CASE REPORT
DOI: 10.5603/OJ.2020.0001

A rare case of posttraumatic bilateral orbital myositis in a young boy — a case report

Ahmad Halawa[1], Mahmoud Al Salem[1], Robert Rejdak[2], Rashed Mustafa Nazzal[2]

[1]Ibn Al Haytham Hospital, Amman, Jordan
[2]Medical University of Lublin, Lublin, Poland

ABSTRACT

Orbital myositis (OM) is a benign inflammatory disease of the orbit characterised by a polymorphous lymphoid infiltrate with varying degrees of fibrosis, without a known local or systemic cause. In this paper, we present a case of a young boy who sustained a trauma to his eyes a few days prior to admission, after which he developed bilateral orbital pain and ocular motility limitation. He underwent the appropriate investigations including orbital imaging and blood laboratory workup, which were all consistent with a diagnosis of posttraumatic bilateral orbital myositis. He was treated with steroids for few weeks, and when the dose of steroids was tapered, he had a relapse of the same disease with a different presentation, which was later controlled with a higher dose of steroids, after which the patient went into remission.

KEY WORDS: myositis; steroids; orbit; trauma

Ophthalmol J 2020; Vol. 5, 1–4

INTRODUCTION

Idiopathic orbital inflammatory disease (IOID) is the term used to describe the disease with an idiopathic cause, spontaneous resolution, benign, non-infectious, space-occupying lesion typically presenting in the third to sixth decade of life with non-granulomatous changes on histopathology. Although orbital myositis is the most common presentation of this disease, other subtypes includes dacryoadenitis, perineuritis, eyelid pseudotumour, inflammation of the anterior orbit (e.g. scleritis), and diffuse orbital inflammation [1].

While IOID is the third most common cause of unilateral proptosis in adults after thyroid eye disease and lymphoproliferative disease [2], it is a relatively rare disease in children. Idiopathic orbital inflammatory disease is a diagnosis of exclusion, hence a wide set of differentials should be considered and ruled out before labelling a patient with this diagnosis, such as thyroid eye disease, lymphoproliferative disease, rhabdomyosarcoma, orbital cellulitis, and metastatic conditions. In this case report, we ruled out all other differential diagnoses by the appropriate laboratory and imaging techniques, and the diagnosis of orbital myositis was made.

CASE PRESENTATION

A 12-year-old boy, previously healthy, presented to our clinic with acute diplopia of two days' duration. The patient's history dates back to 10 days prior to presentation, when he sustained a trauma to his face with a football while playing football. On the next morning he started complaining of bilateral eyelid swelling. Over the following few days he developed deep aching pain in both eyes, associated with generalised fatigue and vomiting.

CORRESPONDING AUTHOR:
Rashed Mustafa Nazzal, Medical University of Lublin, ul. Chmielna 1, 20–079 Lublin, Poland, tel: (+48) 69 027 61 43;
e-mail: rashednazzal@yahoo.com

Copyright © 2019 Via Medica, ISSN 2450–7873

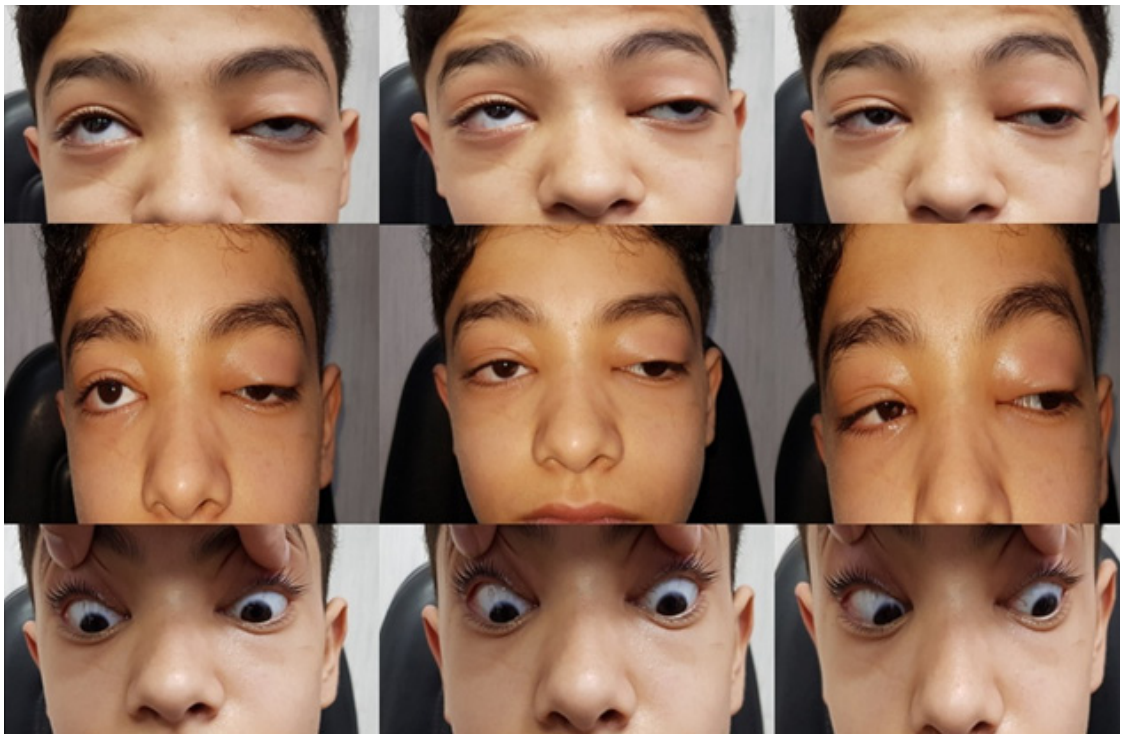

FIGURE 1. Ocular motility at presentation showing limited right abduction and left adduction

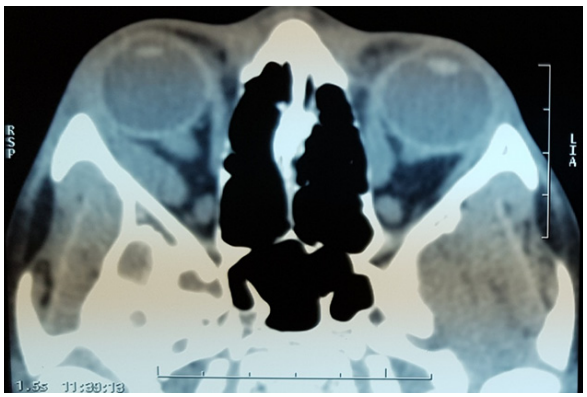

FIGURE 2. Orbital CT scan showing enlarged muscle belly including the tendon (mainly right lateral rectus and left medial rectus)

He eventually developed binocular diplopia. On examination, there was a bilateral eyelid swelling. Anterior and posterior segments exam was within normal limits. Ocular motility exam showed a profound limitation of abduction in the right eye and to a lesser extent limitation of adduction and elevation in the left eye (Fig. 1).

The patient was admitted for further evaluation, and a preliminary diagnosis of orbital cellulitis was suspected, so he was started on intravenous antibiotics.

Orbital CT scan (Fig. 2) revealed prominent enlarged muscles, involving the muscle tendon, mainly the lateral rectus, and superior rectus on the right side and medial rectus and superior rectus on the left side. Blood workup was obtained and included the following: complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), thyroid function test, and workup for connective tissue diseases [rheumatoid factor (RF), antinuclear antibody (ANA), and C- and P-antineutrophil cytoplasmic antibodies (ANCA)], and all were within normal limits.

The diagnosis of IOID was made and the patient was switched from antibiotics to intravenous methylprednisolone (250 mg per day, given slowly with close monitoring over three hours) for three days, after which the patient showed dramatic improvement in symptoms and ocular motility (Fig. 3).

The patient was discharged on oral prednisolone (1 mg/kg) with slow tapering over six weeks. The patient was doing well until he reached the last week of tapering, when he started complaining of recurrence of his deep aching orbital pain with right-eye redness. On examination, there was right episcleritis (Fig. 4) and restriction of ocular motility (Fig. 5). Surprisingly, contrary to what he presented with, this time right abduction was normal and right ad-

FIGURE 3. Ocular motility after improvement

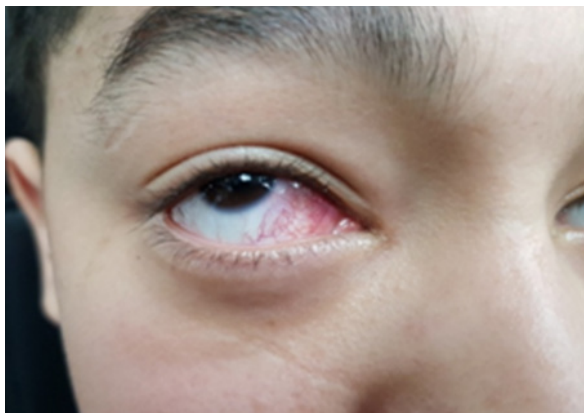

FIGURE 4. Right episcleritis

duction was restricted. The patient was started again on oral prednisolone with a longer tapering period and oral azathioprine as a steroid sparing agent (the dose and the appropriate follow-up were in liaison with a paediatrician). The patient was followed-up for few months, during which he remained in remission even after discontinuation of medications.

DISCUSSION

Nonspecific orbital inflammation was first described in 1905 by Birch-Hirschfeld. Later on, it was named as inflammatory pseudotumor in

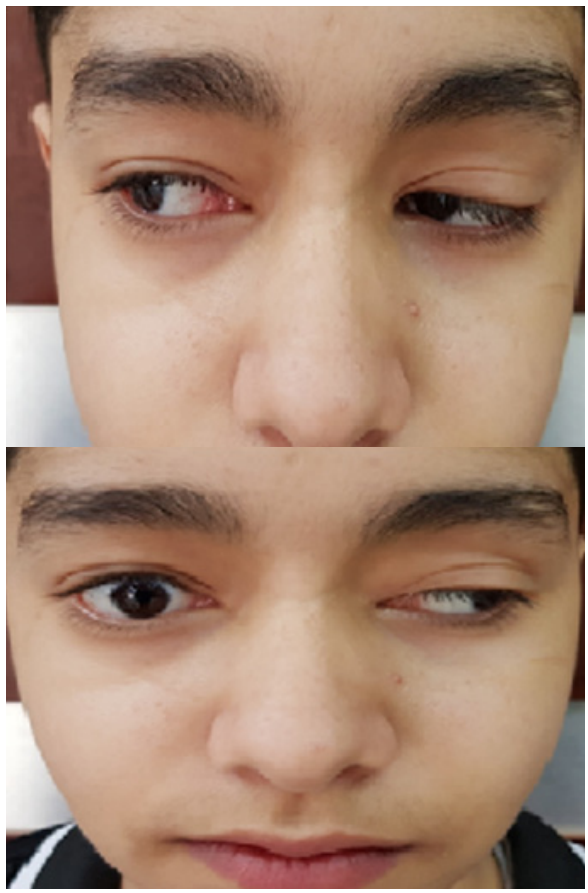

FIGURE 5. Right gaze and left gaze showing limited left adduction on disease recurrence

1954 by Umiker et al. because of its propensity to mimic a malignant process. Presently, the term IOID is usually used. While IOID may account for 5% to 16% of all orbital lesions in adults, it is rare in children, causing a diagnostic dilemma [3]. The pathogenesis of the disease remains controversial; both infectious and immune-mediate aetiologies have been implicated, and association with upper respiratory tract infections and viral illnesses has been described [4, 5]. Of interest, Mottow-Lippe et al. suggested that trauma may cause increased vascular permeability, resulting in release of antigenic substances, which in turn incite an inflammatory cascade [6]. Hence, we believe that trauma was the factor triggering the inflammation in our patient.

The symptoms and clinical findings in IOID may vary widely, but they are dictated by the degree and anatomical location of the inflammation. It can present with deep-rooted boring pain, eyelid swelling, conjunctival injection, ptosis, proptosis, diplopia, and restriction of ocular motility. Affected children more often have constitutional signs and symptoms, such as headache, fever, malaise, emesis, anorexia, lethargy, and abdominal pain [7].

Because IOID is a diagnosis of exclusion, a broad workup is usually done to exclude other causes. The differential diagnosis of idiopathic OM includes the following: infections (viral infections, orbital cellulitis, orbital abscess, Lyme disease, herpes zoster, and syphilis), inflammatory reaction (trauma, foreign body, bisphosphonate-related reaction, and post-vaccinal reaction), Tolosa-Hunt syndrome, thyroid ophthalmopathy, vasculitis (Wegener's granulomatosis, polyarteritis nodosa, rheumatoid arteritis, giant cell arteritis, and Kawasaki disease), systemic lupus erythematosus, sarcoidosis, inflammatory bowel disease, neoplasm, arteriovenous fistulas, and malformations [8]. On radiologic imaging of idiopathic orbital myositis, there is diffuse muscle enlargement involving the muscle tendon, in contrast to thyroid orbitopathy in which the tendons are spared. In addition, in idiopathic orbital myositis, the lateral rectus and medial rectus are the most likely to be involved, while in thyroid disease the lateral rectus is the last rectus muscle to be affected [9].

Systemic corticosteroid therapy is the mainstay treatment in the management of IOID [10]. Of diagnostic significance, idiopathic orbital inflammation is characterised by a rapid and favourable response to systemic corticosteroid treatment.

This disease condition in our patient demonstrated some rare and unusual characteristics, such as bilateral eye involvement in a post-traumatic presentation and ophthalmoplegia — from mainly involving the right lateral rectus at presentation to involving the right medial rectus on disease recurrence.

CONCLUSION

Orbital myositis, as the most important subtype of IOID, is a rare diagnosis that should be kept in mind in patients presenting with ocular pain or diplopia after an ocular trauma. Being a diagnosis of exclusion, IOID should be considered after adequate imaging and laboratory investigations have been performed.

Acknowledgements

None

Statement of competing interests

No competing interests.

REFERENCES

1. Grouteau E, Chaix Y, Armbruster V. [Idiopathic inflammatory orbital myositis and idiopathic inflammatory pseudotumor in children: three cases]. Arch Pediatr. 1998; 5(2): 153–158, doi: 10.1016/s0929-693x(97)86829-7, indexed in Pubmed: 10223136.
2. Belanger C, Zhang KS, Reddy AK, et al. Inflammatory disorders of the orbit in childhood: a case series. Am J Ophthalmol. 2010; 150(4): 460–463, doi: 10.1016/j.ajo.2010.05.012, indexed in Pubmed: 20688313.
3. Mulvihill A, Smith CR, Buncic JR. Pediatric orbital pseudotumour presenting as a painless orbital and periocular mass. Can J Ophthalmol. 2004; 39(1): 77–79, doi: 10.1016/s0008-4182(04)80057-7, indexed in Pubmed: 15040619.
4. Yuen SJ, Rubin PA. Idiopathic orbital inflammation: ocular mechanisms and clinicopathology. OphthalmolClin North Am. 2002; 15(1): 121–6, doi: 10.1016/s0896-1549(01)00003-7, indexed in Pubmed: 12064075.
5. Espinoza GM. Orbital inflammatory pseudotumors: etiology, differential diagnosis, and management. Curr Rheumatol Rep. 2010; 12(6): 443–447, doi: 10.1007/s11926-010-0128-8, indexed in Pubmed: 20803107.
6. Mottow-Lippa L, Jakobiec FA, Smith M. Idiopathic inflammatory orbital pseudotumor in childhood. II. Results of diagnostic tests and biopsies. Ophthalmology. 1981; 88(6): 565–574, doi: 10.1016/s0161-6420(81)34984-7, indexed in Pubmed: 7267028.
7. Stevens JL, Rychwalski PJ, Baker RS, et al. Pseudotumor of the orbit in early childhood. J AAPOS. 1998; 2(2): 120–123, doi: 10.1016/s1091-8531(98)90076-3, indexed in Pubmed: 10530975.
8. Benmiloud S, Boubbou M, Hida M. Bilateral idiopathic orbital myositis in an infant. Int J Res Med. 2013; 2: 112–114.
9. Schoser BG. Ocular myositis: diagnostic assessment, differential diagnoses, and therapy of a rare muscle disease — five new cases and review. ClinOphthalmol. 2007; 1(1): 37–42, indexed in Pubmed: 19668464 .
10. Hankey GJ, Silbert PL, Edis RH, et al. Orbital myositis: a study of six cases. Aust N Z J Med. 1987; 17(6): 585–591, doi: 10.1111/j.1445-5994.1987.tb01264.x, indexed in Pubmed: 3328976.

CASE REPORT
DOI: 10.5603/OJ.2020.0002

A case of an intraocular glass piece that has remained quiescent for four years

Farheen Fatima[1], Zubaida Sirang[2], Azam Ali[1], Nauman Chaudhry[3], Khabir Ahmad[1]

[1]Section of Ophthalmology, Aga Khan University Hospital, Stadium Road, Karachi, Pakistan
[2]Section of Ophthalmology, Mater Misericordiae University Hospital, Dublin, Ireland
[3]Yale School of Medicine, New Haven, United States

ABSTRACT

An intraocular foreign body (IOFB) is mainly acquired via a penetrating globe injury. Some foreign bodies like glass have an inert nature, and the timing of intervention can be delayed, but foreign bodies like metals have a toxic effect on the eye and require urgent removal.

We present a case of a young male with a penetrating globe injury following a road traffic accident. He acquired a foreign body glass piece in his left eye, which was initially missed. Upon thorough examination, it was found at the inferotemporal quadrant of the retina. Considering the inert nature of IOFB and the risks of bleeding and damage to the surrounding intraocular structures, we decided not to remove it. The patient has been stable for four years with good vision in the same eye.

KEY WORDS: intraocular foreign body; IOFB; complications of IOFB

Ophthalmol J 2020; Vol. 5, 5–7

INTRODUCTION

Foreign bodies like glass are easily missed due to their transparent nature. An intraocular foreign body (IOFB) may need urgent removal if there is a risk of developing endophthalmitis [1, 2]. If the IOFB is inert, it is best to observe because there is a risk of intraoperative bleeding and injuring other intraocular structures during removal.

Here, we present a case of a retained intraocular glass piece following a road traffic accident (RTA). It serves as a challenging case because the glass piece was not removed, and it has stayed inert for four years.

CASE REPORT

A 28-year-old healthy male presented with a road traffic accident four years ago. His spectacles broke in the accident and he was uncertain whether the glass pieces had penetrated his left eye.

On initial presentation, visual acuity was 20/20 (–3.25 DS) in the right eye and hand movement in the left. The right eye looked fine, while the left eye had a scleral tear measuring 9 mm from the 1 to the 5 o'clock position with hyphaemia. A foreign body glass piece had penetrated through this tear, which was missed until performing B-scan and CT several weeks after the primary repair.

Four weeks following repair, his visual acuity improved to 20/100 with pinhole in the affected eye. Sutures of primary repair were intact, but traumatic cataract developed and fundoscopy showed vitreous haze. B-scan showed vitreous haze inferiorly (Fig. 1). Computed tomography (CT) orbits showed a radio-opaque foreign body within the anteroinferior aspect of left globe measuring 1.8 × 1.0 cm and

CORRESPONDING AUTHOR:
Zubaida Sirang, Section of Ophthalmology, Mater Misericordiae University Hospital, Dublin, Ireland; e-mail: zubaidasirang@mater.ie

Copyright © 2019 Via Medica, ISSN 2450–7873

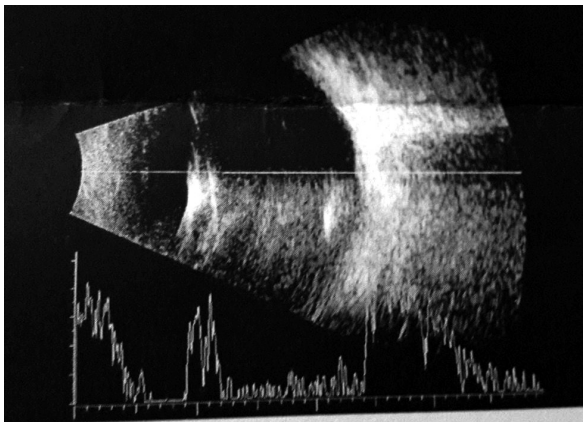

FIGURE 1. B-scan showing vitreous haemorrhage and intraocular foreign body (IOFB) in the left eye

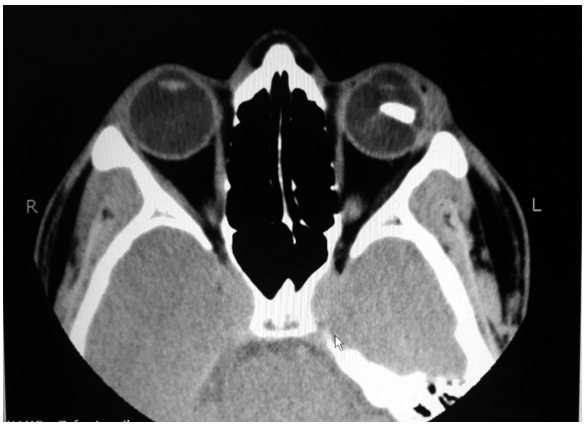

FIGURE 2. Computed tomography (CT) scan showing intraocular foreign body (IOFB) in the left eye

haemorrhage in the posterior chamber (Fig. 2). The traumatic cataract was removed with posterior chamber intraocular lens (PCIOL) placement, and pars plana vitrectomy with air tamponade was performed to remove the vitreous haemorrhage. A glass piece fixed in the inferotemporal quadrant of the retina was visible during vitrectomy, but we decided not to manipulate it because there was a risk of further bleed. On the first postoperative day, his visual acuity was 20/80 with pinhole, anterior chamber was quiet and deep, cornea was clear, and IOL was in place. He was routinely followed, and his visual acuity gradually improved to 20/25 with –3.25DS in his left eye over a period of six months. The glass piece remained quiescent during his yearly follow-up for four years.

DISCUSSION

In all cases of RTA, IOFB needs to be excluded, beginning with the history, with particular emphasis on the mechanism of injury. High suspicion for IOFB should always be maintained [2]. Complete ocular examination is highly important to rule out IOFB, even if there is no evidence — a CT scan needs to be done to rule it out.

An intraocular foreign bodies account for almost 40% of penetrating ocular injuries [3, 4]. Seventy-five per cent of IOFBs lodge in the posterior segment [5]. They can cause damage to the eye by mechanical injury, introducing infection and exerting a toxic effect to the surrounding structures [6].

The decision regarding IOFB removal is determined by several factors, including the risk of endophthalmitis and the nature of the foreign body. If the risk of endophthalmitis is high and the IOFB is metallic in nature, vitrectomy with removal of IOFB should be considered as soon as possible [1, 2]. If the IOFB is dormant, removal can be delayed, and such patients can be followed up regularly.

Hwi et al. reported a case of an infant who acquired an intraocular glass piece following RTA. The glass piece was lodged between the right optic disc and the fovea. It measured 3.5 mm × 4.0 mm, much smaller than in our case, which measured 1.8 cm × 1.0 cm. In this case, the glass piece was not initially removed. It was later removed when the child gained increased mobility and developed cataract [7]. In certain cases, the inert IOFBs can be left in situ and the patient can be observed over time [8, 9].

In our case, the foreign body was not removed because the patient had a vitreous haemorrhage, and removal during vitrectomy could have led to further bleeding by injuring surrounding structures. Considering the risk of intraoperative bleeding and the inert nature of the glass piece, it was left in place. Although our patient had retained IOFB, his visual acuity improved to normal with time, and he has remained stable for four years with yearly follow-up.

CONCLUSIONS

In all cases of RTA, there should be suspicion of IOFB. Intraocular foreign body should always be ruled out by means of CT scan in adjunct with B-scan. The decision regarding the removal of an IOFB can be deferred in cases where the nature of IOFB is inert, it is fixed in place, and there are risks

of bleeding and damage to surrounding intraocular structures.

Statement of ethics

The patient provided written, informed consent for submission of the case report and any accompanying images. This case report was approved by the Ethics Committee of Aga University Hospital, Karachi, Pakistan.

Disclosure statement

The authors declare that they have no conflicts of interest.

REFERENCES

1. Kuhn F, Morris R, Witherspoon CD. Intraocular foreign body (posterior segment) . In: Hampton Roy RD. ed. Masters Techniques in Ophthalmic Surgery. Williams and Wilkins, Baltimore 1995: 1201–1212.
2. Katz G, Moisseiev J. Posterior-segment intraocular foreign bodies: An update on management. Risks of infection, scarring and vision loss are among the many concerns to address. Retinal Physician. 2009.
3. Cazabon S, Dabbs TR. Intralenticular metallic foreign body. J Cataract Refract Surg. 2002; 28(12): 2233–2234, doi: 10.1016/s0886-3350(02)01431-1, indexed in Pubmed: 12498867.
4. Coleman DJ, Lucas BC, Rondeau MJ, et al. Management of intraocular foreign bodies. Ophthalmology. 1987; 94(12): 1647–1653, doi: 10.1016/s0161-6420(87)33239-7, indexed in Pubmed: 3431834.
5. Behrens-Baumann W, Praetorius G. Intraocular Foreign Bodies. 297 consecutive cases. Ophthalmologica. 1989; 198(2): 84–88, doi: 10.1159/000309963, indexed in Pubmed: 2710504 .
6. Ahmadieh H, Soheilian M, Sajjadi H, et al. Vitrectomy in ocular trauma. Factors influencing final visual outcome. Retina. 1993; 13(2): 107–113, indexed in Pubmed: 8337490.
7. Hwi TP, Min TW, Ying CS, et al. Glass piece in the retina after road traffic accident: to remove or not to remove. Sch J Med Case Rep. 2015; 3(9B): 906–910.
8. Greven C, Engelbrecht N, Slusher M, et al. Intraocular foreign bodies: management, prognostic factors, and visual outcomes. Ophthalmology. 2000; 107(3): 608–612, doi: 10.1016/s0161-6420(99)00134-7, indexed in Pubmed: 10711903 .
9. Al-Thowaibi A, Kumar M, Al-Matani I. An overview of penetrating ocular trauma with retained intraocular foreign body. Saudi J Ophthalmol. 2011; 25(2): 203–205, doi: 10.1016/j.sjopt.2011.01.001, indexed in Pubmed: 23960924.

CASE REPORT
DOI: 10.5603/OJ.2020.0003

Acute central serous chorioretinopathy — an uncommon complication of imatinib mesylate (imatinib) therapy in chronic myelogenous leukaemia

Sanjay Kumar Mishra, Ashok Kumar

Department of Ophthalmology, Army College of Medical Sciences and Base Hospital, Delhi, India

ABSTRACT

Imatinib is the most widely used drug in targeted therapy for chronic myelogenous leukaemia (CML). Few ophthalmic side effects like periorbital oedema, epiphora, ptosis, extraocular muscle palsy, blepharoconjunctivitis, glaucoma, papilledema, photosensitivity, retinal haemorrhage, and increased intraocular pressure are described with imatinib therapy. A 35-year-old male, a known case of CML with no ocular complaints, on treatment with imatinib for the preceding six weeks, presented with acute central serous chorioretinopathy in the left eye. Owing to his professional requirements for early visual recovery, he was treated with subthreshold micropulse laser with complete resolution of the subretinal fluid. This case report highlights acute central serous chorioretinopathy as a potential rare complication of imatinib therapy in CML patients, which requires regular and detailed ophthalmic evaluation so as to diagnose and treat it without any residual effects.

KEY WORDS: imatinib mesylate (imatinib); chronic myelogenous leukaemia (CML); central serous chorioretinopathy

Ophthalmol J 2020; Vol. 5, 8–11

INTRODUCTION

Chronic myelogenous leukaemia (CML) is a clonal stem cell disorder of haemopoietic stem cells. It occurs due to reciprocal translocation between chromosomes 9 and 22, t (9; 22), which results in a fusion gene product BCR-ABL on chromosome 22. Chronic myelogenous leukaemia accounts for 15% of adult leukaemias with the median age of diagnosis being 67 years [1]. Imatinib mesylate (imatinib) specifically targets a set of protein tyrosine kinases and is the treatment of choice for patients with CML [2]. Chronic myelogenous leukaemia itself can lead to a varied spectrum of ocular presentations that includes retinal and iris neovascularisation, haemorrhages, glaucoma, vitreous haemorrhages, Roth spots, nerve fibre infarcts, and papilledema [3, 4].

Imatinib treatment can also lead to certain ophthalmic side effects like periorbital oedema, epiphora, ptosis, extraocular muscle palsy, blepharoconjunctivitis, glaucoma, papilledema, photosensitivity, retinal haemorrhage, and increased intraocular pressure [5]. We report an unusual complication in the form of acute central serous chorioretinopathy in a patient of CML, who was started on imatinib therapy six weeks earlier, as well as its management.

CORRESPONDING AUTHOR:
Ashok Kumar, Department of Ophthalmology, Army College of Medical Sciences and Base Hospital, Delhi Cantt, 110010 Delhi, India;
e-mail: smileashok@rediffmail.com

Copyright © 2019 Via Medica, ISSN 2450–7873

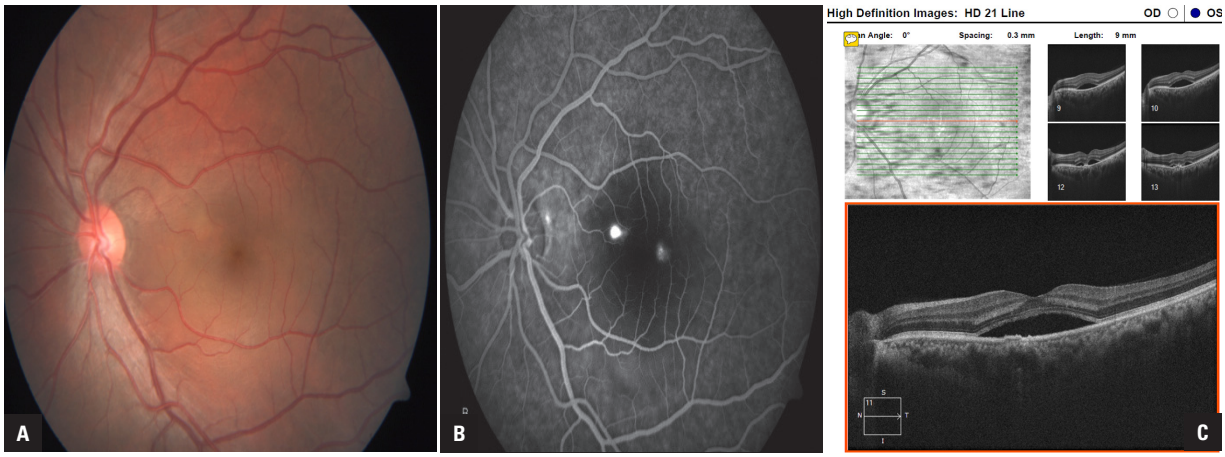

FIGURE 1A. Colour fundus photograph of the left eye showing large (around 6 DD size) neurosensory detachment in posterior pole involving foveal centre. **B.** Fundus fluorescein angiogram of the same patient showing a single ink blot leak close to the foveal centre with some transmitted florescence. **C.** Spectral domain optical coherence tomography (SD-OCT) of the same patient confirming large neurosensory detachment involving the foveal centre

To the best of our knowledge, it is first case of documentation of this vision-affecting complication in a patient of CML on imatinib therapy.

CASE REPORT

A 35-year-old Indian male, an active military soldier, a known case of CML on treatment, presented with diminution of vision in left eye for the preceding week. He was started on imatinib 400 mg (Tab) once daily as target therapy for CML about six weeks earlier, after BCR-ABL was detected as positive. The patient did not have any history of steroid use and it was not documented in his treatment history. On evaluation he had best corrected visual acuity of 6/6 in his right eye and 6/36 in his left eye, with no ocular abnormality in the right eye. Left eye examination revealed normal anterior segment with large 6 DD size neurosensory detachment in the posterior pole involving foveal centre with no evidence of any retinal haemorrhages or features of active vasculitis (Fig. 1A). Fundus fluorescein angiogram showed a single ink blot leak close to the foveal centre, with spectral domain optical coherence tomography (SD-OCT) confirming large neurosensory detachment involving the foveal centre (Fig. 1B and C).

Observation for spontaneous resolution is a standard treatment in patients of central serous chorioretinopathy. Owing to blast crisis, it was not possible to reduce the dosage of imatinib therapy, which was continued for the subsequent eight weeks. However, being an active military soldier, early visual recovery was required, so he was subjected to subthreshold micropulse laser using a 532 nm green laser (Suprascan, Multispot Photocoagulator, Quantel medicals, Clermont-Ferrand, France) using 5% duty cycle with 250 mW power (titrated to 1/3 of power producing a just detectable burn outside the vascular arcades), duration 0.02 ms, and 36 confluent spots to focal leak. The patient was subsequently evaluated at 1 week, 4 weeks, and 8 weeks post laser with BCVA, OCT, and Fundus autofluorescence, with substantial improvement in visual status and no adverse effects of laser treatment. He had complete resolution of neurosensory detachment, which was confirmed on OCT with BCVA improving to 6/6 in LE without any side effects of subthreshold laser therapy at 8 weeks post treatment (Fig. 2A and B).

DISCUSSION

Imatinib is the most common drug used for the targeted therapy of CML. In addition to inherent ophthalmic manifestation of CML, certain ophthalmic side effects like periorbital oedema, epiphora, ptosis, extraocular muscle palsy, blepharoconjunctivitis, glaucoma, papilledema, photosensitivity, retinal haemorrhage, and increased intraocular pressure are described with imatinib therapy [5]. Montero et al. also reported serous retinal detachment along with retinal haemorrhages in a 35-year-old woman but without angiographic evidence of any focal leak in a CML patient not on any therapy [6]. Nakashima et al. reported that imatinib induced interstitial

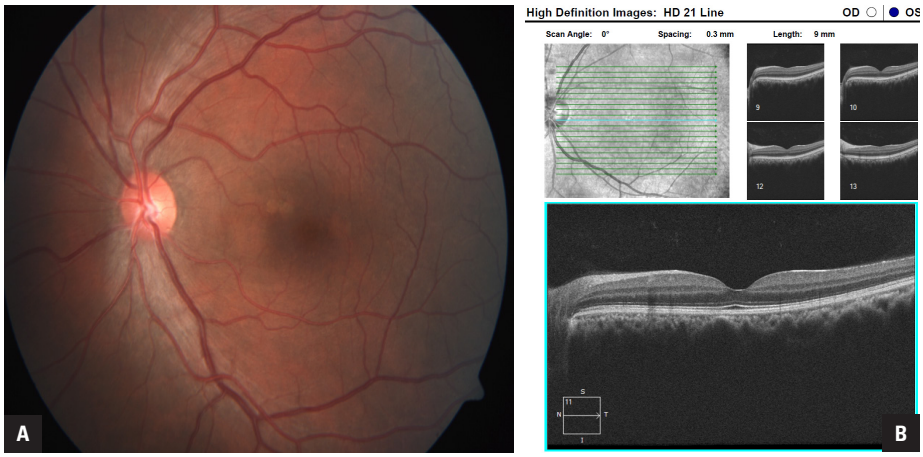

FIGURE 2A. Colour fundus photograph of patient same patient eight weeks post-subthreshold laser showing resolved neurosensory detachment with normal appearing fovea. **B.** Spectral domain optical coherence tomography (SD-OCT) of the left eye of the same patient showing normal fovea with completely resolved neurosensory detachment

lung disease after discontinuation of therapy in a patient who received treatment for 10 weeks [7].

Our patient developed diminution of vision in the left eye around six weeks after starting on imatinib therapy with FFA showing a single ink blot leak on the papillomacular bundle close to the foveal centre. He underwent subthreshold micropulse laser treatment of the focal leak because early visual recovery was warranted owing to his professional requirement, with full recovery of vision and complete resolution of neurosensory detachment over the subsequent eight weeks.

Imatinib usually does not cross the blood-ocular barrier; but can do so subsequent to damage to ocular or retinal microvasculature. It can lead to a vasculitis-like picture in which the effect on the retinal vasculature is seen early. Fluid retention is a common adverse effect and one of the important dose-limiting toxicities mainly occurring in the periorbital area, and pleural and pericardial cavity [8]. The most popular theory that can explain serous detachment is that imatinib inhibits the platelet-derived growth factor receptor (PDGFR), which regulates interstitial fluid homeostasis , and which probably also occurs in choroidal vasculature manifesting with central serous retinopathy [9].

Hence, it is a well-known fact that patients of CML are at high risk of loss of vision due to development of glaucoma or retinal complications. The role of imatinib cannot be ruled out in causation of acute central serous retinopathy, especially in view of the important, documented side effect of fluid retention. It is imperative that CML patients on imatinib therapy should undergo regular detailed ophthalmic examinations so as to diagnose and treat potential vision-affecting complications, as demonstrated in our present case.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethics approval and consent to participate

Ethics approval and consent to participate are not applicable in this case report.

Acknowledgement

Nil.

REFERENCES

1. Singhal MK, Sengar M, Nair R. Summary of the published Indian data on chronic myeloid leukemia. South Asian J Cancer. 2016; 5(3): 162–165, doi: 10.4103/2278-330X.187593, indexed in Pubmed: 27606306.
2. O'Brien SG, Guilhot F, Larson RA, et al. IRIS Investigators. Imatinib compared with interferon and low-dose cytarabine for newly diagnosed chronic-phase chronic myeloid leukemia. N Engl J Med. 2003; 348(11): 994–1004, doi: 10.1056/NEJMoa022457, indexed in Pubmed: 12637609.
3. Rennie I. Ophthalmic manifestations of childhood leukaemia. Br J Ophthalmol. 1992; 76(11): 641, doi: 10.1136/bjo.76.11.641, indexed in Pubmed: 1477035.
4. Sharma T, Grewal J, Gupta S, et al. Ophthalmic manifestations of acute leukaemias: the ophthalmologist's role. Eye (Lond). 2004; 18(7): 663–672, doi: 10.1038/sj.eye.6701308, indexed in Pubmed: 15002029.
5. Fraunfelder FW, Solomon J, Druker BJ, et al. Ocular side-effects associated with imatinib mesylate (Gleevec). J Ocul Pharmacol Ther. 2003; 19(4): 371–375, doi: 10.1089/10807680332279426, indexed in Pubmed: 12964961.
6. Montero J, Cervera E, Palomares P, et al. Serous retinal detachment as a presenting feature of chronic myelogenous leukemia. Retin Cases Brief Rep. 2010; 4(4): 394–396, doi: 10.1097/ICB.0b013e3181b5ef71, indexed in Pubmed: 25390928.

7. Nakashima S, Kakugawa T, Motomura H, et al. Development of imatinibmesylate-induced interstitial lung disease 2 weeks after discontinuation of the treatment: a case report. Multidiscip Respir Med. 2012; 7(1): 48, doi: 10.1186/2049-6958-7-48, indexed in Pubmed: 23174134.
8. Thanopoulou E, Judson I. The safety profile of imatinib in CML and GIST: long-term considerations. Arch Toxicol. 2012; 86(1): 1–12, doi: 10.1007/s00204-011-0729-7, indexed in Pubmed: 21717109.
9. Pietras K, Ostman A, Sjöquist M, et al. Inhibition of platelet-derived growth factor receptors reduces interstitial hypertension and increases transcapillary transport in tumors. Cancer Res. 2001; 61(7): 2929–2934, indexed in Pubmed: 11306470.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0004

Wang Koch-adjusted axial length in SRK/T formula for ocular biometry in high myopia: a prospective study

Fouad Chraibi, Hassan Moutei, Ahmed Bennis, Meriem Abdellaoui, Idriss Andaloussi Benatiya

University Hospital Hassan II and University Sidi Mohamed Ben Abdellah, Fez, Morocco

ABSTRACT

BACKGROUND: The aim of this study was to prospectively assess refractive results of cataract surgery in highly myopic eyes using the SRKT formula and Wang Koch-adjusted axial length.

MATERIAL AND METHODS: Prospectively, we recruited consecutive candidates for cataract surgery having an axial length equal to 27 mm and longer. We performed biometry by using Wang and Koch-adjusted axial length applied to the SRKT formula. The main outcome measures were: mean of refractive error, mean of absolute refractive error, and percentage of eyes that achieved a refractive error of ± 0.5D and ± 1D.

RESULTS: Fifteen eyes of nine patients were involved in the study. The mean refractive error was -0.01D ± 0.4D, and the mean absolute refractive error was + 0.35D ± 0.20D. Refractive errors of ± 0.5D and ± 1D were achieved, respectively, in 86.6% and in 100% of eyes.

CONCLUSIONS: Wang Koch's axial length adjustment applied to the SRKT formula is a reliable alternative in high myopic cataract patients.

KEY WORDS: cataract; high myopia; Wang Koch adjustment; SRK/T formula; refractive error; absolute refractive error

Ophthalmol J 2020; Vol. 5, 12–16

INTRODUCTION

Phacoemulsification is a functional rehabilitation surgery but also, and increasingly, a refractive surgery. Eye biometry is an important step in the process. There are still some challenging cases of eye biometry such as in cases of keratoconus, after refractive surgery, and in cases of extreme axial length.

In the present paper, we focus on eye biometry in high myopic cataract surgery candidates. Conventional formulas used to perform biometry tend to underestimate the power of implant in cases of high myopia yielding postoperative hypermetropia [1].

In high myopia, part of the problem is that the measurement of the axial length (AL) is inaccurate, particularly in the case of associated myopic staphyloma. Optical biometry can partially compensate for this issue but does not completely alleviate it because of certain intrinsic deficiencies of the used formulas.

The new generation of formulas, including Barrett Universal II and Hill-RBF, enable the best results but necessitate optical biometry — a technology not available in all centres, especially in developing countries.

CORRESPONDING AUTHOR:
Dr Fouad Chraibi, University Hospital Hassan II and University Sidi Mohamed Ben Abdellah, 30000 Fez, Morocco;
e-mail: fouadchraibi@gmail.com

Copyright © 2019 Via Medica, ISSN 2450–7873

For this reason, we analyse prospectively Wang Koch's axial length optimisation method for the SRK/T formula in high myopic cataract surgery candidates.

MATERIAL AND METHODS

This study was conducted following the declarations of Helsinki and after obtaining the patient's informed consent.

This was a prospective study that spanned from November 2018 to August 2019; all patients with high myopia (AL ≥ to 27 mm) and who are candidates to cataract surgery by phacoemulsification had had ultrasonic or optical (Lenstar Ls 900; Haag-Streit AG, Koeniz, Switzerland) eye biometry depending on the transparency of the media.

Following the recommendations of Wang et al., we used the constant a = 118.4 as advocated by the ULIB (User Group for Laser Interference Biometry) optimised for the formula SRK/T and adapted to the implant that we used.

Keratometry was measured either with an automatic refractometer or during the acquisition of optical ocular biometry. Patients with keratometric astigmatism of over 1.5D were excluded from the study.

In patients with high myopia, the recommended post-operative target refraction is –0.75D to –3D, or even up to –5D in cases of high myopia with macular lesion [2]. In our series and after discussion with our patients, the refractive target was –2D, except for one patient who preferred emmetropia as postoperative target refraction.

The initial calculation of the intraocular lens power (IOLm; m for measured) was performed based on the SRK/T formula using the measured axial length. In the second step, the second calculation of adjusted IOL power (IOLa; a for adjusted) was based on a computed axial length according to the method of Wang Koch for the SRK/T formula:

Adjusted axial length = 0.8453 × measured axial length + 4.0773 mm.

For implants with intermediate steps of 0.5D, which are not provided by the manufacturer in the range of powers from –10D to +10D, we increased the value of the power of the used IOL (IOLu; u for used) by +0.5D (example: if the power of IOLa = –2.5D, which is not available, the power of IOLu will be –2D).

All patients are operated by coaxial phacoemulsification by the same surgeon (FC), with a 2.4 mm upper temporal incision and implantation of a hydrophobic acrylic implant (Eyecryl Plus, Biotech) for all patients. No early intraoperative or postoperative complications occurred. On the other hand, we excluded cases that required a stitch at the end of the surgery for its probable effect on the induced astigmatism and final spherical equivalent.

Postoperative refraction was assessed two months after surgery.

The main measured outcomes are the average of the refractive error, the average of the absolute refractive error, the percentage of refractive errors between –0.5D and +0.5D (± 0.5D), and the percentage of refractive errors between –1D and + 1D (± 1D).

The biometric refractive error is equal to the postoperative refraction (spherical equivalent) minus the targeted refraction. The absolute biometric refractive error corresponds to the difference between the postoperative refraction and the target refraction in absolute value. The calculation of the mean of the absolute biometric refractive errors makes it possible to assess the precision of the measurements of the formula used [3].

RESULTS

The total number of eyes was 15 eyes of nine patients whose ages ranged from 42 to 56 years with an average of 52 years; the sex ratio was 0.8 (4 men and 5 women).

The measured axial length was on average 30.44 mm ± 2.35 mm (from 27.18 mm to 34.37 mm) (Tab. 1), and the adjusted axial length according to Wang Koch's formula was 29.81 mm ± 1.99 mm (from 27.05 mm to 33.13 mm). The average of the power of IOLm was 5.66D ± 4.98D (from –1.75D to +12.5D), and the average power of the IOLa was 7.23D ± 4.28D (from 1D to 13.5D).

The mean of the refractive error was –0.01D ± 0.4D, ranging from –0.5D to +0.75D, with an overall trend towards relative emmetropia.

The mean of the absolute refractive error was +0.35D ± 0.20D, ranging from 0 to +0.75D, confirming the high precision of the adjusted formula

Table 1. Demographic characteristics of the study sample

Parameter	Value
Number of eyes	15
Age (years)	
Average ± SD	52 ± 4.7
Extremes	42–56
Sex	
Female	5
Male	4
Sex ratio	0.8
Axial length [mm]	
Average ± SD	30.44 ± 2.35
Extremes	27.18–34.37
Power LIOm [D]	
Average ± SD	5.66 ± 4.98
Extremes	–1.75 to +12.5

SD – standard deviation; LIOm – measured power of the artificial lens

(Tab. 2). The percentage of the refractive error within ± 0.5D was 86.6% and within ± 1D in 100% of cases.

DISCUSSION

In 2015, L. Wang and D. Koch proposed a method for optimising ocular biometry formulas in high myopia by modifying the axial length according to the following original formula [4]:

Optimised axial length = 0.8981 × AL (in mm) + 2.5637 mm.

However myopic refractive results were of significant proportion, and these same authors proposed in 2018 a new regression for the adjustment of the axial length in SRK/T, as follows:

Axial length optimised = 0.8453 × measured axial length + 4.0773 mm [5].

In our study, the average of biometric refractive error was almost zero (a trend toward relative emmetropia), and the average of the absolute biometric refractive error was + 0.33D ± 0.21D. The percentage of postoperative refractions were within ± 0.5D and ± 1D in 86.6% and 100% of cases, respectively. Yokoi et al. [6], using the SRK/T formula without adjustment of the axial length in

Table 2. The different parameters before and after adjusting the axial length

Eye	LAm	LAa	LIOm	LIOa	Liu	MRE	MARE
1	33.52	32.41	–1.75	1	1	–0.25	0.25
2	33.41	32.31	–1.5	1	1	0.50	0.50
3	27.34	27.18	11.5	12	12	–0.25	0.25
4	27.18	27.05	11	11.5	11.5	0.00	0.00
5	29.89	29.34	6.5	8	8	0.50	0.50
6	29.57	29.07	7	8.5*	9	–0.50	0.50
7	34.37	33.13	–1	1.5*	2	0.25	0.25
8	34.22	33.00	–1.5	1	1	0.75	0.75
9	30.54	29.89	4.5	6	6	0.25	0.25
10	30.87	30.17	6	7.5*	8	–0.25	0.25
11	28.67	28.31	10.5	11.5	11.5	–0.25	0.25
12	28.49	28.15	10	11	11	–0.25	0.25
13	28.14	27.86	12.5	13.5	13.5	–0.25	0.25
14	31.12	30.38	3	5	5	0.75	0.75
15	29.34	28.87	8.5	9.5 *	10	–0.25	0.25
Avg	30.44	29.81	5.68	7.23	7.36	–0.01	0.35
SD	02.35	1.99	4.98	4.28	4.27	0.40	0.20

LAm — axial length measured in mm; LAa — axial length adjusted in mm; LIOm — power of the implant measured in D; LIOa — power of the implant adjusted in D; Liu — power of the implant used in D; MRE — mean refractive error; MARE — the mean of the absolute refractive error; Avg — average; SD — standard deviation; *not available

high myopic patients (AL ≥ 26.5 mm) in 84 eyes, found an average postoperative biometric refractive error of +0.45D ± 0.79D (hypermetropic shift) with an average of the absolute refractive error of +0.72 D ± 0.47D; and a postoperative refraction of ± 1D in only 70% of cases.

On the other hand, our refractive results meet the standards set by the study of the Swedish National Register of cataract surgery establishing postoperative reactive values of ± 0.5D in at least 71.0% of the eyes and of ± 1.0D in 93.0% of the cases as the optimal results [7].

Among all the currently available formulas in high myopia, the benchmark is represented by the Barrett Universal II formula, which according to the literature provides the lowest average postoperative refractive error (–0.09D ± 0.42D to +0.05D ± 0.46D) and the best percentage of a postoperative refraction of ± 0.5D (77%) [8–11]. We consider that the results obtained in our series using adjustment of the axial length according to the Wang Koch method are close to the performance of the Barrett Universal II formula, which is rather modern and sophisticated but which requires technology not yet available for routine practice in developing countries.

Third- and fourth-generation formulas (SRKT, Hoffer Q, Holiday I and II) tend to underestimate the power of the implant with consequent hyperopia. This outcome is more noticeable in eyes with an axial length ≥ at 31 mm [6] and in cases of negative IOL power [12].

Aboulafia et al. [13]. state that in highly myopic patients with an axial length of more than 26 mm, a threshold value of IOL power of 6D allows segregation of high myopic patients into two groups at different risk of postoperative hyperopic refractive error. Those having less than 6D as IOL power will have a higher risk of postoperative refractive error. Indeed, in their assessment of the SRK/T formula, the average refractive error was close to 0D (–0.05D ± 0.35D) in the group of IOL powers of 6D and more, while in the group of IOL powers less than 6D the average refractive error was +0.82D ± 0.53D. After adjusting the axial length according to the Wang Koch method applied to SRK/T, the average refractive error was –0.31D ± 0.36D for group 6D and more and +0.02D ± 0.49D for the group of less 6D.

Our study is certainly prospective but nevertheless has certain limits. First, the small size of our series due to numerous self-imposed restrictions during the process of patient recruitment for the study. Second, the lack of homogeneity of measurements given the use of optical biometry and ultrasound depending on the transparency of the media in the same series. And finally, the unavailability by the manufacturer of some intermediate IOL power values with steps of +0.5D in the range –10D to +10D.

CONCLUSION

Wang Koch's axial length adjustment for high myopia cataract candidates is a reliable alternative to the more sophisticated formulas such as Barrett Universal II. Special attention is advised regarding eyes with an axial length of ≥ 27 mm, particularly those with an AL ≥ 31D, as well as in cases of IOL power < 6D, particularly those of negative IOL power values.

Conflict of interests

The authors declare that they have no conflict of interests in relation to this article.

REFERENCES

1. Zuberbuhler B, Seyedian M, Tuft S. Phacoemulsification in eyes with extreme axial myopia. J Cataract Refract Surg. 2009; 35(2): 335–340, doi: 10.1016/j.jcrs.2008.10.044, indexed in Pubmed: 19185252.
2. Hayashi K, Hayashi H. Optimum target refraction for highly and moderately myopic patients after monofocal intraocular lens implantation. J Cataract Refract Surg. 2007; 33(2): 240–246, doi: 10.1016/j.jcrs.2006.10.045, indexed in Pubmed: 17276264.
3. Hoffer KJ, Aramberri J, Haigis W, et al. Protocols for studies of intraocular lens formula accuracy. Am J Ophthalmol. 2015; 160(3): 403–405.e1, doi: 10.1016/j.ajo.2015.05.029, indexed in Pubmed: 26117311.
4. Wang Li, Shirayama M, Ma XJ, et al. Optimizing intraocular lens power calculations in eyes with axial lengths above 25.0 mm. J Cataract Refract Surg. 2011; 37(11): 2018–2027, doi: 10.1016/j.jcrs.2011.05.042, indexed in Pubmed: 22018365.
5. Wang Li, Koch DD. Modified axial length adjustment formulas in long eyes. J Cataract Refract Surg. 2018; 44(11): 1396–1397, doi: 10.1016/j.jcrs.2018.07.049, indexed in Pubmed: 30274847.
6. Yokoi T, Moriyama M, Hayashi K, et al. Evaluation of refractive error after cataract surgery in highly myopic eyes. Int Ophthalmol. 2013; 33(4): 343–348, doi: 10.1007/s10792-012-9690-6, indexed in Pubmed: 23315193.
7. Behndig A, Montan P, Stenevi U, et al. Aiming for emmetropia after cataract surgery: Swedish National Cataract Register study. J Cataract Refract Surg. 2012; 38(7): 1181–1186, doi: 10.1016/j.jcrs.2012.02.035, indexed in Pubmed: 22727287.
8. Wang Q, Jiang Wu, Lin T, et al. Accuracy of intraocular lens power calculation formulas in long eyes: a systematic review and meta-analysis. Clin Exp Ophthalmol. 2018; 46(7): 738–749, doi: 10.1111/ceo.13184, indexed in Pubmed: 29498180.
9. Melles RB, Holladay JT, Chang WJ. Accuracy of Intraocular Lens Calculation Formulas. Ophthalmology. 2018; 125(2): 169–178, doi: 10.1016/j.ophtha.2017.08.027, indexed in Pubmed: 28951074.
10. Liu J, Wang Li, Chai F, et al. Comparison of intraocular lens power calculation formulas in Chinese eyes with axial myopia. J Cataract Refract Surg. 2019; 45(6): 725–731, doi: 10.1016/j.jcrs.2019.01.018, indexed in Pubmed: 31146930.

11. Zhou D, Sun Z, Deng G. Accuracy of the refractive prediction determined by intraocular lens power calculation formulas in high myopia. Indian J Ophthalmol. 2019; 67(4): 484–489, doi: 10.4103/ijo.IJO_937_18, indexed in Pubmed: 30900579.
12. Zaldivar R, Shultz MC, Davidorf JM, et al. Intraocular lens power calculations in patients with extreme myopia. J Cataract Refract Surg. 2000; 26(5): 668–674, doi: 10.1016/s0886-3350(00)00367-9, indexed in Pubmed: 10831895.
13. Abulafia A, Barrett GD, Rotenberg M, et al. Intraocular lens power calculation for eyes with an axial length greater than 26.0 mm: comparison of formulas and methods. J Cataract Refract Surg. 2015; 41(3): 548–556, doi: 10.1016/j.jcrs.2014.06.033, indexed in Pubmed: 25708208.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0005

Risk factors associated with development of senile cataract

Pragati Garg, Ritika Mullick, Bharti Nigam, Priyanka Raj

Department of Ophthalmology, Era's Lucknow Medial College and Hospital, Lucknow, India

ABSTRACT

BACKGROUND: Cataract is the most common cause of reversible blindness worldwide, which has been associated with various causative risk factors. Hence, we aim to study the factors that might play a role in cataractogenesis.
MATERIAL AND METHODS: A total of 240 eyes of 240 subjects were included for the study, which consisted of 120 cases with age-related cataract and 120 age-matched controls, and in them various factors like blood pressure, body mass index (BMI), smoking, sun exposure, and serum cholesterol were studied.
RESULTS: A statistically significant difference between the two groups was found with respect to smoking profile ($p = 0.007$), sun exposure ($p = 0.001$), and serum cholesterol ($p < 0.001$). Subjects who were smokers, had a longer exposure to sun, and had higher serum cholesterol level were found to be positively associated with development of cataract. No significant association between BMI ($p = 0.384$) and blood pressure ($p > 0.05$) was observed.
CONCLUSION: Higher cholesterol levels, increased sun exposure, and smoking habit play a role in the development of senile cataract, and these are modifiable risk factors. Hence, control of these might help in delaying formation and progression of cataract.

KEY WORDS: cataract; serum cholesterol; blood pressure; risk factor; smoking

Ophthalmol J 2020; Vol. 5, 17–24

INTRODUCTION

Cataract is the most common cause of reversible blindness worldwide. According to the World Health Organisation (WHO), around 253 million people in the world are visually impaired, of whom 90% of the global burden of visual impairment is concentrated in developing countries [1]. Visual impairment caused by cataract leads to not only economic loss, but also impaired quality of life. Cataract is responsible for 50–80% of bilateral blindness in India [2–4].

Owing to its large impact and public health considerations, cataract has always been a target of continuous epidemiologic research. Insights into causative factors amenable to intervention, genetic factors that predispose to disease, and avenues for novel treatment serve to reduce the disease burden [5].

Extensive research has established smoking, diabetes, and ultraviolet (UV) light exposure as the causative risk factors for age-related cataract, while recent studies have identified other potential risk factors like corticosteroid, exogenous oestrogen [6, 7], nutrition [8, 9], dietary fat and serum lipid [10, 11], and genetics [12, 13], which might play a role in the development and progression of cataract.

The focus of identification of newer risk factors of cataract is basically driven by the underlying pathogenesis and pathophysiology behind the cataract. Cataractogenesis, is a multifactorial disease

CORRESPONDING AUTHOR:
Dr. Priyanka Raj, Junior Resident, Era's Lucknow Medial College and Hospital, Sarfarazganj, Lucknow, Uttar Pradesh, India 226003;
e-mail: drpriyankarajy@gmail.com

Copyright © 2019 Via Medica, ISSN 2450–7873

process that may be initiated or promoted by oxidative damage. Conversely, serum lipids have been shown to have a direct relationship with oxidative stress, and so they seem to play a causative role in the development and progression of cataract. Hence, this study was carried out to analyse the factors that potentially play a role in cataractogenesis.

MATERIAL AND METHODS

This is a hospital-based case control study, carried out in the Department of Ophthalmology of a tertiary care centre in Lucknow, North India. Over a period of 18 months we recruited 240 subjects for the purpose of this study, which included 120 individuals aged 50 years or above with age-related cataract as cases, and 120 age-matched non-cataractous controls, after obtaining informed and written consent according to the Declaration of Helsinki.

We excluded subjects with corneal opacities that obscured the grading of the cataract, patients with a history of smoking > 10 pack years, alcohol consumption 20–140 g/day, diabetes or hypertension, and patients with secondary cataract. Controls were demographically matched with the cases without cataract and followed the exclusion criteria. The study was approved by Institutional Ethics Committee.

For the purpose of the study, detailed history regarding signs and symptoms of cataract, family history of cataract, history of any medicine intake and systemic disease that might influence cataract, any history of intraocular surgeries, and socioeconomic status was obtained. The patients were then subjected to systemic examination for height, weight, body mass index (BMI), blood pressure, and ocular examination for best corrected visual acuity by Snellen's chart, and torch light and slit lamp examination for grading of cataract, which was done according to the Lens Opacities Classification System III (LOCS III) into: nuclear cataract, cortical cataract, and posterior subcapsular cataract. Evaluation of serum cholesterol was done by taking a 5 mL blood sample from each participant in an EDTA vial and sending it to the Department of Biochemistry.

The statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. P values, indicating the level of significance, were defined as significant ($p < 0.05$), highly significant ($p < 0.01$), and very highly significant ($p < 0.001$).

RESULTS

The present study was carried out to assess the environmental risk factors and cholesterol levels in the serum of patients with cataract, and to understand their significance. For this purpose, a case-control study was planned in which 120 cases with senile cataract aged ≥ 50 years and 120 demographically matched healthy controls were enrolled and distributed into Group I and Group II, respectively.

Ages of patients in Group I ranged from 50 to 85 years whereas those of controls ranged from 50 to 78 years. The majority of Group I (62.5%) as well as Group II (65.8%) subjects were aged 50–60 years. The mean age of cases was 60.98 ± 7.93 years and that of controls was 59.22 ± 7.15 years. Statistically, there was no significant difference between the two groups with respect to age ($p = 0.071$). In Group I the majority of patients were females (52.5%) whereas in Group II the majority were males (54.2%), and the male-to-female ratios in the two groups were 0.9 and 1.18, respectively. The difference between two groups was not significant statistically ($p = 0.602$) (Tab. 1).

In Group I, a total of 63 (52.5%) had involvement of right eye whereas the remaining 57 (47.5%) had involvement of the left eye. The majority had nuclear sclerotic cataract, among which the most common was Grade 3 cataract (23.3%) followed by those having grade 4 (22.5%), grade 1 (11.7%), and grade 2 (10%) cataract, respectively. Posterior subcapsular cataract was present in 20.0% of the subjects, and cortical cataract was found in 12.5% (Fig. 1).

in Group I the mean systolic and diastolic blood pressure values were 123.82 ± 12.38 and 78.17 ± 8.37 mmHg, respectively, whereas in Group II these values were 124.20 ± 11.64 and 77.52 ± 8.99 mmHg, respectively. On evaluating the data statistically, the difference between two groups was not found to be significant ($p > 0.05$) (Tab. 2).

In Group I the BMI ranged from 17.10 to 32.40 kg/m^2 whereas in Group II the BMI ranged from 18.1 to 31.7 kg/m^2. In Group I the majority (63.3%) had BMI within the range 18.5–24.9 kg/m^2 followed by 25.0–29.9 kg/m^2 (26.7%), < 18.5 kg/m^2 (5.8%), and > 30 kg/m^2 (4.2%). In Group II also, the majority (71.7%) had BMI within the range 18.5–24.9 kg/m^2 followed by 25.0–29.9 kg/m^2 (22.5%), < 18.5 kg/m^2 (3.3%), and > 30 kg/m^2 (2.5%). The mean BMI of Group I

Table 1. Age distribution between cases and controls

	Group I Cases (n = 120)		Group II Controls (n = 120)		Statistics
	No.	%	No.	%	
Age [years]					
50–60	75	62.5	79	65.8	t = 1.812 p = 0.071
61–70	32	26.7	31	25.8	
> 70	13	10.8	10	8.3	
Mean age [years] ± SD (range)	60.98 ± 7.93 (50–85)		59.22 ± 7.15 (50–78)		
Gender					χ^2 = 1.067 p = 0.302
M:F	0.9		1.18		

SD — standard deviation

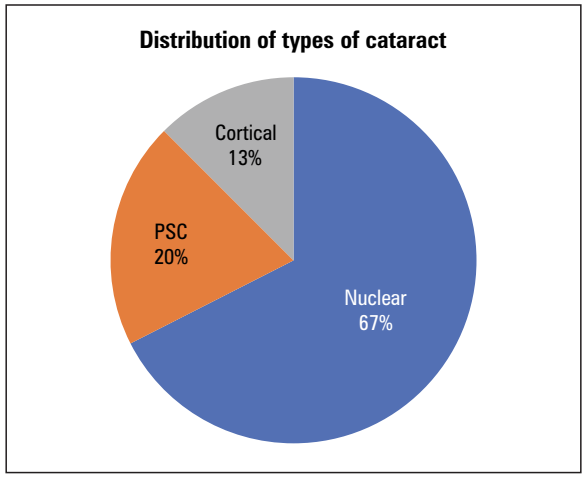

FIGURE 1. Type of cataract; PSC — posterior subcapsular cataract

patients was 23.39 ± 3.09 kg/m^2 as compared to 23.04 ± 3.12 kg/m^2 for Group II subjects. Statistically, there was no significant difference between the two groups with respect to BMI (p = 0.384) (Tab. 3).

In Group I, a total of 57 (47.5%) were non-smokers, 17 (14.2%) were smokers of up to five packs/year, and 46 (38.3%) were smokers of 5–10 packs/year. Compared to this, the majority of Group II (59.2%) subjects were non-smokers, 25 (20.8%) were smokers of up to five packs/year, and 24 (20%) were smokers of 5–10 packs/year. Statistically, the difference between two groups was found to be significant (p = 0.007). The majority of Group I patients had duration of sun exposure > 6 hrs/week (65.8%) whereas the majority of Group II subjects had duration of sun exposure < 6 hrs/week (55.8%). On comparing the data statistically, the difference between the two groups was found to be significant (p = 0.001) (Tab. 3).

Compared to Group II, Group I subjects had significantly higher mean cholesterol levels (p < 0.001). Mean serum cholesterol levels were minimum grade 3 (170.11 ± 26.12 mg/dL) and maximum grade 2 (192.92 ± 33.71 mg/dL); however, the difference among different grades was not statistically significant (p = 0.093) (Tab. 4).

Total cholesterol had area under curve (AUC) = 0.603. The sensitivity and specificity ranged from 61.7% and 52.5%, respectively (Fig. 2).

On evaluating the role of different variables found to be significantly associated with cataract in univariate assessment through a multivariate predictive model for cataract, neither smoking, sun exposure, nor cholesterol were shown to have any significant association with cataract (Tab. 5).

Table 2. Systolic and diastolic blood pressure between the two groups

Parameter	Group I Cases (n = 120)		Group II Controls (n = 120)		Statistical significance	
	Mean	SD	Mean	SD	t	p
SBP [mmHg]	123.82	12.38	124.20	11.64	0.247	0.805
DBP [mmHg]	78.17	8.37	77.52	8.99	0.580	0.563

SBP — systolic blood pressure; DBP — diastolic blood pressure; SD — standard deviation

Table 3. Comparison of various risk factors between cases and controls

Characteristics	Group I Cases (n = 120)		Group II Controls (n = 120)		Statistical significance
	No.	%	No.	%	
BMI					
< 18.5	7	5.8	4	3.3	t = 0.872 p = 0.384
18.5–24.9	76	63.3	84	71.7	
25.0–29.9	32	26.7	27	22.5	
≥ 30	5	4.2	3	2.5	
Mean BMI [kg/m²] ± SD (range)	23.39 ± 3.09 (17.10–32.40)		23.04 ± 3.12 (18.1–31.7)		
Sun exposure					
< 6 hrs/week	41	34.2	67	55.8	χ^2 = 11.38 p = 0.001
> 6 hrs/week	79	65.8	53	44.2	
Smoking habit					
No	57	47.5	71	59.2	χ^2 = 9.969 (df = 2) p = 0.007
Up to 5 packs/year	17	14.2	25	20.8	
5–10 packs/year	46	38.3	24	20.0	

BMI — body mass index; SD — standard deviation

Table 4. Comparison of serum cholesterol levels between cases and controls

Group I Cases (n = 120)						Group II Controls (n = 120)	Statistical significance
179.72 ± 28.90 (110–280)						153.59 ± 31.11 (100–220)	t = 6.625 p < 0.001
PSC (n = 24)	Cortical (n = 15)	Nuclear (n = 81)					
179.38 ± 22.34	170.93 ± 22.45	181.44± 31.52					F = 0.837 p = 0.436
		Grade 1 (n = 14)	Grade 2 (n = 12)	Grade 3 (n = 28)	Grade 4 (n = 27)		
		189.86 ± 40.92	192.92 ± 33.71	170.11 ± 26.12	183.74 ± 28.06		F = 2.214 p = 0.093

PSC — posterior subcapsular cataract

DISCUSSION

Despite cataract being one of the most common causes of preventable blindness, there is limited understanding regarding the exact aetiology and pathogenesis. Cataract is often referred to as a multi-aetiological process. Laboratory investigations suggest that age-related cataract might result from oxidative stress after sunlight exposure [14]. Animal and observational studies suggest that a diet low in antioxidant micronutrients may increase the risk of lens opacification. Cholesterol levels have also been shown to produce oxidative stress [15]. Incidentally, cholesterol levels and cataract have both been shown to be age related, and hence a temporal relationship cannot be ruled out. Taking into account the oxidative stress-induced pathogenesis of cataract, it may be hypothesised that levels of antioxidant micronutrients might be lower while cholesterol levels might be higher among cataract patients.

In order to test this hypothesis, the present study was planned as a case-control study in which 120 patients of senile cataract (aged > 50 years) were included as cases and an equal number of age- and sex-matched individuals without cataract were included as controls. Serum total cholesterol levels were included as representative of an oxidative stress-inducing condition. The mean age of patients was 60.98 ± 7.93 years, and the majority were females (52.5%).

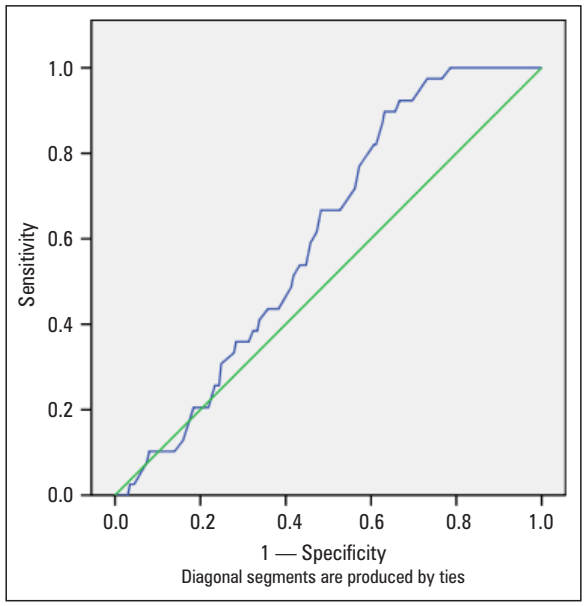

FIGURE 2. Area under curve for cholesterol. ROC — receiver operating characteristic curve

In the present study, the BMI of patients ranged from 17.10 to 32.40 kg/m^2. The mean BMI of patients was 23.39 ± 3.09 kg/m^2, and the majority of patients were within normal BMI range (63.3%). Compared to the present study, Nourmohammadi et al. [16] found the mean BMI of patients to be 24.02 ± 4.10 kg/m^2, while Abbaszadeh et al. [17] reported a mean BMI of cataract patients of 25.04 ± 3.69 kg/m^2. Compared to this, western studies report relatively high BMI in cataract patients. In the Italian-American Clinical Trial of Nutritional Supplements and Age-related Cataract (CTNS) [26], the majority of patients were overweight (55%) and almost one quarter (23.6%) were obese. Karppi et al. [18] reported a mean BMI of cataract patients of 27.5 ± 4.4 kg/m^2 in their study among the elderly Finnish population. These findings in general suggest that while BMI could be a risk factor for cataract in western populations, it does not seem to be very significant in Asian populations. Bearing in mind the probable role of micronutrients in the determination of BMI, there could be differences in micronutrient levels among different populations.

The controls were statistically matched to cases with respect to age, gender, and BMI, thus showing that these factors did not have a confounding effect.

In the present study, the eye with the higher grade of cataract was included among cases. With respect to the side involved, both right (52.5%) and left (47.5%) eyes were involved almost equally. As such, no predisposition of side of eye with cataract has been reported in literature. The present study, showing almost equal distribution of left and right sides, also showed that the side involved is determined by chance rather than by any particular side-related risk. The present study did not include any diabetic or hypertensive patient as per the exclusion criteria of the study. Consecutively, the systolic and diastolic blood pressure values of two cases and controls were matched statistically.

In the present study, the majority of cataract patients were smokers (52.5%). Among smokers (n = 63) too, majority smoked 5–10 packs/year (46/63; 73.0%). In present study we excluded those smoking > 10 pack-years. Smoking is known to be a risk factor for development of age-related cataract [19]. Smoking might also induce oxidative stress [20, 21] and affect the level of antioxidant micronutrients and lipids [22, 23] under different health conditions. On the other hand, the proportion of smokers and those with smoking habit 5–10 packs/year was significantly lower in controls. These findings suggested that smoking habit was a confounding factor in our study.

In the present study, the majority of cases (65.8%) had sunlight exposure > 6 hrs/week as compared to 44.2% of controls. Thus, the proportion of those having sunlight exposure > 6 hrs/week

Table 5. Multivariate assessment

Variables	B	SE	Wald	df	Sig.	Exp (B)	95.0% CI for Exp(B)	
							Lower	Upper
Smoking	–.413	.222	3.456	1	.063	.661	.428	1.023
Sun exposure	–.017	.404	.002	1	.967	.984	.446	2.170
Cholesterol	–.002	.007	.064	1	.800	.998	.986	1.011
Constant	–.945	1.317	.515	1	.473	2.573		

B — ????: SE — standard error; Wald. — ???; df — degree of freedom; Sig. — significance; **Exp — ????:** CI — confidence interval

was significantly higher in cases as compared to that in controls. Laboratory investigations have suggested that age-related cataract might result from oxidative stress after sunlight exposure [24, 25]. The findings of the present study also validated this proposition.

Mean serum cholesterol levels were significantly higher in cases as compared to those in controls. In their study, Karppi et al. [18] did not find a significant difference between those having nuclear cataract and those not having cataract for cholesterol level; however, their study was a cross-sectional study among cataract patients in a significantly older age group and having a significantly lower proportion of males as compared to those not having controls. Moreover, in their study, a significant difference between the two groups was also found for alcohol consumption. Owing to these confounding effects, the antioxidant micronutrient and lipid levels in their study might have been affected. In the present study we identified smoking and sunlight exposure as possible reasons for inducing oxidative stress and affecting antioxidant micronutrient levels.

We also found that increased cholesterol levels are associated with cataract risk. A number of previous studies have also endorsed this association in different populations [26–34].

We also investigated cholesterol levels among different types of cataract (posterior capsular, nuclear, and cortical cataract cases) but did not find a significant difference in cholesterol levels among different cataract types. Also, with respect to cholesterol levels, a number of studies supported that all types of cataract are affected by higher cholesterol levels too. However, Al-Talqani et al. [26] found that dyslipidaemia was associated significantly with nuclear and cortical cataract, but it was not associated significantly with posterior subcapsular cataract. Cholesterol representing approximately 40% of the total lipids of human lens fibres, and intrinsic or extrinsic factors modifying its level and/or repartition may alter optical lens properties. Some cholesterols can be present as crystals, which have been found in plasma membranes isolated from the lens, and which may play functional roles in normal and pathological lens. The formation of these crystals is related to the lipid composition of the lens and seems to depend on the presence of sphingomyelin and dihydrosphingomyelin. The part played by cholesterol in the development of cataract is also supported by observations performed in various pathologies associated with defects in cholesterol metabolism. Thus, patients with Smith-Lemli-Opitz syndrome, mevalonic aciduria, or cerebrotendinous xanthomatosis characterised by mutations in enzymes of cholesterol metabolism (7- dehydrocholesterol reductase, mevanolate kinase, and CYP27A1, resp.) often develop cataract [27]. Moreover, with regards to oxidative damage, because the lipid lens composition is devoid of oxidisable polyunsaturated fatty acids, and because there is a high content of dihydrosphingomyelin that is less prone to oxidation, this particular lipid composition favours cholesterol autoxidation. Thus, because human lens membrane contains the highest cholesterol levels of any known biological membranes, and because human lens is continuously in a strong photoxidative environment, chronic exposure to UV light and ozone can lead to the formation of some cholesterol oxide derivatives (also named oxysterols) [28, 29], which might contribute to disruption of cholesterol repartition and homeostasis in human lens fibres.

Hiller et al. [30] reported a longitudinal data series to find the association between serum lipids and age-related lens opacities. In this multistage analysis fasting hypertriglyceridaemia (≥ 250 mg/dL) was associated with an increased risk of posterior subcapsular cataract (PSC) in men ($p = 0.02$). High-density lipoprotein cholesterol levels ≤ 35 mg/dL were associated with PSC cataract in men at a borderline level of significance ($p = 0.09$). No associations were noted between serum lipid/lipoprotein variables and risk of cortical or nuclear cataract. These findings suggested that hypertriglyceridaemia, a potentially modifiable factor, is associated with the development of PSC cataract in men.

Heydari et al. [31] evaluated the relationship between cataract development and serum lipids, glucose, and antioxidants in a case-control study. They found that plasma TG ($p = 0.02$), cholesterol ($p = 0.001$), and low-density lipoprotein cholesterol (LDL-C) ($p = 0.04$) were significantly higher in the cataract group than in the control group.

Park et al. [32] conducted an analysis of data from the Korea National Health and Nutrition Examination Surveys (2008–2010). Reduced high-density lipoprotein cholesterol (HDL-C), elevated fasting glucose, and elevated triglycerides (TG) were also significantly associated with cataract in women [aOR, 95% CI; 1.27 (1.07–1.50), 1.23 (1.01–1.50), and 1.26 (1.04–1.52), respectively]. In the subgroup analysis for cataract subtype, MetS and reduced HDL-C were significantly associated with nuclear cataract in women [aOR,

95% CI; 1.25 (1.07–1.55) and 1.25 (1.03–1.52), respectively]. However, such associations were not found in men.

In a similar study Uppu and Gupta [33] also found a significant difference between the case and control groups for all the lipids including total cholesterol, TG, LDL, and very low-density lipoprotein (VLDL) but not HDL levels ($p < 0.001$). No significant difference was observed between the two groups for serum fasting glucose levels. The authors were of the view that oxidative stress may play an import role in the senile cataract.

Al-Talqani et al. [26] also found a significant association between the prevalence of dyslipidaemia ($p < 0.05$) with nuclear and cortical cataract, but it was not significant (> 0.05) for posterior subcapsular cataract.

Li et al. [34] in a case control study found that the serum LDL-C, TG, cholesterol, and apolipoprotein A (APOA) levels were significantly higher ($p < 0.05$) in the cataract group than in the control group. The findings of the study thus showed that lipid levels pose a significant risk of age-related cataract.

In the present study, among different grades of nuclear cataract, we also did not find a significant difference in cholesterol levels, and we did not find any significant association between the grade of nuclear cataract and lipid levels. One of the reasons for this could be the lower number of cases in lower grades (Grade I and II) in our series.

In view of these findings, we attempted to derive cut-off values for total cholesterol levels for discrimination between cataract and non-cataract subjects. We found that total cholesterol levels were least sensitive and specific (61.7% sensitivity and 52.5% specificity) at a cut-off of > 169.5 mg/dL.

In previous studies, despite showing the role of cholesterol levels, no such discriminant role had been analysed. In the present study, despite deriving these cut-off values, we feel that they have limited practical value because it was carried out as a case-control study and included subjects falling within predefined inclusion and exclusion criteria. Bearing in mind the fact that cholesterol levels play roles also in other diseases, the diagnostic/discriminant value of these parameters has limited practical application and more such studies are needed to confirm the usefulness of these cut-off values.

In the present study, on binary logistic regression, taking smoking, sun exposure, and cholesterol levels as independent predictors of cataract, none of them showed a significant association with cataract.

CONCLUSION

The present study thus endorsed the findings that antioxidant micronutrients and cholesterol levels play a significant role in causation of senile cataract, as proposed by various previous studies. The present study also highlighted that increased sun exposure and smoking habit could play a detrimental role in oxidative stress, which affected the antioxidant levels and lipid levels and thus played a role in the pathogenesis of cataract.

Acknowledgements

None.

Conflict of interest

Authors declare that there was no conflict of interest in the publication of this study.

REFERENCES

1. World Health Organization. Blindness and visual impairment. WHO Fact Sheet dated 11 October, 2017. http://www.who.int/en/news-room/fact-sheets/detail/blindness-and-visual-impairment (1st May, 2018).
2. Thulasiraj RD, Nirmalan PK, Ramakrishnan R, et al. Blindness and vision impairment in a rural south Indian population: the Aravind Comprehensive Eye Survey. Ophthalmology. 2003; 110(8): 1491–1498, doi: 10.1016/S0161-6420(03)00565-7, indexed in Pubmed: 12917162.
3. Thulasiraj RD, Rahamathulla R, Saraswati A, et al. The Sivaganga eye survey: I. Blindness and cataract surgery. Ophthalmic Epidemiol. 2002; 9(5): 299–312, doi: 10.1076/opep.9.5.299.10334, indexed in Pubmed: 12528915.
4. Nirmalan PK, Thulasiraj RD, Maneksha V, et al. A population based eye survey of older adults in Tirunelveli district of south India: blindness, cataract surgery, and visual outcomes. Br J Ophthalmol. 2002; 86(5): 505–512, doi: 10.1136/bjo.86.5.505, indexed in Pubmed: 11973242.
5. West SK, Valmadrid CT, West SK, et al. Epidemiology of risk factors for age-related cataract. Surv Ophthalmol. 1995; 39(4): 323–334, doi: 10.1016/s0039-6257(05)80110-9, indexed in Pubmed: 7725232.
6. Younan C, Mitchell P, Cumming RG, et al. Hormone replacement therapy, reproductive factors, and the incidence of cataract and cataract surgery: the Blue Mountains Eye Study. Am J Epidemiol. 2002; 155(11): 997–1006, doi: 10.1093/aje/155.11.997, indexed in Pubmed: 12034578.
7. Mukesh BN, Le A, Dimitrov PN, et al. Development of cataract and associated risk factors: the Visual Impairment Project. Arch Ophthalmol. 2006; 124(1): 79–85, doi: 10.1001/archopht.124.1.79, indexed in Pubmed: 16401788.
8. Wu SY, Leske MC. Antioxidants and cataract formation: a summary review. Int Ophthalmol Clin. 2000; 40(4): 71–81, doi: 10.1097/00004397-200010000-00006, indexed in Pubmed: 11064858.
9. Leske MC, Chylack LT, Wu SY, et al. The Lens Opacities Case-Control Study. Risk factors for cataract. Arch Ophthalmol. 1991; 109(2): 244–251, doi: 10.1001/archopht.1991.01080020090051, indexed in Pubmed: 1993036.
10. Hiller R, Sperduto RD, Reed GF, et al. Serum lipids and age-related lens opacities: a longitudinal investigation: the Framingham Studies. Ophthalmology. 2003; 110(3): 578–583, doi: 10.1016/S0161-6420(02)01762-1, indexed in Pubmed: 12623825.
11. Jahn CE, Janke M, Winowski H, et al. Identification of metabolic risk factors for posterior subcapsular cataract. Ophthalmic Res.

1986; 18(2): 112–116, doi: 10.1159/000265424, indexed in Pubmed: 3737111.
12. Familial aggregation of lens opacities: the Framingham Eye Study and the Framingham Offspring Eye Study. Am J Epidemiol. 1994; 140(6): 555–564, indexed in Pubmed: 8067349.
13. Heiba IM, Elston RC, Klein BE, et al. Evidence for a major gene for cortical cataract. Invest Ophthalmol Vis Sci. 1995; 36(1): 227–235, indexed in Pubmed: 7822150.
14. Young RW. The family of sunlight-related eye diseases. Optom Vis Sci. 1994; 71(2): 125–144, doi: 10.1097/00006324-199402000-00013, indexed in Pubmed: 8152745.
15. Rao V, Kiran R. Evaluation of correlation between oxidative stress and abnormal lipid profile in coronary artery disease. J Cardiovasc Dis Res. 2011; 2(1): 57–60, doi: 10.4103/0975-3583.78598, indexed in Pubmed: 21716754.
16. Nourmohammadi I, Modarress M, Khanaki K, et al. Association of serum alpha-tocopherol, retinol and ascorbic acid with the risk of cataract development. Ann Nutr Metab. 2008; 52(4): 296–298, doi: 10.1159/000148189, indexed in Pubmed: 18663288.
17. Abbaszadeh M, Aidenloo NS, Motarjemizadeh Q, et al. Lack of association between plasma levels of vitamin C and nuclear cataract. Bull Env Pharmacol Life Sci. 2016; 6(1): 1–5.
18. Karppi J, Laukkanen JA, Kurl S. Plasma lutein and zeaxanthin and the risk of age-related nuclear cataract among the elderly Finnish population. Br J Nutr. 2012; 108(1): 148–154, doi: 10.1017/S0007114511005332, indexed in Pubmed: 22005336.
19. Ye J, Lou LX, He JJ, et al. Smoking and risk of age-related cataract: a meta-analysis. Invest Ophthalmol Vis Sci. 2012; 53(7): 3885–3895, doi: 10.1167/iovs.12-9820, indexed in Pubmed: 22599585.
20. Isik B, Ceylan A, Isik R. Oxidative stress in smokers and non-smokers. Inhal Toxicol. 2007; 19(9): 767–769, doi: 10.1080/08958370701401418, indexed in Pubmed: 17613085.
21. Donohue JF. Ageing, smoking and oxidative stress. Thorax. 2006; 61(6): 461–462, doi: 10.1136/thx.2005.053058, indexed in Pubmed: 16738041.
22. Gepner AD, Piper ME, Johnson HM, et al. Effects of smoking and smoking cessation on lipids and lipoproteins: outcomes from a randomized clinical trial. Am Heart J. 2011; 161(1): 145–151, doi: 10.1016/j.ahj.2010.09.023, indexed in Pubmed: 21167347.
23. Sinha AK, Misra GC, Patel DK. Effect of cigarette smoking on lipid profile in the young. J Assoc Physicians India. 1995; 43(3): 185–188, indexed in Pubmed: 11256905.
24. Young RW. The family of sunlight-related eye diseases. Optom Vis Sci. 1994; 71(2): 125–144, doi: 10.1097/00006324-199402000-00013, indexed in Pubmed: 8152745.
25. Ayala MN, Michael R, Söderberg PG. Influence of exposure time for UV radiation-induced cataract. Invest Ophthalmol Vis Sci. 2000; 41(11): 3539–3543, indexed in Pubmed: 11006249.
26. Al-Talqani HM, Taher AA, Jabouri BB. Dyslipidemia and cataract in adult Iraqi patients . EC Ophthalmol. 2017; 5(5): 162–171.
27. Cenedella R. Cholesterol and cataracts. Surv Ophthalmol. 1996; 40(4): 320–337, doi: 10.1016/s0039-6257(96)82007-8, indexed in Pubmed: 8658343.
28. Wentworth P, Nieva J, Takeuchi C, et al. Evidence for ozone formation in human atherosclerotic arteries. Science. 2003; 302(5647): 1053–1056, doi: 10.1126/science.1089525, indexed in Pubmed: 14605372.
29. Dreyfus MA, Tolocka MP, Dodds SM, et al. Cholesterol ozonolysis: kinetics, mechanism, and oligomer products. J Phys Chem A. 2005; 109(28): 6242–6248, doi: 10.1021/jp050606f, indexed in Pubmed: 16833964.
30. Hiller R, Sperduto RD, Reed GF, et al. Serum lipids and age-related lens opacities: a longitudinal investigation: the Framingham Studies. Ophthalmology. 2003; 110(3): 578–583, doi: 10.1016/S0161-6420(02)01762-1, indexed in Pubmed: 12623825.
31. Heydari B, Kazemi T, Zarban A, et al. Correlation of cataract with serum lipids, glucose and antioxidant activities: a case-control study. West Indian Med J. 2012; 61(3): 230–234, doi: 10.7727/wimj.2011.103, indexed in Pubmed: 23155978.
32. Park YH, Shin JAh, Han K, et al. Gender difference in the association of metabolic syndrome and its components with age-related cataract: the Korea National Health and Nutrition Examination Survey 2008-2010. PLoS One. 2014; 9(1): e85068, doi: 10.1371/journal.pone.0085068, indexed in Pubmed: 24416342.
33. Li S, Li D, Zhang Y, et al. Association between serum lipids concentration and patients with age-related cataract in China: a cross-sectional, case-control study. BMJ Open. 2018; 8(4): e021496, doi: 10.1136/bmjopen-2018-021496, indexed in Pubmed: 29626052.

CASE REPORT
DOI: 10.5603/OJ.2020.0006

Magnetic resonance imaging evaluation of retro-bulbar optic nerve in patients with optic disc pit maculopathy

Katarzyna Baltaziak[1], Lucyna Baltaziak[2], Rashed Mustafa Nazzal[2], Robert Rejdak[2], Tomasz Pikuła[3]

[1]Medical Students Ophthalmology Interest Group, General Ophthalmology Clinic, Medical University of Lublin, Lublin, Poland
[2]Department of General Ophthalmology, Medical University of Lublin, Lublin, Poland
[3]Department of Interventional Radiology and Diagnostic Imaging, Medical University of Lublin, Poland

ABSTRACT

BACKGROUND: Optic disc pit (ODP) is a congenital anomaly characterized by indented area of the optic nerve head most likely originating from the incomplete closure of the superior edge of the embryonic fissure. Maculopathy can occasionally complicate this anomaly as intra-retinal and sub-retinal fluid at the macula. In result, maculopathy is associated with a poor visual prognosis due to a serous macular detachment, formation of macular hole, or atrophy of the retinal pigmented epithelium. In this case series, we report of three patients with unilateral ODP.
CASE REPORT: We attempted to analyze the morphologic changes seen in the ODP and evaluate patients with a complete ophthalmologic evaluation, fundus color photography, spectral-domain optical coherence tomography (SD-OCT) scanning, and magnetic resonance imaging (MRI) of globe and orbit. Magnetic resonance imaging scan was done for optic disc diameter (ODD) and optic nerve sheath diameter (ONSD).
CONCLUSION: We noticed that in the patient who presented with neurosensory detachment in the macula, the ONSD is larger than in the fellow eye and is larger than the remaining two patients with ODP and without neurosensory detachment of the retina.

KEY WORDS: optic disc pit; OCT; MRI; maculopathy; optic nerve

Ophthalmol J 2020; Vol. 5, 25–28

INTRODUCTION

Optic disc pit (ODP) is a rare inherited anomaly of the head of the optic nerve. It typically appears in one eye (although 15% are bilateral). Optic disc pit presents as oval, hypo-pigmented discolored scooping of the optic disc, most frequentlyin the temporal or inferio-temporal segment of the optic disc. At times, it can be found in other sector of the optic nerve [1]. The incidence of ODP is 1 in 10,000 people without gender predilection [2]. Optic disc pit is usually asymptomatic, but if large enough, it can be associated with visual field defects. In the absence of associated maculopathy, vision is typically unaffected [1, 2].

Regarding the origin of the fluid that causes the maculopathy, the exact mechanism remains unclear and several competing theories have suggested it might originate from liquified vitreous humor between the retina is the vitrous membrane, leakage of serum from blood vessels at the base of the pit or leakage of the cerebrospinal fluid (CSF) from the choroid [3–5].

The aim of this study was to review the ODP case series including the natural history of the disease to

CORRESPONDING AUTHOR:
Katarzyna Baltaziak, Medical University of Lublin, ul. Chmielna 1, 20–079 Lublin, Poland; e-mail: k.baltaziak@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

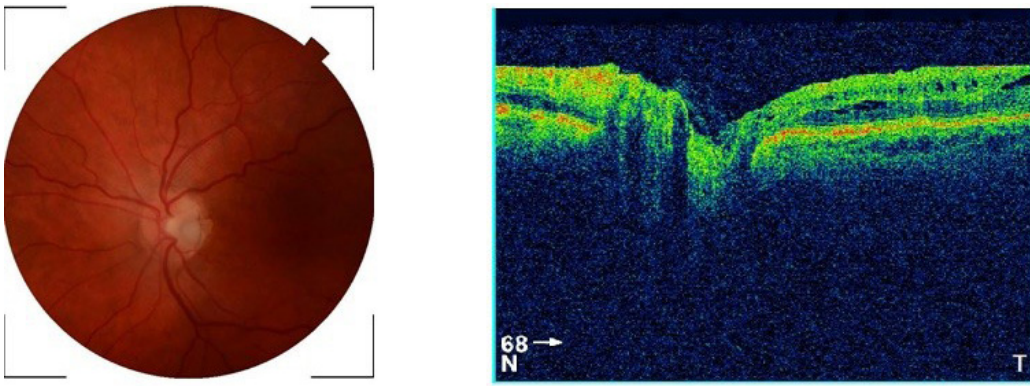

FIGURE 1. Coloured fundus photography and optical coherence tomography (OCT) of the optic disco of left eye for the Case 1

gain better understanding of clinical and pathological circumstances involved in development of the ODP-related maculopathy, and at least in part to develop insights into the prediction of when and if ODP patients may develop maculopathy.

CASE REPORTS

We attempted to analyze the morphologic changes seen in the ODP and evaluate patients with a complete ophthalmologic evaluation, fundus color photography, spectral-domain optical coherence tomography (SD-OCT) scanning, and Magnetic resonance imaging (MRI) of globe and orbit. MRI scan was done for optic disc diameter (ODD) and optic nerve sheath diameter (ONSD).

CASE 1

A 70-year-old woman with chief complaint of gradual worsening of vision over the last few months. On examination, she was found to have a best corrected visual acuity of 0.4. Fundus examination showed optic disc pit complicated by maculopathy which was confirmed by OCT (Fig. 1). MRI scan was done for optic disc diameter (ODD) and optic nerve sheath diameter (ONSD) and both measurements were within normal limits (Fig. 4A).

CASE 2

A 42-year-old man presented to our clinic for check-up. The visual acuity was 1.0 and the fundus examination showed an incidental finding of ODP in his left eye as illustrated in the colored fundus photograph and OCT (Fig. 2). And MRI scan was obtained also and measurements for ODD and ONSD were within normal limits (Fig. 4B).

CASE 3

A 41-year-old woman, presented with gradual worsening of vision in left eye. The visual acuity was 0.1 in the left eye. Fundus exam showed macular neurosensory detachment confirmed by OCT, and associated optic nerve pit; there was also areas of RPE pigmentary changes (Fig. 3). To measure the

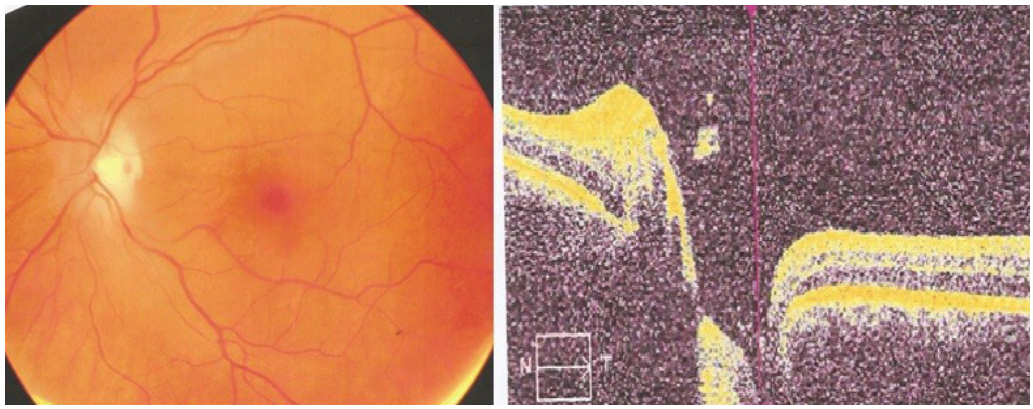

FIGURE 2. Coloured fundus photography and optical coherence tomography (OCT) of the optic disco of left eye for the Case 2

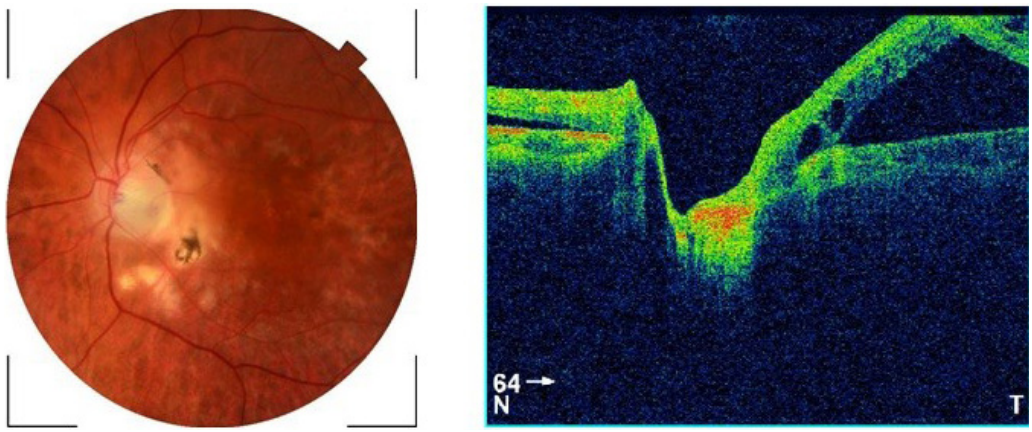

FIGURE 3. Coloured fundus photography and optical coherence tomography (OCT) of the optic disco of left eye for the Case 3

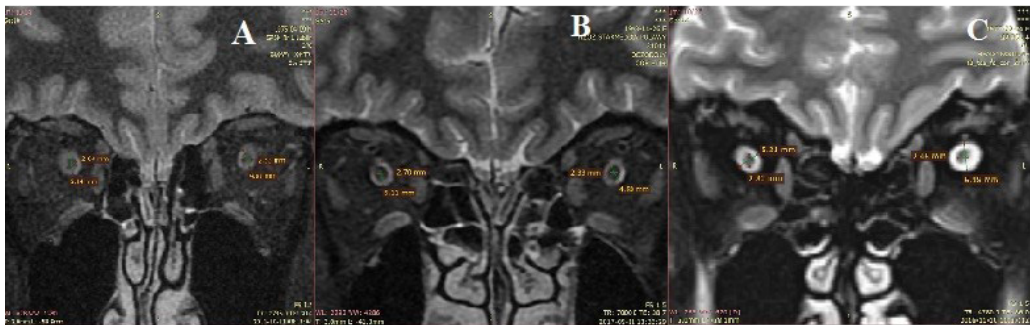

FIGURE 4. Constructive interference in steady state T2-weighted sequences imaging (CISS MRI) for the three patients. **A.** Case 1; **B.** Case 2; **C**. Case 3

Table 1. Demographics of the patients

Patient	Eye	Gender	Visual acuity	Symptoms	Location of the ONP
1	Left	Female	0.4	Bluring of vision	Temporal
2	Left	Male	1.0	Asymptomatic	Inferiotemporal
3	Left	Female	0.1	Decreased of vision	Inferiotemporal

OPN — optic nerve pit

size of the ONSD we used MRI scans targeting the retro-bulbar part of the optic nerve. Based on the radiologist recommendation we used a special protocol called constructive interference in steady state T2-weighted sequences (CISS MRI), which has demonstrated the increase in 3D dimensions of abnormally swollen ONSD on the CISS MRI (Fig. 4C).

Summary of patient demographics is shown in Table 1.

DISCUSSION

It has been always known that maculopathy is a well-recognized complication of optic disc pit, which usually results in poor visual outcome [2]. In this case series of three patients, we evaluated the patients with full ophthalmological examination in addition to MRI scan for the retro-bulbar part of the optic nerve.

Geeraerts et al. showed that the mean ONSD in healthy people was (5.08 ± 0.52 mm), while the normal ODD in healthy people was (2.70 ± 0.23 mm; p = 0.26) [6].

In our cases, we compared the diameter of the ODD in both eyes of the same patient, and between the three patients and they were all within normal limits. Then, we measured the ONSD that surrounds the retro-bulbar part of the optic nerve

Table 2. Summary of measurements by magnetic resonance imagong (MRI)				
Patient	OND [mm]		ONSD [mm]	
	Right eye	Left eye	Right eye	Left eye
1	2.6	2.5	5.1	4.6
2	2.7	2.3	5.1	4.8
3	2.8	2.5	5.2	6.2

OND — optic nerve diameter; ONSD — optic nerve sheath diameter

between both eyes of the same patient and among the three patients (Tab. 2). In this case series, we used the other eye as a control group. We noticed that in the third patient who presented with neurosensory detachment in the macula, the ONSD is larger in the left eye than the left eye and is larger than all three patients. This was better illustrated by doing a modified protocol in the MRI scan known as CISS — is a fully refocused fast-gradient echo sequence that is mainly used in the assessment of the central nervous system structure and lesions. Advantages of steady-state imaging are short acquisition times, high signal-to-noise ratio, and better contrast-to-noise ratio. In addition, a cisternographic effect of CISS allows assessments of cranial nerves which was relevant in this study [7].

Whether this result is of clinical significance or not, needs further study. We are aware of the very small sample size in this report. But such an association has never been reported before, hence further studies might be needed to reach a clinical significance.

Medical management of ODP maculopathy remains challenging although there are reports of spontaneous resolution of the disease. Nevertheless, the current management of the ODP maculopathy involves several surgical approaches and presents possibility of postsurgical complications for affected patients undergoing vitrectomy due to the ODP maculopathy. Alternatives to vitrectomy include either gas tamponade or laser photocoagulation. Other less frequently performed options including scleral buckling and inner fenestration, have been also reported [8].

Acknowledgements

None.

Conflict of interests

None.

REFERENCES

1. Wiethe T. Ein Fall von angelborener Difformitaet der Sehnerven-papille. Arch Augenheilkd. 1882; 11: 14–19.
2. Gass JD. Serous detachment of the macula. Secondary to congenital pit of the optic nervehead. Am J Ophthalmol. 1969; 67(6): 821–841, doi: 10.1016/0002-9394(69)90075-0, indexed in Pubmed: 5795739.
3. Irvine AR, Crawford JB, Sullivan JH, et al. The pathogenesis of retinal detachment with morning glory disc and optic pit. Trans Am Ophthalmol Soc. 1986; 84(3): 280–292, indexed in Pubmed: 3590472.
4. Gowdar JP, Rajesh B, Giridhar A, et al. An insight into the pathogenesis of optic disc pit-associated maculopathy with enhanced depth imaging. JAMA Ophthalmol. 2015; 133(4): 466–469, doi: 10.1001/jamaophthalmol.2014.6093, indexed in Pubmed: 25675311.
5. Moisseiev E, Moisseiev J, Loewenstein A. Optic disc pit maculopathy: when and how to treat? A review of the pathogenesis and treatment options. Int J Retina Vitreous. 2015; 1: 13, doi: 10.1186/s40942-015-0013-8, indexed in Pubmed: 27847606.
6. Geeraerts T, Newcombe VFJ, Coles JP, et al. Use of T2-weighted magnetic resonance imaging of the optic nerve sheath to detect raised intracranial pressure. Crit Care. 2008; 12(5): R114, doi: 10.1186/cc7006, indexed in Pubmed: 18786243.
7. Gonçalves F, Amaral L. Constructive Interference in Steady State Imaging in the Central Nervous System. Eur Neurol Rev. 2011; 6(2): 138, doi: 10.17925/enr.2011.06.02.138.
8. Chatziralli I, Theodossiadis P, Theodossiadis GP. Optic disk pit maculopathy: current management strategies. Clin Ophthalmol. 2018; 12: 1417–1422, doi: 10.2147/OPTH.S153711, indexed in Pubmed: 30127591.

CASE REPORT
DOI: 10.5603/OJ.2020.0007

Uveitis presenting with iris bombe in a patient with HIV: the importance of multi-disciplinary management — a case study

Thomas RP Taylor[1], Neil Shah[2], Rashmi Akshikar[2]

[1]Barts Health NHS Trust, Academic Foundation Program, Royal London Hospital, London, United Kingdom
[2]Imperial College Healthcare NHS Trust, London, United Kingdom

ABSTRACT

This case study concerns a 53-year-old female presenting to an eye-hospital in London with uveitis, on a background of well-controlled HIV. After investigation, no cause for the uveitis was found other than the HIV itself, and the patient was treated with immunosuppressants. Because of the nature of her underlying HIV infection, help was sought from HIV specialists, who gave advice on the management, including alteration of corticosteroid dosing due to the risk of drug-interactions between her uveitis and HIV treatments. Of particular concern was the risk of cytochrome P450 3A inhibition by cobicistat and the potential for iatrogenic Cushing syndrome through elevated steroid doses. This case is used as an example to highlight the importance of the multi-disciplinary team in the management of complex conditions, as well as to add to the literature in support of the HIV virus itself as a cause of uveitis.

KEY WORDS: uveitis; HIV; iris bombe; multi-disciplinary; inflammation

Ophthalmol J 2020; Vol. 5, 29–32

CASE PRESENTATION

A 53-year-old Afro-Caribbean female with a background of well-controlled human immunodeficiency virus (HIV) suffered subacute onset left sided ocular pain and loss of vision.

One year prior to presentation, she had a suspected reactivation of ocular (retinal) toxoplasmosis treated appropriately. Diagnosed over 25 years ago, her HIV was known to be triple-class antiretroviral drug resistant (TC-DR). Despite extensive antiretroviral therapy changes, she was well controlled on Symtuza (combination of darunavir, cobicistat, emtricitabine, and tenofovir alafenamide) at the time of presentation. Her most recent CD4 count was 840 cells/mm^3 with an undetectable HIV-1 viral load.

At presentation with a five-day history of worsening ocular pain, floaters, and loss of vision, her left intraocular pressure (IOP) was 42 mmHg, and her visual acuity was CF in the affected eye. Extensive corneal oedema was present (Fig. 1) with iris bombe demonstrated in three quadrants as well as a large crystalline lens on B-scan ocular ultrasound. With no clinical fundal view, B-scan also showed a retinal traction band expanding temporally with no retinal detachment. A diagnosis of hypertensive uveitis and iris bombe was made, with particular note of the immunocompromised state.

She had no other systemic symptoms. In particular, she had no weight loss, fever, night sweats, rashes, or cough, which could point to an aetiology. There was no history of, or high-risk contact with,

CORRESPONDING AUTHOR:
Dr. Thomas RP Taylor, Barts Health NHS Trust, Academic Foundation Program, Royal London Hospital, Whitechapel Road, London, UK E1 1RD; e-mail: thomasrptaylor@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

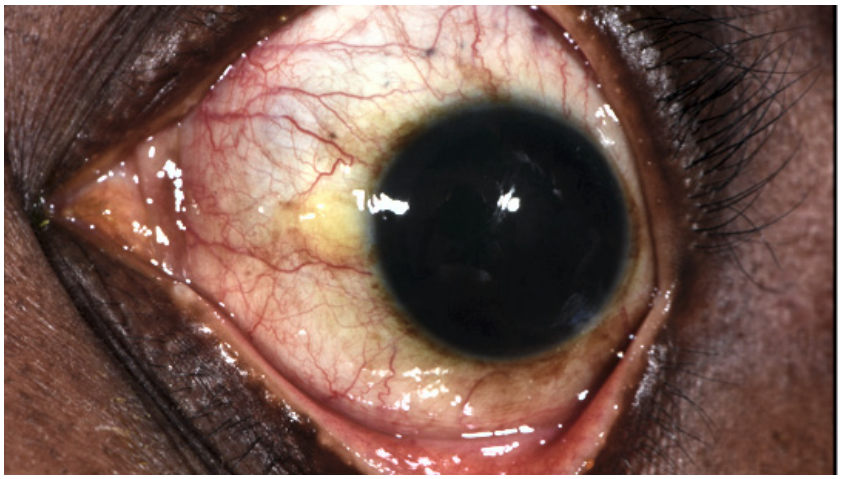

FIGURE 1. Affected eye showing significant corneal oedema

mycobacterium tuberculosis (TB). Extra-ocular clinical examination was within normal limits, with no lymphadenopathy.

Intraocular pressure lowering was immediately attempted with intravenous acetazolamide. Topical carbonic anhydrase inhibitor, beta blockers, anti-muscarinic, prostaglandin analogues, and alpha agonists [dorzolamide and timolol (Cosopt), atropine, latanoprost and iopidine, respectively] were also administered to aid this. Oral and topical steroids were started to treat the uveitis, the underlying cause of the raised IOP and loss of vision. As she was on a protease inhibitor, this was all in close discussion with the HIV team and specialist pharmacists, to prevent adverse effects on HIV control. Anti-emetics, analgesics, and benzodiazepines were also prescribed for symptom relief.

Over three days, her ocular pain settled, intraocular pressure reduced to 10 mm Hg, and she was discharged with a reducing regime of oral prednisolone as well as a topical steroid and non-steroidal anti-inflammatory drops as a steroid-sparing alternative. Unfortunately, her visual acuity remained CF in the left eye despite treatment.

In the following two months, her IOP became persistently high at 34 mm Hg despite oral acetazolamide. An emergency micropulse diode laser trabeculoplasty (MDLT), using laser to alter the trabecular network and aid flow of the aqueous humour and thus reduce IOP, was successfully performed. Due to persistent inflammation, a dense cataract has formed. She now awaits a surgical iridectomy and cataract surgery with intravitreal steroid to open up the iridocorneal angle further and improve visual acuity.

Despite extensive testing, no cause of the aetiology of her uveitis was found. Her repeated HIV-1 viral load was less than 20 and CD4 count 373 cells/mm^3.

Throughout her treatment, the HIV team were very closely involved. Whilst on immunosuppressive steroids, it was decided to intensify her current HIV therapy with the addition of dolutegravir, an integrase inhibitor. She remains systemically well from an HIV perspective at present, and ongoing collaborative care remains essential because long-term immunosuppression for ocular pathology is likely.

DISCUSSION

This patient presented with uveitis (inflammation of the iris, ciliary body, and choroid) leading to raised IOP after developing iris bombe. This is where inflammation causes the iris to become adherent to the crystalline lens, preventing aqueous humour outflow. Raised IOP is dangerous due to its potential to cause irreversible optic neuropathy (glaucoma).

Uveitis is associated with many conditions including autoinflammatory disorders, infectious diseases, or it may be idiopathic. HIV is a disease commonly associated with uveitis, and it is estimated that 70–80% of patients with untreated HIV will develop an ocular condition at some point, of which half will be inflammation or uveitis [1].

Uveitis and other ocular complications of HIV are typically caused by opportunistic infections such as tuberculosis, syphilis, and toxoplasmosis, as well as malignant processes such as lymphoma secondary to progressive immune dysfunction. However, there

are also reports of uveitis occurring in HIV-infected patients without any suspected causative agents other than the HIV virus itself [2, 3]. This implicates that the eye itself could be a sanctuary for HIV.

Certain drugs used to treat HIV are also associated with a risk of uveitis, particularly medications containing rifabutin [4] or cidofovir [5]. Symtuza, however, is not associated with this risk. Only one published study has found a weak link between a similar class of medication containing three of the four constituent drugs and uveitis. In all cases, the uveitis resolved without stopping the drug [6]. Given no evidence to the contrary, it is likely that the HIV infection itself was the causative organism in this case, although intraocular fluid was not sent for culture to confirm this.

Anterior uveitis in HIV tends to be asymptomatic [7]. A case series of symptomatic uveitis in HIV found four other patients over a four-year period in one hospital with CD4 counts over 200 cells/mm^3 and symptomatic uveitis with no concurrent illness [7]. Other symptomatic cases, which were associated with other aetiologies, such as tuberculosis and herpes zoster, all had CD4 counts < 200 cells/mm^3.

This case highlights the comparative rarity of a patient with well-controlled HIV developing a symptomatic uveitis without clear underlying aetiology, as well as the importance of cooperation between ophthalmic and infectious disease specialists in the treatment of this condition.

The mainstay of treatment of non-infective uveitis is corticosteroids, which can be given via several routes, commonly topical and oral [8]. They need slow tapering over a period of weeks so as not to cause rebound inflammation when they are withdrawn. Drugs to paralyse the ciliary body are also given to relieve pain and prevent adhesions. If an infective cause is suspected, an appropriate antimicrobial is also added.

Despite the theoretical concerns over the use of immunosuppressive drugs such as corticosteroids in patients who are already immunosuppressed, studies have shown that short-term steroid use in HIV-positive individuals is relatively safe, well tolerated, and not associated with effects on HIV-1 RNA levels or CD4 cell counts [9, 10]. Corticosteroid use is generally only a concern when high doses are used, or when the CD4 count is very low [11].

The issue with co-prescribing corticosteroids in patients being treated for HIV is not therefore a risk of worsening HIV control; instead, care must be taken due to drug-drug interactions between corticosteroids and HIV treatments. Cobisistat, one of the components of Symtuza, acts as a boosting agent for the effects of the protease inhibitor darunavir. Its main mechanism of action is inhibition of the enzyme cytochrome P450 3A (CYP3A), the liver enzyme that breaks down darunavir [12]. Inhibition of this enzyme therefore leads to increased levels and prolonged effects of darunavir. Many other drugs are also metabolised by CYP3A, the most relevant of which in this case are corticosteroids. Through the same mechanism of action, Cobisistat therefore increases plasma concentrations of corticosteroids given as treatment for uveitis and could risk development of steroid-associated side effects. This includes Cushing syndrome and secondary adrenal suppression through the hypothalamic-pituitary-adrenal axis.

There has been a reported case of this occurring in a patient on a CYP3A inhibitor and corticosteroid eye drops, which led to serious complications including avascular necrosis of the hip [13]. Conversely, there is also a theoretical risk that the steroid (dexamethasone) eye drops could alter the efficacy of the protease inhibitor darunavir. This is because dexamethasone can act as an inducer of the CYP3A enzyme, of which darunavir is a substrate, which could worsen HIV control [14]. Accordingly, care must be taken when co-prescribing these medications because they have the potential to cause serious, irreversible side-effects as well as the worsening of underlying HIV control. Specialists must thus be involved to ensure safe prescribing.

In our patient, the dose of oral corticosteroids was reduced by a third to compensate for the increased systemic exposure. Punctal occlusion was also taught to minimise systemic absorption of topical dexamethasone drops. The decision was also made to intensify HIV treatment with the addition of dolutegravir to counteract the potential reduction in efficacy through the induction of darunavir. Dolutegravir is not primarily metabolised by CYP3A and is therefore not subject to the same drug interactions discussed here [15].

Without input from multi-disciplinary specialists, this patient could have been at greater risk of serious iatrogenic complications.

CONCLUSION

This case showcases that ocular inflammatory emergencies, such as iris bombe, can present in the

absence of obvious causal aetiology, and it adds to the literature in support of the HIV-1 virus itself as a cause of uveitis. Multi-disciplinary teamwork is key in the management of complex uveitis, especially with immunosuppressed individuals on medications pre-disposing to dangerous drug-drug interactions.

Statement of competing interests

The authors report no competing interests.

REFERENCES

1. Cunningham ET, Margolis TP. Ocular manifestations of HIV infection. N Engl J Med. 1998; 339(4): 236–244, doi: 10.1056/NEJM199807233390406, indexed in Pubmed: 9673303.
2. Rothova A, Schneider M, de Groot-Mijnes JDF. Human immunodeficiency virus-induced uveitis: intraocular and plasma human immunodeficiency virus-1 RNA loads. Ophthalmology. 2008; 115(11): 2062–2064, doi: 10.1016/j.ophtha.2008.04.034, indexed in Pubmed: 18562005.
3. Rosberger D, Heinemann MH, Friedberg D, et al. Uveitis associated with human immunodeficiency virus infection. Am J Ophthalmol. 1998; 125(3): 301–305, doi: 10.1016/s0002-9394(99)80135-4, indexed in Pubmed: 9512146.
4. Nichols C. Mycobacterium avium Complex Infection, Rifabutin, and Uveitis — Is There a Connection? Clin Infect Dis. 1996; 22(Suppl 1): S43–S49, doi: 10.1093/clinids/22.supplement_1.s43, indexed in Pubmed: 8785256.
5. Davis JL, Taskintuna I, Freeman WR, et al. Iritis and hypotony after treatment with intravenous cidofovir for cytomegalovirus retinitis. Arch Ophthalmol. 1997; 115(6): 733–737, doi: 10.1001/archopht.1997.01100150735008, indexed in Pubmed: 9194724.
6. Gaur A, Kizito H, Prasitsueubsai W, et al. Safety, efficacy, and pharmacokinetics of a single-tablet regimen containing elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide in treatment-naive, HIV-infected adolescents: a single-arm, open-label trial. Lancet HIV. 2016; 3(12): e561–e568, doi: 10.1016/s2352-3018(16)30121-7, indexed in Pubmed: 27765666.
7. Verma S, Hughes JD, Mabey D, et al. Symptomatic anterior uveitis in HIV-positive patients. Int J STD AIDS. 1999; 10(4): 268–274, doi: 10.1258/0956462991913925, indexed in Pubmed: 12035782.
8. Uveitis — NICE CKS. Cks.nice.org.uk. (2019) . https://cks.nice.org.uk/uveitis#!backgroundsub:1.
9. McComsey GA, Whalen CC, Mawhorter SD, et al. Placebo-controlled trial of prednisone in advanced HIV-1 infection. AIDS. 2001; 15(3): 321–327, doi: 10.1097/00002030-200102160-00004, indexed in Pubmed: 11273211.
10. Andrieu JM, Lu W, Levy R. Sustained Increases In Cd4 Cell Counts In Asymptomatic Human. J Infect Dis. 1995; 171(3): 523–530, doi: 10.1093/infdis/171.3.523, indexed in Pubmed: 7876597 .
11. Nelson MR, Erskine D, Hawkins DA, et al. Treatment with corticosteroids — a risk factor for the development of clinical cytomegalovirus disease in AIDS. AIDS. 1993; 7(3): 375–378, doi: 10.1097/00002030-199303000-00011, indexed in Pubmed: 8097096.
12. Tseng A, Foisy M. Important Drug-Drug Interactions in HIV-Infected Persons on Antiretroviral Therapy: An Update on New Interactions Between HIV and Non-HIV Drugs. Curr Infect Dis Rep. 2012; 14(1): 67–82, doi: 10.1007/s11908-011-0229-1, indexed in Pubmed: 22125049.
13. Molloy A, Matheson NJ, Meyer PAR, et al. Cushing's syndrome and adrenal axis suppression in a patient treated with ritonavir and corticosteroid eye drops. AIDS. 2011; 25(10): 1337–1339, doi: 10.1097/QAD.0b013e328347c09c, indexed in Pubmed: 21659797.
14. HIV insite (2019). Interactions with Dexamethasone. http://hivinsite.ucsf.edu/insite?page=ar-00-02&post=8¶m=138..
15. Castellino S, Moss L, Wagner D, et al. Metabolism, excretion, and mass balance of the HIV-1 integrase inhibitor dolutegravir in humans. Antimicrob Agents Chemother. 2013; 57(8): 3536–3546, doi: 10.1128/AAC.00292-13, indexed in Pubmed: 23669385.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0010

The frequency of refractive errors required to be corrected in childhood among Turkish children

Mahmut Atum[1], Burçin Çakir[1], Erdinç Bozkurt[2], Erkan Çelik[1], Gürsoy Alagöz[1]

[1]Department of Ophthalmology, Sakarya University Education and Research Hospital, Sakarya, Turkey
[2]Department of Ophthalmology, Kars Kafkas University, Kars, Turkey

ABSTRACT

BACKGROUND: The aim of this study is to investigate the distribution of refractive errors needed to be correct in childhood.

MATERIAL AND METHODS: Children applied and received glasses prescriptions were recruited. Age, gender, spherical, cylindrical error, and spherical equivalent (SE) were noted. The refractive errors were classified as myopic, hyperopic and cylindrical errors according to the SE and prescriptions. Cylindrical errors were subdivided into myopic, hyperopic. Children were classified into 4 groups. Group 1, 2, 3 and 4 composed of children whose ages were between 0–5, 6–10, 11–15 and 16–18 years, respectively.

RESULTS: There were 846 children in group 1, 3931 in group 2, 5948 in group 3, 3896 in group 4, and a total of 14621 children. The rates of myopia and hyperopia were 72.4% and 27.6%. Myopic and hyperopic astigmatism were found in 29.1% and 11.3% of children. Myopia, myopic astigmatism increased with age ($p < 0.05$). The hyperopia rate decreased with decreasing age ($p < 0.05$). The frequency of myopia, myopic astigmatism was higher in both male and female children ($p < 0.05$). The rate of myopia was higher in females ($p < 0.05$). There was no statistically significant difference in terms of cylindrical value between genders. The statistically significant difference was found in terms of mean SE among all groups and a negative correlation was present between age and mean SE. A lower negative correlation was stated between age and cylindrical value.

CONCLUSION: Corrected myopic and myopic astigmatism errors were higher than hyperopic refractive errors. The prevalence of myopia increased by age and was higher in females. The need for glasses was highest in children whose age range was between 11 and 15 years.

KEY WORDS: refractive errors; astigmatism; myopia; hyperopia; childhood

Ophthalmol J 2020; Vol. 5, 33–37

INTRODUCTION

The most common cause of visual impairment worldwide is uncorrected refractive errors (myopia, hyperopia, and astigmatism). Approximately 153 million people are thought to be affected [1]. Uncorrected refractive errors may lead to amblyopia in childhood and cause persistent visual impairment. Refractive status should be checked in both preschool and school-age children [2]. Studies have been previously performed on the prevalence of refractive errors in childhood in different regions [2–5]. Rajavi et al. reported in a study conducted in Iran that they had 3.5% hyperopia, 22.6% myopia and 4.9% astigmatism in children

CORRESPONDING AUTHOR:
Mahmut Atum, Department of Ophthalmology, Sakarya University Education and Research Hospital, Sakarya, Turkey; Korucuk Mah. 54100 Sakarya, Turkey, tel: (+90) 555 809 62 75; e-mail: mahmutatum@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

aged 7–12 years. They also observed an increase in myopia and decrease in hyperopia as the children aged [6]. Another study conducted in Germany also revealed an increase in myopia and decrease in hyperopia with age for patients between 2 and 35 years old [7]. The prevalence of myopia has been increasing steadily and is estimated to afflict approximately 1 billion people in the 2050 year according to a study by Holden et al. [8]. These studies reveal the refractive status of children, but not the refractive errors which need to be corrected. Mild hyperopia in children (below 3 diopters) without ocular deviation and with sufficient accommodation does not need to be corrected. Also, moderate myopia in preschool-aged children may be observed without intervention. Caca et al. investigated the refractive status of 21062 children and 22.7% needed correction of a refractive error. The age range was between 6–14 years [9]. The need for refractive error correction and the prevalence of corrected refractive errors in children is important to evaluate the real effect of refractive status on children's vision. To our knowledge, there is no study in the literature evaluating the prevalence of corrected refractive errors in children aged 0 to 18 years old.

MATERIAL AND METHODS

This study was conducted at the Departments of Ophthalmology of two major hospitals (Sakarya Training and Research Hospital, Yenikent State Hospital) in the Sakarya province in Turkey between January 2016 and December 2018. Prior approval from the Institutional Review Board (IRB number:71522473/050.01.04/19) was received and written informed consent was obtained from the parents of each participant. The study was performed in adherence to the Declaration of Helsinki.

Children between 0 to 18 years of age who were treated at the two hospitals and received a prescription for glasses after an ophthalmological examination were recruited for this study. Children with a previous history of refractive surgery were not included in this study.

All the children underwent a full ophthalmological examination including a best-corrected visual acuity measurement by Snellen chart, cycloplegic refraction, biomicroscopic examination for the anterior segment and fundus evaluation. Autorefractometers (Tonoref 3; Nıdek Co., Ltd, Gamagori, Japan, and Canon RK-F2 Full Auto Ref-Keratometer; Canon, Tokyo, Japan) in the hospitals were used for measuring refractive errors. Examination for ocular deviation and dynamic retinoscopy was also performed. According to the results of the examination, a prescription for glasses was written and registered in the hospitals' information systems. The results of a dynamic retinoscopy and improvement in the best corrected visual acuity as the primary data used to determine if glasses should be prescribed to a child.

Age, gender, spherical and cylindrical errors, and spherical equivalent (SE) were noted. The SE was calculated as the sum of the spherical and half of the cylindrical value. Records of the glasses prescriptions were taken from the information systems and investigated retrospectively. The refractive errors were classified as myopic, hyperopic, and cylindrical errors according to the SE and prescriptions, respectively. Cylindrical errors were subdivided into myopic astigmatism and hyperopic astigmatism. The study was classified into four groups based on age range. Groups 1, 2, 3 and 4 were composed of children whose ages were between 0–5, 6–10, 11–15, and 16–18 years, respectively.

STATISTICAL ANALYSIS

Statistical analyses were performed using the SPSS program version 17 (SPSS Inc, Chicago, IL, USA). Descriptive statistics were used for data analyses. The Pearson correlation analysis was used for detecting the correlation between the refractive errors of the eyes of each child. Numerical data were given as mean ± standard deviation. Distribution according to age and gender was given as a percentage. Kolmogorov-Smirnov analysis was used for testing the normality of distribution. Parametric tests (the Student t test) were used for variables with normal distribution and non-parametric tests (Mann-Whitney U test) were chosen for variables without normal distribution. A p value of < 0.05 was considered statistically significant.

RESULTS

This current study was composed of 14621 children in total, if which 5656 (38.7%) were female and 8965 (61.3%) were male. The mean ages of males and females were 11.58 ± 4.26 and 12.70 ± 3.85 years, respectively, and the overall mean age was 12.27 ± 4.05 years. A statistically significant difference was present in terms of the mean ages of male and female children ($p < 0.05$). As mentioned in the materials and methods section, the children were divided into 4 groups. There were 846 (5.8%)

Table 1. Distribution of refraction errors by age groups and gender (n, %)

	Myopia	Hyperopia	Total	Myopic astigmatism	No astigmatism	Hyperopic astigmatism	Total
Group 1 (0–5 y)	135 (16.0%)	711 (84.0%)	846 (100.0%)	138 (16.3%)	372 (44.0%)	336 (39.7%)	846 (100.0%)
Group 2 (6–10 y)	2211 (56.2%)	1720 (43.8%)	3931 (100.0%)	1034 (26.3%)	2119 (53.9%)	778 (19.8%)	3931 (100.0%)
Group 3 (11–15 y)	4817 (81.0%)	1131 (19.0%)	5948 (100.0%)	1769 (29.7%)	3788 (63.7%)	391 (6.6%)	5948 (100.0%)
Group 4 (16–18)	3426 (87.9%)	470 (12.1%)	3896 (100.0%)	1315 (33.8%)	2436 (62.5%)	145 (3.7%)	3896 (100.0%)
Total (0–18)	10589 (72.4%)	4032 (27.6%)	14621 (100.0%)	4256 (29.1%)	8715 (59.6%)	1650 (11.3%)	14621 (100.0%)
Male	3771 (66.7%)	1885 (33.3%)	5656 (100.0%)	1815 (32.1%)	3001 (53.1%)	840 (14.9%)	5656 (100.0%)
Female	6818 (76.1%)	2147 (23.9%)	8965 (100.0%)	2441 (27.2%)	5714 (63.7%)	810 (9.0%)	8965 (100.0%)

children in group 1, group 2 included 3931 (26.9%) children, Group 3 included 5948 (40.7%) children, and there were 3896 (26.6%) children in Group 4. A high positive correlation was found between the two eyes of children and the data obtained from the right eye were used in the analyzes ($r = 0.814$, $p = 0.000$).

Myopia was present in 10,589 (72.4%) children and hyperopia was present in 4032 (27.6%) children. Myopic astigmatism was found in 4256 (29.1%) children and 1650 (11.3%) children had hyperopic astigmatism. In 8715 (59.6%) children astigmatism was not present.

While the myopia rate was 16% and the myopic astigmatism rate was 16.3% in Group 1, these rates were 87.9 % and 33.8% in Group 4, respectively. It was observed that myopia and myopic astigmatism increased with age ($p < 0.05$). The rates of hyperopia and hyperopic astigmatism were 84.0% and 39.7% in Group 1 and 12.1%, and 3.7% in Group 4, respectively. The hyperopia rate decreased with age ($p < 0.05$).

The distribution of corrected refractive errors in all age groups and genders is summarized in Table 1. When the distribution of refractive errors according to gender was investigated, the frequency of myopia and myopic astigmatism was higher than hyperopia and hyperopic astigmatism in both male and female children ($p < 0.05$). In addition, the rate of myopia was higher in females ($p < 0.05$).

The mean SE was –0.65 ± 2.22 diopter (D) and ranged between –17.50 D and +18.00 D. The mean cylindrical value was –0.16 ± 0.90 D and ranged between –7.00 D and +6.25 D. A statistically significant difference was found in terms of mean SE among all groups and a negative correlation was present between age and the mean SE ($r = –0.375$, $p < 0.05$). Similarly, a lower negative correlation was stated between age and cylindrical value ($r= –0.162$, $p < 0.05$) (Fig. 1).

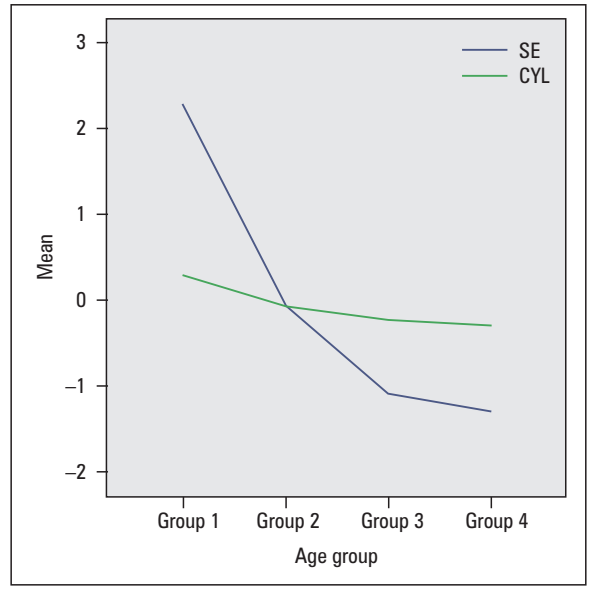

FIGURE 1. Mean values of refraction errors according to age groups in diopters (Group 1: 0–5 years, Group 2: 6–10 years, Group 3: 11–15 years and Group 4: 16–18 years). D — diopter; SE — spherical equivalent; CYL — cylinder

The mean SE and cylindrical value were –0.43 ± 2.45 D and –0.15 ± 1.03 D in males and

Table 2. Comparison of spherical equivalent (SE) and cylinder (CYL) values according to age groups						
		Group 1 (n = 846)	Group 2 (n = 3931)	Group 3 (n = 5948)	Group 4 (n = 3896)	p
Mean SE (D)		2.25 ± 2.76	–0.05 ± 2.30	–1.07 ± 1.88	–1.26 ± 1.77	< 0.05
95% CI for Mean SE	Lower	2.06	–0.12	–1.12	–1.32	
	Upper	2.44	–0.02	–1.03	–1.20	
Mean CYL (D)		0.31 ± 1.25	–0.06 ± 1.09	–0.21 ± 0.78	–0.29 ± 0.69	< 0.05
95% CI for Mean CYL	Lower	0.2312	–0.0961	–0.2369	–0.3159	
	Upper	–0.4012	–0.0278	–0.1971	–0.2721	

Group 1: 0–5 years, Group 2: 6–10 years, Group 3: 11–15 years and Group 4: 16–18 years; D — diopter; SE — standard error; CI — confidence interval

–0.80 ± 2.04 D and 0.17 ± 0.80 in females, respectively. While the frequency of myopia was higher in females, there was no statistically significant difference in terms of cylindrical value between males and females ($p < 0.05$ and $p = 0.363$, respectively). Table 2 summarizes the mean SE and cylindrical values classified according to age group.

DISCUSSION

This current study revealed the rate of corrected myopic and myopic astigmatism errors were higher than hyperopic refractive errors. Robaei et al. found the rate of 12-year-old Australian children requiring glasses was 19.0%. The rates of myopia, hyperopia, and astigmatism were 46.3%, 10.9%, and 21.8%, respectively [10]. Gaete et al. found school-aged children needed glasses at a rate of 34.4%. They did not investigate the distribution of refractive errors [11]. Robaei et al. also investigated the patterns of glasses use in 6-year-old Australian school children and found the rate of glasses use was 4.4%. Hyperopia with or without astigmatism was the most frequent reason for glasses use (40.3%) [12]. These reports supported our findings. We found a higher hyperopic corrected refractive error in children between 0 and 5 years old and this refractive error gradually decreased with age. We also observed the need for glasses was lower in children between 0 and 10 years old. This result indicated that hyperopic refractive errors were less often corrected. Huang et al. found myopia started in children at approximately 7 years old, increased with age, and had a significant association with visual acuity [13]. Gursoy et al. investigated refractive errors in 7- to 8-year-old children and the need for glasses for myopia and hyperopia were 0.8% and 1.0%, respectively. The narrow and young age range may cause this result. In this study, the need for glasses was 20.4% of all children [14].

When we investigated the rate of corrected refractive errors in children, we observed the need for glasses was highest in children whose age range was between 11 and 15 years (Group 3). The growth of children in this age range is faster than in other periods. Chen et al. found the prevalence of myopia exhibited an increased tendency with height development in children [15]. These factors may be responsible for our findings.

Glasses need for myopia was higher in girls than boys in this study. Lin et al. found a lower prevalence and lesser degree of myopia among boys. Goldschmidt et al. reported higher myopia prevalence in girls. But Alemam et al. found myopia was more prevalent in males. The behavioral differences of children in different regions may lead to these variations [16–18].

CONCLUSION

The need for glasses increased gradually by age 15 and a minimal decline was observed between 15- and 18-year-old children. The prevalence of myopia increased with age and was higher in females. This current study is unique in terms of investigating the distribution of the need for glasses in childhood according to age, gender, and classification of refractive errors.

Acknowledgments

We are grateful to Atilla Akgül, one of the staff of the Sakarya Provincial Health Directorate, for his contributions to the data collection.

Conflicts of interest

The Authors declare that there is no conflict of interest.

REFERENCES

1. Resnikoff S, Pascolini D, Mariotti SP, et al. Global magnitude of visual impairment caused by uncorrected refractive errors in 2004. Bull World Health Organ. 2008; 86(1): 63–70, doi: 10.2471/blt.07.041210, indexed in Pubmed: 18235892.
2. Tongue AC. Refractive errors in children. Pediatr Clin North Am. 1987; 34(6): 1425–1437, doi: 10.1016/s0031-3955(16)36365-9, indexed in Pubmed: 3317238.
3. Maul E, Barroso S, Munoz SR, et al. Refractive Error Study in Children: results from La Florida, Chile. Am J Ophthalmol. 2000; 129(4): 445–454, doi: 10.1016/s0002-9394(99)00454-7, indexed in Pubmed: 10764851.
4. Mehari ZA, Yimer AW. Prevalence of refractive errors among schoolchildren in rural central Ethiopia. Clin Exp Optom. 2013; 96(1): 65–69, doi: 10.1111/j.1444-0938.2012.00762.x, indexed in Pubmed: 22784031.
5. Gomez-Salazar F, Campos-Romero A, Gomez-Campaña H, et al. Refractive errors among children, adolescents and adults attending eye clinics in Mexico. Int J Ophthalmol. 2017; 10(5): 796–802, doi: 10.18240/ijo.2017.05.23, indexed in Pubmed: 28546940.
6. Rajavi Z, Sabbaghi H, Baghini AS, et al. Prevalence of Amblyopia and Refractive Errors Among Primary School Children. J Ophthalmic Vis Res. 2015; 10(4): 408–416, doi: 10.4103/2008-322X.176909, indexed in Pubmed: 27051485.
7. Jobke S, Kasten E, Vorwerk C. The prevalence rates of refractive errors among children, adolescents, and adults in Germany. Clin Ophthalmol. 2008; 2(3): 601–607, doi: 10.2147/opth.s2836, indexed in Pubmed: 19668760.
8. Holden BA, Fricke TR, Wilson DA, et al. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016; 123(5): 1036–1042, doi: 10.1016/j.ophtha.2016.01.006, indexed in Pubmed: 26875007.
9. Caca I, Cingu AK, Sahin A, et al. Amblyopia and refractive errors among school-aged children with low socioeconomic status in southeastern Turkey. J Pediatr Ophthalmol Strabismus. 2013; 50(1): 37–43, doi: 10.3928/01913913-20120804-02, indexed in Pubmed: 22966784.
10. Robaei D, Kifley A, Rose KA, et al. Refractive error and patterns of spectacle use in 12-year-old Australian children. Ophthalmology. 2006; 113(9): 1567–1573, doi: 10.1016/j.ophtha.2006.02.066, indexed in Pubmed: 16857261.
11. Gaete MI, Lira RP, Lynch de Moraes LF, et al. [Association between the need for optical correction prescription and other ocular conditions in school children]. Arq Bras Oftalmol. 2007; 70(6): 949–952, doi: 10.1590/s0004-27492007000600012, indexed in Pubmed: 18235905.
12. Robaei D, Rose K, Kifley A, et al. Patterns of spectacle use in young Australian school children: findings from a population-based study. J AAPOS. 2005; 9(6): 579–583, doi: 10.1016/j.jaapos.2005.07.005, indexed in Pubmed: 16414527.
13. Huang YoP, Singh A, Lai LiJu. The Prevalence and Severity of Myopia among Suburban Schoolchildren in Taiwan. Ann Acad Med Singapore. 2018; 47(7): 253–259, indexed in Pubmed: 30120433.
14. Gursoy H, Basmak H, Yaz Y, et al. Vision screening in children entering school: Eskisehir, Turkey. Ophthalmic Epidemiol. 2013; 20(4): 232–238, doi: 10.3109/09286586.2013.808672, indexed in Pubmed: 23865604.
15. Chen J, Chen Z, Lin S, et al. Correlation analysis for school-age children's height and refractive errors. Adv Clin Exp Med. 2018; 27(8): 1125–1130, doi: 10.17219/acem/78773, indexed in Pubmed: 30088701.
16. Goldschmidt E. [On the etiology of myopia. An epidemiological study]. Acta Ophthalmol (Copenh). 1968: Suppl 98, indexed in Pubmed: 4886009.
17. Mohammed Alemam A, Aldebasi MH, Rehmatullah A, et al. Prevalence of Myopia among Children Attending Pediatrics Ophthalmology Clinic at Ohud Hospital, Medina, Saudi Arabia. J Ophthalmol. 2018; 2018: 3708409, doi: 10.1155/2018/3708409, indexed in Pubmed: 30524756.
18. Lin LL, Shih YF, Tsai CB, et al. Epidemiologic study of ocular refraction among schoolchildren in Taiwan in 1995. Optom Vis Sci. 1999; 76(5): 275–281, doi: 10.1097/00006324-199905000-00013, indexed in Pubmed: 10375241.

CASE REPORT
DOI: 10.5603/OJ.2020.0012

Primary apocrine adenocarcinoma of the orbit with lacrimal sac invasion

Mona Mohammad[1], Rashed Mustafa Nazzal[5], Maysa AlHussaini[2], Niveen Abdullah[2], Alaa Saleh[3], Sana' Muhsen[4], Robert Rejdak[6], Yacoub A. Yousef[1]

[1]Department of Surgery/Ophthalmology, King Hussein Cancer Center (KHCC), Amman, Jordan
[2]Department of Pathology, King Hussein Cancer Center (KHCC), Amman, Jordan
[3]Department of and Radiology, King Hussein Cancer Center (KHCC), Amman, Jordan
[4]Ophthalmology Department, Jordan University Hospital, University of Jordan, Amman, Jordan
[5]Shami Eye Center, Amman, Jordan
[6]Medical University of Lublin, Lublin, Poland

ABSTRACT

BACKGROUND: Orbital adenocarcinoma usually is metastatic and rarely can be primary disease of the orbit with no clear standard of care. Herein, we report a case of primary apocrine adenocarcinoma in the orbit with invasion into lacrimal sac in a young patient.

CASE REPORT: A 38-year-old male presented with enlarging lump in the left eye. Ocular imaging studies showed an orbital mass with invasion into the lacrimal sac and surrounding muscles. The lesion was found to be adenocarcinoma with apocrine differentiation in both pathology and immunohistochemistry. Full body imaging studies showed no extra ocular spread and no other tumors to suggest orbital metastasis. The patient was treated with orbital exenteration and was given adjuvant local radiotherapy and systemic chemotherapy because of positive margins and high risk pathological features. On serial exams over 5 years follow up, the patient was free of local recurrence or distant metastasis.

CONCLUSION: Orbital adenocarcinoma can present as a primary orbital tumor in young adults originating from apocrine glands, and aggressive surgical resection can be lifesaving management.

KEY WORDS: adenocarcinoma; apocrine; metastasis; orbit

Ophthalmol J 2020; Vol. 5, 38–41

INTRODUCTION

There are two types of sweat glands: apocrine and eccrine. Unlike eccrine glands, apocrine glands are distributed in limited areas in the body including the axilla, anogenital areas, mammary glands, and eyelids [1]. Characteristically, these glands secrete by decapitation; part of the cytoplasm of the glandular cell is pushed off into the glandular lumen [2]. The glands of Moll are modified apocrine glands that lie in the base of the follicles of the eyelashes [3].

Adenocarcinoma (AC) is a rare, slow-growing skin carcinoma with apocrine differentiation arising from apocrine glands. This is rarely seen in the orbit, but common in the axilla and the anogenital region [4]. Adenocarcinoma in the orbit is usually metastasis from breast or lung adenocarcinoma, but can be rarely primary in the ocular region, where they are usually derived from Moll glands of the eyelid [5]. Adenocarcinoma should be recognized and treated properly because of a high rate of both local recurrence and distant metastasis [6]. Herein

CORRESPONDING AUTHOR:
Yacoub A. Yousef, MD, Consultant Ocular Oncologist, King Hussein Cancer Center, Department of Surgery/Ophthalmology, Queen Rania Al Abdullah Street, P.O. Box 1269, Amman 11941, Jordan, tel: (962) 7 87228749, fax: (962) 6 5345 567; e-mail: yyousef@Khcc.jo, drjaqub@yahoo.com

Copyright © 2020 Via Medica, ISSN 2450–7873

we are reporting an extremely rare case of primary orbital adenocarcinoma in a young patient who was cured by orbital exenteration.

CASE REPORT

A 38-year-old previously healthy male patient referred to the ophthalmology department at King Hussein Cancer Centre (KHCC) with a slowly-enlarging, painless lump in the medial corner of the left eye of four months duration. On clinical examination, best corrected visual acuity was 20/20 in both eyes. A mass overlying the left caruncle was grossly visible. It was not attached to eyelids. Motility testing revealed a limitation of abduction in the left eye. This was associated with binocular diplopia on left gaze. Hertel exophthalmometry showed no proptosis. Slit-lamp examination of both the anterior and posterior segments was normal. Examination of the right eye was unremarkable. Intraocular pressure was normal in both eyes. Palpation of regional lymph nodes showed no palpable preauricular, submandibular or cervical nodes.

Orbital magnetic resonance imaging (MRI) with contrast was requested. It showed an intensely enhancing mass involving the anterior aspect of the left orbit medially. It measured 2.3 × 1.1 centimeters (cm) in the axial plane. The mass was invading the lacrimal sac and the upper part of the left nasolacrimal duct. It abutted the anterior eye globe, medial rectus, and inferior oblique muscles. The mass was inseparable from the overlying skin but was not arising from the skin (Fig. 1). Orbital computed tomography CT scan with contrast showed focal destruction of the lacrimal bone (Fig. 2).

Systemic staging including a whole body CT scan did not reveal any tumors elsewhere. A bone scan was done and it showed no convincing evidence of osteoblastic metastases. No tumorous lesions suggestive of primary apocrine adenocarcinoma were found elsewhere in the skin, particularly in axillae or around the nipples. Incisional biopsy for the left orbital mass was undertaken. The pathology examination revealed a moderately differentiated apocrine adenocarcinoma (Fig. 3).

On immunohistochemistry, tumor cells were positive for androgen receptor (AR), cytokeratin 7 (CK7), cytokeratin 19 (CK19), cytokeratin 18 (CK18), epithelial membrane antigen (EMA), polyclonal carcinoembryonic antigen (CEA), gross cystic disease fluid protein 15 (GCDFP-15), CD99 and MUC1 immunostains. They were

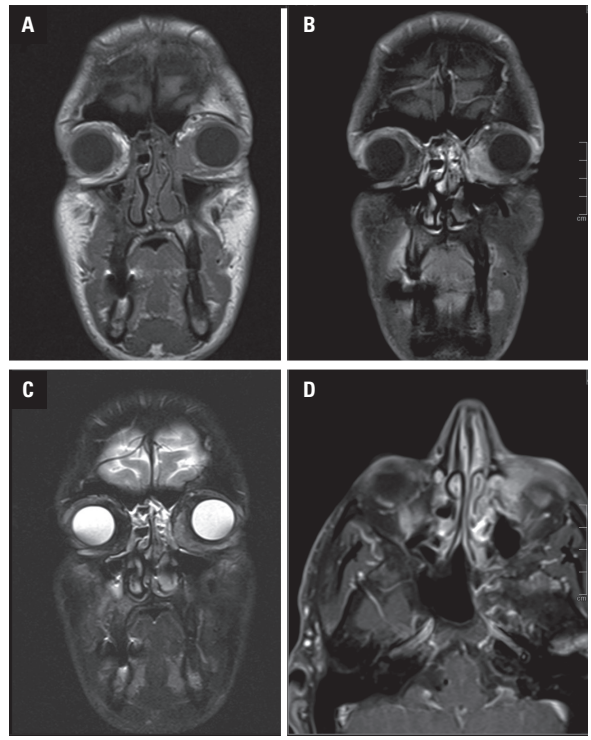

FIGURE 1. **A.** Orbit MRI coronal view T1; **B.** T1 post contrast fat sat; **C.** Short TI inversion recovery (STIR); **D.** Axial T1 post contrast fat sat. A lobulated mass at left medial canthus invading the lacrimal sac and the medial orbital rim. The mass is inseparable from anterior eye globe, medial rectus and inferior oblique muscles. The mass is invading the lacrimal sac and the upper part of the left nasolacrimal duct

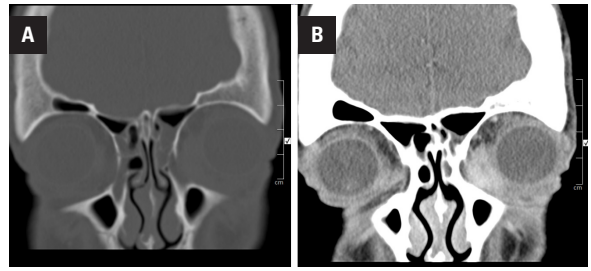

FIGURE 2. **A.** Orbit CT with contrast coronal views bone; **B.** Soft tissue (**B**) windows. A lobulated soft tissue mass (arrow) at left medial canthus, invading the left lacrimal sac (**A**) with focal destruction of the lacrimal bone (**B**)

negative for cytokeratin 20 (CK-20), monoclonal carcinoembryonic antigen (CEA), CDX-2, prostate-specific antigen (PSA), renal cell carcinoma (RCC), PAX8, vimentin, thyroid transcription factor-1 (TTF-1), hepatocyte specific antigen (Hep Par-1), Sal-like protein 4 (SALL4), MUC2, MUC5, thyroglobulin, CA19-9, S100 protein, CD34, surfactant, estrogen receptor (ER), and factor VIII-re-

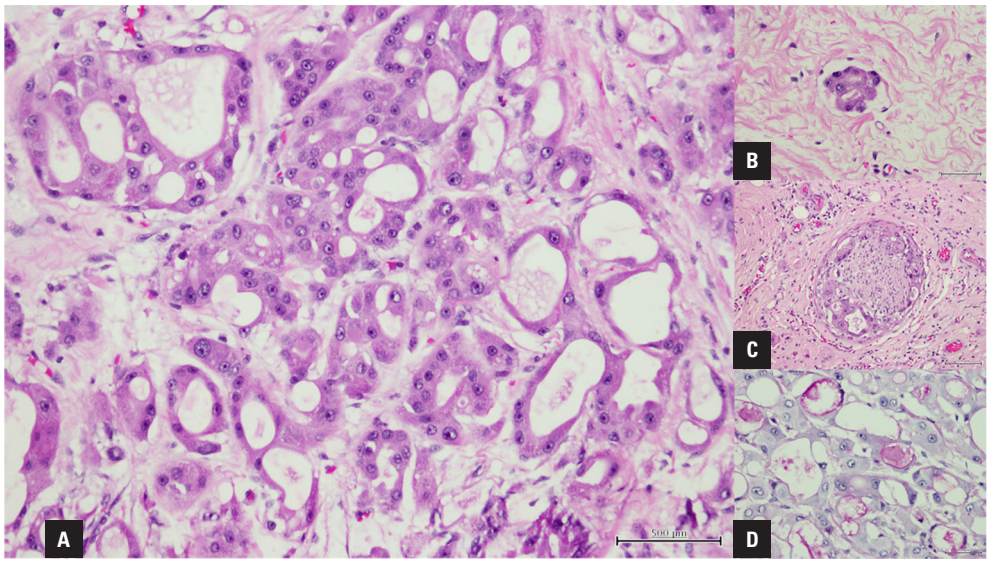

FIGURE 3. **A.** The tumor is composed of well-formed glands, with an irregular lumen and pseudopapillary structures lined by cells with abundant acidophilic granular cytoplasm, large vesicular nuclei with single prominent nucleoli. Secretion decapitation at the apical border of the tumor cells is seen focally. The lumens contain secretions. In addition, few cells show intracytoplasmic vacuoles containing mucin droplets, (H&E X20). **B.** Tumor lymphatic permeation (H&E X40). **C.** Perineural invasion (H&E X40). **D.** PAS/PASD special stain highlighted the mucin within the glands and in the cytoplasm of some of the cells (PAS/PASD stain, X40)

lated antigen. These results ruled out systemic metastasis to the orbit or other primary tumors in the breast or skin.

Based on all of the above findings, the final diagnosis was left orbital primary apocrine adenocarcinoma. Therefore, we proceeded with left eyelid-sparing orbital exenteration. Histopathology of the left orbit showed moderately differentiated apocrine adenocarcinoma with positive margins and lymphovascular invasion (pT3bN0). Given these high-risk pathological features, the patient was given adjuvant chemoradiotherapy; 66 Gray (Gy) in 33 fractions to the left socket and intravenous Cisplatin.

Follow up with serial orbit and neck MRI scans, showed no local recurrence or regional lymph nodes enlargement. The patient has been disease-free for the last 5 years with no signs of local or systemic recurrence of the tumor.

DISCUSSION

Apocrine adenocarcinoma (AC) is a rare, slow-growing skin carcinoma with apocrine differentiation arising from apocrine glands. AC occurs most commonly in the axilla followed by the anogenital region [4]. These tumors may arise rarely in the ocular region, where they are usually derived from Moll glands of the eyelid [5]. AC should be recognized and treated properly because of a high rate of both local recurrence and distant metastasis [6].

Kipkie and Haust described the following criteria for the histologic diagnosis of apocrine adenocarcinoma: Periodic acid-Schiff (PAS) positive, strongly eosinophilic cytoplasm, decapitation secretion, iron-positive intracellular pigment, and occurrence in areas where apocrine glands are normally located. The PAS-positive malignant apocrine epithelial cells often have diastase-resistant granules containing iron [7].

Immunohistochemistry has a role in diagnosing these tumors, particularly in poorly differentiated specimens. GCDFP-15 as a specific tissue marker of apocrine epithelium was found to stain apocrine-related neoplasms in 84% of the specimens [8].

Apocrine adenocarcinoma may represent a primary skin tumor, or be secondary to various internal adenocarcinomas that metastasize to the skin [9]. In a major review of 19 cases of AC of the eyelid published by Figueira et al., fifty-three percent of cases had tumors limited to the eyelids. Most patients (18 out of 19) presented with a painless blue-brown eyelid lump. Local orbital and periorbital invasion was described in 47% of the patients [10]. In a case reported by Hoang et al., apocrine adenocarcinoma in the lacrimal sac presented as a masquerading chronic dacryocystitis [11]. In another case reported

by Shintaku et al., the neoplasm was located in the subcutaneous tissue of the eyelid in the medial canthus and showed a subconjunctival spread in the lacrimal caruncle [12].

In this case report, the patient had no eyelid skin mass as is the usual case for these tumors. Instead, the tumor occurred primarily in the caruncle with local invasion to the lacrimal sac. Given the fact that there are no apocrine glands in the lacrimal sac region [13], we think that the tumor probably originated in the Moll's gland of the eyelid near the region of the medial canthus and subsequently exhibited a subconjunctival spread into the lacrimal caruncle instead of moving anteriorly toward the eyelid skin. This is similar to the case published by Shintaku et al. [12] The other possibility is that the tumor could have arisen from embryonic epithelial remnants within the orbit.

The possibility of a secondary tumor was excluded by the normal results of the systemic workup and immunohistochemistry. This is consistent with the final diagnosis of the presented case as a primary apocrine adenocarcinoma of the caruncle with lacrimal sac invasion.

Acknowledgments/Disclosure

None.

REFERENCES

1. Weedon D. Skin Pathology. Churchill Livingstone, Sydney 2002: 877888.
2. Gesase AP, Satoh Y. Apocrine secretory mechanism: recent findings and unresolved problems. Histol Histopathol. 2003; 18(2): 597–608, doi: 10.14670/HH-18.597, indexed in Pubmed: 12647810.
3. Stoeckelhuber M, Stoeckelhuber BM, Welsch U. Human glands of Moll: histochemical and ultrastructural characterization of the glands of Moll in the human eyelid. J Invest Dermatol. 2003; 121(1): 28–36, doi: 10.1046/j.1523-1747.2003.12328.x, indexed in Pubmed: 12839560.
4. Paties C, Taccagni GL, Papotti M, et al. Apocrine carcinoma of the skin. A clinicopathologic, immunocytochemical, and ultrastructural study. Cancer. 1993; 71(2): 375–381, doi: 10.1002/1097-0142(19930115)71:2<375::aid-cncr2820710218>3.0.co;2-4, indexed in Pubmed: 7678545.
5. Barker-Griffith AE, Streeten BW, Charles NC. Moll gland neoplasms of the eyelid: a clinical and pathological spectrum in 5 cases. Arch Ophthalmol. 2006; 124(11): 1645–1649, doi: 10.1001/archopht.124.11.1645, indexed in Pubmed: 17102015.
6. Warkel RL, Helwig EB. Apocrine gland adenoma and adenocarcinoma of the axilla. Arch Dermatol. 1978; 114(2): 198–203, indexed in Pubmed: 629545.
7. Kipkie GF, Haust MD. Carcinoma of apocrine glands; report of case. AMA Arch Derm. 1958; 78(4): 440–445, doi: 10.1001/archderm.1958.01560100014003, indexed in Pubmed: 13582185.
8. Mazoujian G, Pinkus GS, Davis S, et al. Immunohistochemistry of a gross cystic disease fluid protein (GCDFP-15) of the breast. A marker of apocrine epithelium and breast carcinomas with apocrine features. Am J Pathol. 1983; 110(2): 105–112, indexed in Pubmed: 6130702.
9. Hood CI, Font RL, Zimmerman LE. Metastatic mammary carcinoma in the eyelid with histiocytoid appearance. Cancer. 1973; 31(4): 793–800, doi: 10.1002/1097-0142(197304)31:4<793::aid-cncr2820310406>3.0.co;2-a, indexed in Pubmed: 4350331.
10. Figueira EC, Danks J, Watanabe A, et al. Apocrine adenocarcinoma of the eyelid: case series and review. Ophthalmic Plast Reconstr Surg. 2013; 29(6): 417–423, doi: 10.1097/IOP.0b013e3182a64fe5, indexed in Pubmed: 24217473.
11. Hoang A. Apocrine Adenocarcinoma of Lacrimal Sac Presenting as Chronic Dacryocystitis. J Ophthal Clin Res. 2017; 4(1): 1–2, doi: 10.24966/ocr-8887/100027.
12. Shintaku M, Tsuta K, Yoshida H, et al. Apocrine adenocarcinoma of the eyelid with aggressive biological behavior: report of a case. Pathol Int. 2002; 52(2): 169–173, doi: 10.1046/j.1440-1827.2002.01323.x, indexed in Pubmed: 11940224.
13. Kominami R, Yasutaka S, Taniguchi Y, et al. Anatomy and histology of the lacrimal fluid drainage system. Okajimas Folia Anat Jpn. 2000; 77(5): 155–160, doi: 10.2535/ofaj1936.77.5_155, indexed in Pubmed: 11218713.

CASE REPORT
DOI: 10.5603/OJ.2020.0009

Combined hamartoma of the retina and retinal pigment epithelium in a 6-year-old girl — a case report

Dorota Borowicz[1], Katarzyna Biela[1], Ewa Teresińska[1], Tomasz Bentkowski[1], Waldemar Kędziora[1], Katarzyna Nowomiejska[2], Robert Rejdak[2]

[1]Pope John Paul II Independent Public Provincial Hospital, Zamość, Poland
[2]Department of General Ophthalmology, Medical University of Lublin, Lublin, Poland

ABSTRACT

Combined hamartoma of the retina and retinal pigment epithelium (CHRRPE) is a rare, benign, usually one-sided disease that can cause significant painless vision loss. Combined hamartoma of the retina and retinal pigment epithelium is most commonly found in isolated forms, but reports are also available describing compounds with neurofibromatosis types 1 and 2. CHRRPE has increased retinal pigmentation, tortuous vessels, and the presence of epiretinal membranes.
In our article, we present a case report of a 6-year-old girl who was diagnosed with CHRRPE.

KEY WORDS: hamartoma of the retina and retinal pigment epithelium

Ophthalmol J 2020; Vol. 5, 42–45

INTRODUCTION

Combined hamartoma of the retina and retinal pigment epithelium (CHRRPE) is a rare, benign, usually one-sided tumor that can cause significant painless vision loss and strabismus. Combined hamartoma of the retina and retinal pigment epithelium is most commonly found in isolated forms, but reports are also available describing compounds with neurofibromatosis types 1 and 2. The classic clinical symptoms of CHRRPE increased retinal pigmentation, tortuous vessels, and the presence of epiretinal membranes. The diagnosis of CHRRPE is established by combining classic clinical signs with diagnostic features on ultrasonography (noncalcified mass) and pleated, thickened retina with disorganized of the photoreceptor on optical coherence tomography (OCT). This tumor can resemble choroidal melanoma or retinoblastoma.

We report a case of CHRRPE with poor visual acuity and strabismus.

CASE REPORT

A 6-year-old girl was admitted to the Ophthalmological Emergency Room due to slow, painless decrease of visual acuity in the left eye and left eye esotropia. The mother of the girl did not notice the beginning of the deterioration of vision and the incorrect position of the left eye. Parents denied the injury, the child's general health was normal, the girl was born without complications at delivery. On exam, the best-corrected visual acuity was 20/20 OD and 20/250 OS. The anterior seg-

CORRESPONDING AUTHOR:
Dorota Borowicz, Independent Public Provincial Hospital. Pope John Paul II Zamość; e-mail: dorotajjj2@wp.pl

Copyright © 2020 Via Medica, ISSN 2450–7873

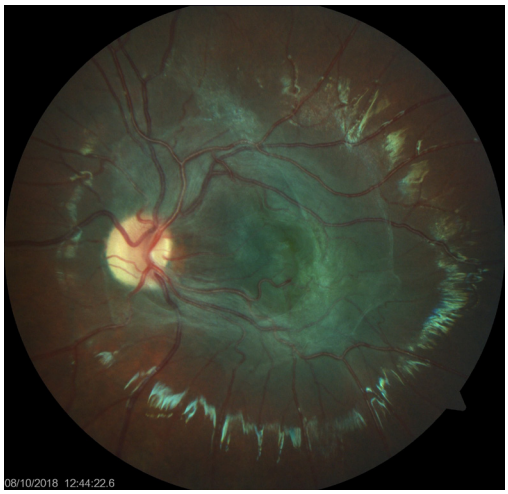

FIGURE 1. In the fundoscopy of the left eye, an area of increased pigmentation of the retinal pigment epithelium was observed, vascular arcades were distorted and shifted towards the macula. Within the lesion a shimmering gray epiretinal membrane was visible

ment was unremarkable OU. In the fundoscopy of the left eye, an area of increased pigmentation of the retinal pigment epithelium was observed, vascular arcades were distorted and shifted towards the macula. Within the lesion a shimmering gray epiretinal membrane was visible. The retinal periphery was normal (Fig. 1). There wasno deviation in the fundoscopy of the right eye. Optical coherent tomography of the left eye showed a significant thickening of the retina with hyporeflective shading of normal retinal layers and with the presence of the epiretinal membrane. The right eye OCT was normal (Fig. 2). Type B ultrasound showed a lobular lesion in the macula region with a calcified plaque on the lesion surface. The patient was referred to the Ophthalmological Oncology Clinic in Cracow where the diagnosis was confirmed based on a clinical examination and additional tests, i.e. OCT, ultrasound. The patient remains under constant ophthalmological control, her condition is stable.

DISCUSSION

Embryologically, the retinal pigment epithelium (RPE) develops from the outer layer of the optic cup — the ectoderm, and the neurosensory retina from the inner layer. In the inner layer, the cells adherent to the intraretinal space differentiates into photoreceptors and the cells of the next layer form Muller cells as well as bipolar cells and ganglion cell axons. Retinal and pigmented epithelial hamartoma is, therefore, a congenital lesion in which the developmental disorders of all separately developing retinal layers occurs [1, 2].

Histologically, CHRRPE consists of pigmented, glial and vascular cells in various propor-

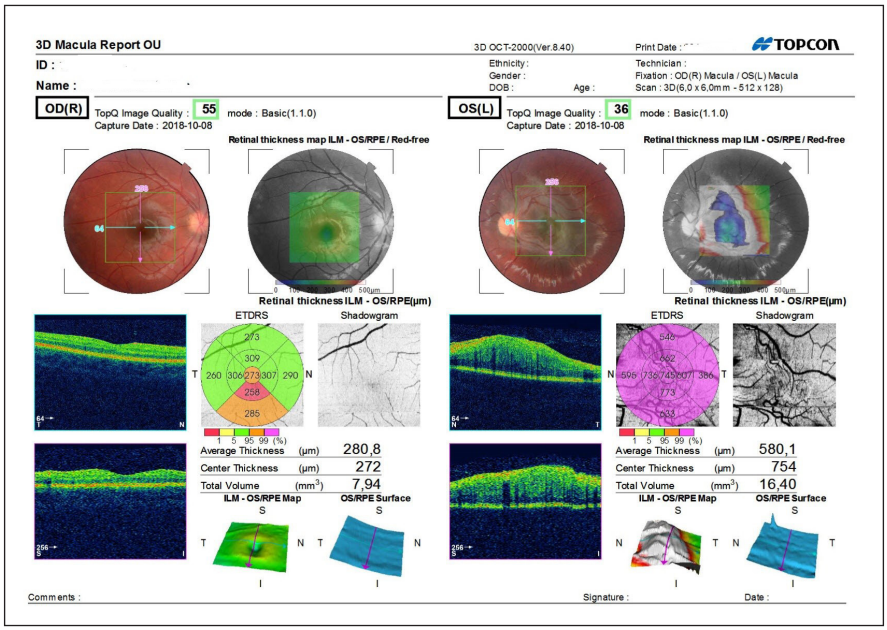

FIGURE 2. Optical coherent tomography (OCT) of the left eye showed a significant thickening of the retina with hyporeflective shading of normal retinal layers and with the presence of the epiretinal membrane. The right eye OCT was normal

tions. It is most often located near the optic nerve (76%), macula (17%) and in the peripheral retina (17%) [3].

Gass was the first to use the term retinal hamartoma and RPE in 1973. He was the first to describe clinical features of CHRRRPE as:

— slightly elevated dark gray lesion affecting the retina, RPE and surrounding vitreous;
— expansion towards the peripher;
— connecting to the neighboring RPE;
— surrounded by dense gray-white retina;
— showing internal surface compression;
— without peripheral RPE and choroidal atrophy;
— no retinal detachment, haemorrhage, vitreous effusion [4].

According to Gass, CHRRPE was initially divided into two subcategories depending on the presence or absence of involvement of the optic disc. [5] These two types of CHRRPE have slightly different histological features. CHRRPE, which does not include the optic disc, shows no RPE cell migration, less RPE overgrowth, less retinal capillary proliferation, and less retinal disorganization.

Based on current imaging studies, including optical coherent tomography (OCT), common features of CHRRPE lesions include tumor involvement of the internal and intermediate layers of the retina (the inner layer of the retina to the outer plexus layer) with varying amounts of thickened gray-white retinal tissues and epiretinal membranes, the displacement of the surrounding retina and blood vessels, no choroid involvement [6, 7].

In 2018 Dedania et al. proposed a new clinical classification system for the assessment and follow-up of patients with CHRRPE. The use of a uniform classification system is intended to facilitate the assessment and comparison of the results of various tests, to determine the frequency of follow-up visits and/or to take therapeutic measures. Changes are classified based on location, fundus features and OCT.

Location of the lesion: zone 1 — macula/per-macular zone, zone 2 — medium retinal periphery, zone 3 — distal retinal periphery.

Retinal assessment during fundoscopy: stage 1 — no retinal vitreous traction, stage 2 — the presence of retinal traction and/or dissection, stage 3 — retinal detachment.

Retinal morphology in OCT: A — epiretinal membrane, B — changes in the deeper layers of the retina, and C — changes on the entire retinal thickness and in RPE.

In patients under 12 years, a full ophthalmologic and morphological assessment is recommended at least every 6 months, with more frequent observation (2–4 months) in patients with macular/perimacular lesions (zone 1) or with retinal traction, dissection or detachment retina (stages 2 and 3). Surgical intervention is recommended in patients with deterioration or loss of vision secondary to retinal vitreous traction or retinal detachment. Routine assessment in patients with lesions in zone 3 is less common, every 6 or every 12 months, depending on the stage of the change [8].

There are no known risk factors. The Caucasian breed seems to dominate. As for gender, in the study by Schachat et al. men and women were equally affected (31 men and 29 women) [9]. However, in the article Shields et al. the majority of patients were men (68%).

Shields et al. report the most common presenting signs were decreased vision (40%) and strabismus (28%) in 79 eyes with CHRRPE in a retrospective analysis. The mean vision (logMAR) for the macular tumors' location (51%) was 1.2, compared with 0.61 in patients with extramacular tumors location (49%). At 4 years follow-up, visual acuity loss of 3 Snellen lines or more appeared in 60% of patients with macular CHRRPE, compared with 13% of peripheral CHRRPE [10]. The visual acuity loss and strabismus are the most frequent presenting signs as in our patient.

CHRRPE are usually unilateral changes. Bilateral lesions are more commonly associated with phacomatoses, including NF type 1, NF type 2, tuberous sclerosis and basal cell nevus syndrome [11, 12]. Although CHRRPE is more common in patients with NF type 2, in practice these changes are more commonly seen in patients with NF type 1 due to the higher incidence of NF1. [11] It is recommended to perform genetic tests in patients diagnosed with CHRRPE, especially in patients with binocular presence of characteristic lesions. In hamartomic differentiation, retinoblastoma, melanoma, RPE adenoma, RPE adenocarcinoma should be considered.

CONCLUSIONS

Classical clinical symptoms, as a painless loss of vision, combined with fundoscopy and diagnostic imaging using optical coherence tomography, allow diagnosis of the disease. The highest risk of blindness or loss of vision are in the presence of CHR-

RPE with macular/perimacular region involvement with simultaneous retinal vitreous traction, retinal detachment or dissection.

Assessment of anatomy and morphology of the lesion allows it to be properly classified. This facilitates observation of the patient, determining the time interval between subsequent controls and the inclusion of early therapeutic intervention that can protect against vision loss.

REFERENCES

1. Shields CL, Manalac J, Das C, et al. Review of spectral domain-enhanced depth imaging optical coherence tomography of tumors of the retina and retinal pigment epithelium in children and adults. Indian J Ophthalmol. 2015; 63(2): 128–132, doi: 10.4103/0301-4738.154384, indexed in Pubmed: 25827543.
2. Chawla R, Kumar V, Tripathy K, et al. Combined Hamartoma of the Retina and Retinal Pigment Epithelium: An Optical Coherence Tomography-Based Reappraisal. Am J Ophthalmol. 2017; 181: 88–96, doi: 10.1016/j.ajo.2017.06.020, indexed in Pubmed: 28669779.
3. Nowomiejska K, Zarnowski T, Rejdak R, et al. Combined Hamartoma of the Optic Disc and Retinal Pigment Epithelium — 3 Years of the Follow-Up with Semi-Automated Kinetic Perimetry. Open J Ophthalmol. 2012; 02(04): 116–118, doi: 10.4236/ojoph.2012.24025.
4. Gass JD. An Unusual Hamartoma of the Pigment Epithelium and Retina Simulating Choroidal Melanoma and Retinoblastoma, " Transactions of the American Ophthalmological Society. Transactions Am Ophthalmol Soc. 1973; 71: 175–183.
5. Agarwal A. Gass' atlas of macular diseases. Vol. 1. Elsevier, St. Louis 2012. . http://site.ebrary.com/id/10521767EW. (2015 Feb 8).
6. Arepalli S, Pellegrini M, Ferenczy SR, et al. Combined hamartoma of the retina and retinal pigment epithelium: findings on enhanced depth imaging optical coherence tomography in eight eyes. Retina. 2014; 34(11): 2202–2207, doi: 10.1097/IAE.0000000000000220, indexed in Pubmed: 25102194.
7. Shields CL, Thangappan A, Hartzell K, et al. Combined hamartoma of the retina and retinal pigment epithelium in 77 consecutive patients visual outcome based on macular versus extramacular tumor location. Ophthalmology. 2008; 115(12): 2246–2252.e3, doi: 10.1016/j.ophtha.2008.08.008, indexed in Pubmed: 18995912.
8. Dedania VS, Ozgonul C, Zacks DN, et al. ovel classification system for combined hamartoma of the retina and retinal pigment epithelium. Retina. 2018; 38(1): 12–19, doi: 10.1097/IAE.0000000000001499, indexed in Pubmed: 28098730.
9. Schachat AP, Shields JA, Fine SL, et al. Combined hamartomas of the retina and retinal pigment epithelium. Ophthalmology. 1984; 91(12): 1609–1615, doi: 10.1016/s0161-6420(84)34094-5, indexed in Pubmed: 6521994.
10. Shields CL, Thangappan A, Hartzell K, et al. Combined hamartoma of the retina and retinal pigment epithelium in 77 consecutive patients visual outcome based on macular versus extramacular tumor location. Ophthalmology. 2008; 115(12): 2246–2252.e3, doi: 10.1016/j.ophtha.2008.08.008, indexed in Pubmed: 18995912.
11. Mason JO, Kleiner R. Combined hamartoma of the retina and retinal pigment epithelium associated with epiretinal membrane and macular hole. Retina. 1997; 17(2): 160–162, indexed in Pubmed: 9143046.
12. Kaye LD, Rothner AD, Beauchamp GR, et al. Ocular findings associated with neurofibromatosis type II. Ophthalmology. 1992; 99(9): 1424–1429, doi: 10.1016/s0161-6420(92)31789-0, indexed in Pubmed: 1407974.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0013

Comparison between traditional and electronic ETDRS charts

Claudio Campa

Ophthalmic Surgery Unit, University Hospital of Ferarra, Cona, Ferrara, Italy

ABSTRACT

BACKGROUND: The aim of the study was to compare the visual acuity (VA) score obtained in both normal subjects and patients with different eye diseases by using TOPCON CP-22 electronic ETDRS charts (i.e. E-ETDRS) and standard ETDRS charts (S-ETDRS).

MATERIAL AND METHODS: The primary outcome of this observational prospective study was the difference in median VA score (in letters) recorded in 60 patients by using both E-ETDRS and S-ETDRS. There were 60 subjects enrolled in the study: 20 normal, 20 with diabetic retinopathy and 20 with age-related macular degeneration.

RESULTS: Median number of letters read was 72.5 S-ETDR and 77 for E-ETDR ($p < 0.01$). A subgroup analysis disclosed that the difference in VA score between the 2 devices was more pronounced ($p < 0.01$) when considering healthy subjects compared to patients affected by diabetic retinopathy ($p = 0.02$) or age-related macular degeneration ($p = 0.04$).

CONCLUSIONS: Small but significant discrepancies between the 2 devices have been detected, especially when recording high VA values.

KEY WORDS: visual acuity measurements; electronic ETDRS charts; traditional ETDRS charts; age-related macular degeneration; diabetic retinopathy

Ophthalmol J 2020; Vol. 5, 46–50

INTRODUCTION

Since their first introduction more than 30 years ago [1], ETDRS charts have represented always the gold standard for visual acuity measurement. These charts are based on the Bailey-Lovie principles: letters of approximately equal legibility, equal letters per line and a regular progression in letter size between lines. These features assure many advantages compared to the most popular Snellen charts: visual acuity (VA) measurement is always accurate regardless of initial vision; test-retest variability (TRV) is low, thus increasing the ability to detect subtle change in vision; acuity score can be easily used in statistical analysis. In the era of anti-VEGF therapy for many retinal diseases, where improvement of visual acuity is common, the ability to measure even small changes in vision has become an important tool to determine the response to treatment. This explains why the ETDRS charts are being used more and more often not only in clinical trials but also in routine clinical practice.

The original ETDRS charts are printed on opaque, washable polystyrene and mounted on an illuminator cabinet which uses fluorescent tubes which should be replaced annually and "burned in" (i.e., left on continuously for 96 hours) before using the ETDRS light box (Fig. 1A).

Recently many companies have launched into the market LCD screens with both Snellen and ETDRS charts. These devices are very convenient

CORRESPONDING AUTHOR:
Claudio Campa, MD, PhD, Unità operativa di Oculistica, Azienda Ospedaliero Universitaria di Ferrara, Via A. Moro 8, 44124 Cona, Ferrara, Italy, tel: (+39) 05 32 206 338, fax: (+39) 053 2 247365; e-mail: claudiocampa@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

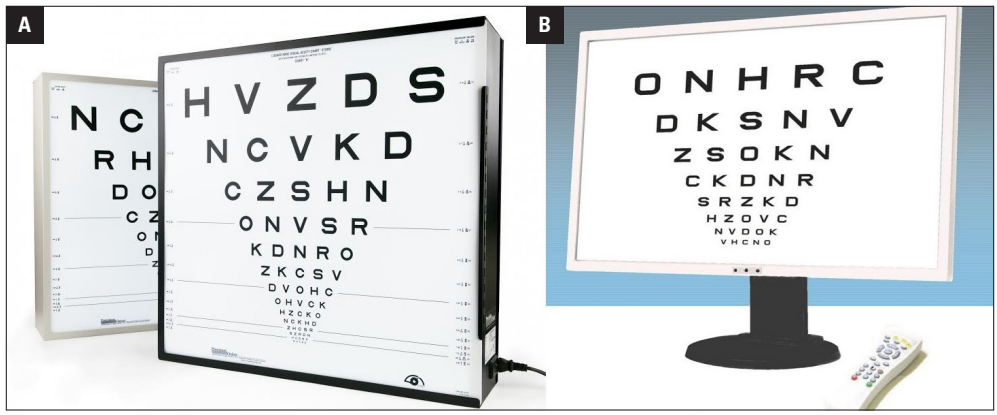

FIGURE 1. **A.** Original ETDRS chart (S-ETDRS). **B.** Electronic Topcon CP-22 (E-ETDRS)

because they do not require any maintenance, allow a quickly switch form one test to another and can be used at different distances.

Unfortunately most of them have not been validated in clinical studies, so it is difficult to assume that visual acuity recorded on LCD screen ETDRS charts is equivalent to that performed with standard ETDRS charts.

Topcon CP-22 is (Topcon, Japan) is a led LCD system which incorporates all important visual acuity and colour vision tests. It has a 22" wide screen with high resolution, high contrast and a high brightness (Fig. 1B).

Aim of this study was to compare the VA score obtained in both normal subjects and patients with different eye diseases by using CP-22 (i.e. electronic ETDRS charts E-ETDRS) and standard ETDRS charts (S-ETDRS).

MATERIAL AND METHODS

This was an observational single centre study. The primary outcome of the study was the change in median visual acuity score recorded between E-ETDRS and S-ETDRS. We decided to use the median for the primary outcome because it is better suited for skewed distributions to derive at central tendency since it is much more robust and sensible. For sample size calculation we considered significant a difference of 6 ETDRS letters, since it has been demonstrated that the test-retest reliability falls within 5 letters for the majority of patients for both methods (89% and 87% for E- and S-ETDRS, respectively) [2]. With an estimated standard deviation of the difference of 0.05 [3], a value for alpha of 0.01 and a power of the test of 0.9, the required number of patients when using a two-tailed t-test was 5.

Patients enrolled in the study were divided into 3 groups of 20 subjects each: group A, B and C. Only one eye (right) was investigated. The research was performed in compliance with the guidelines of the Declaration of Helsinki. An informed consent was obtained from the subjects after explanation of the nature and possible consequences of the study.

Inclusion criteria for all groups were age > 18 years and visual acuity better than 2.00 logMAR in the study eye. Additional inclusion criteria were diabetic retinopathy (any grade, with or without maculopathy) for group B and age related macular degeneration (dry or exudative) for group C, respectively. Exclusion criterion for all groups was the inability to sign an informed consent. Additional exclusion criteria were: for group A any ocular disease except refractive errors; for group B ocular diseases different from diabetic retinopathy; for group C ocular diseases different from age related macular degeneration. Each subject enrolled in the study underwent two visits performed by the same examiner (C.C.) in two different days, 7–10 days a part. During the first visit the study eye was refracted on ETDRS chart R (No. 2110, Precision Vision, La Salle, Illinois). Once obtained the optimal refractive correction, best corrected visual acuity was measured on E-ETDRS and S-ETDRS, in random order chosen by flipping a coin (simple randomization).

During examination room illumination was kept constant and before starting each test luminance in the centre of VA chart was checked in order to avoid values > 161.4 lux (with retroillumination/monitor

off). For S-ETDRS we used chart 1 (No. 2111, Precision Vision, La Salle, Illinois) at 4 meters. For E-ETDRS the monitor of CP-22 was placed at 2 meters, according to manufacture instructions. When the subject could not see at least 20 letters at these distances then both charts were placed at 1 meter and +0.50 sphere was added to the refraction.

With both charts we used the same VA line presentation testing procedure, which has been widely described in the TAP study visual acuity protocol [4].

At the second visit the VA of study eye was re-tested on both chart (chosen with a random order) using the refraction determined at the previous visit. Patients experiencing any visual symptoms in the interval between the 2 visits had to exit the study.

Origin Pro 8 (Origin Lb Corporation) was used for all the statistical analyses. After analysing data distribution with Shapiro-Wilk test, either Wilcoxon or paired t-test was used for comparisons.

RESULTS

Sixty subjects completed the study. Demographic and baseline characteristics are shown in Table 1. When considering the whole study population the median number of letters read at the first visit on S-ETDRS and E-ETDR was 77 and 72.5, respectively ($p < 0.01$). Analysing in details the VA score in each group (Fig. 2), mean number of letters read with S-ETDRS and E-ETDRS was 90.2 and 83.2 in group A ($p < 0.01$), 68.7 and 66.4 ($p = 0.02$) in group B, and 66.5 letters and 62 on E-ETDRS ($p = 0.04$) in group C, respectively.

With the second visit we evaluated the test-retest reliability of both charts. As shown in Figure 3 there was a significant difference ($p < 0.05$) between the two devices, with a mean difference of 0.75 letters for E-ETDRS and 2.81 for S-ETDRS.

DISCUSSION

With this study we have demonstrated that small but significant differences between S-ETDR and E-ETDRS (namely TOPCON CP-24) do exist. When considering the whole group of subjects investigated, in fact we found a mean discrepancy of 5.5 letters between the two devices. This disparity was even more pronounced when taking into considerations the group with the highest VA (i.e. healthy subjects), with a mean difference of 7 letters. These differences are not only statistically but also clinically significant: indeed a change of 5 or

Table 1. Demographic and baseline characteristics of study population

	Group A	Group B	Group C
Mean age (± SD) (years)	41 (± 8.1)	52.5 (± 4.7)	69.3 (± 5.2)
Sex (M/F)	12/8	12/8	10/10
Mean refractive errors (± SD) Spherical equivalent	–1.12 (±0.3)	–1.07 (± 0.5)	–0.73 (± 0.2)

SD — standard deviation

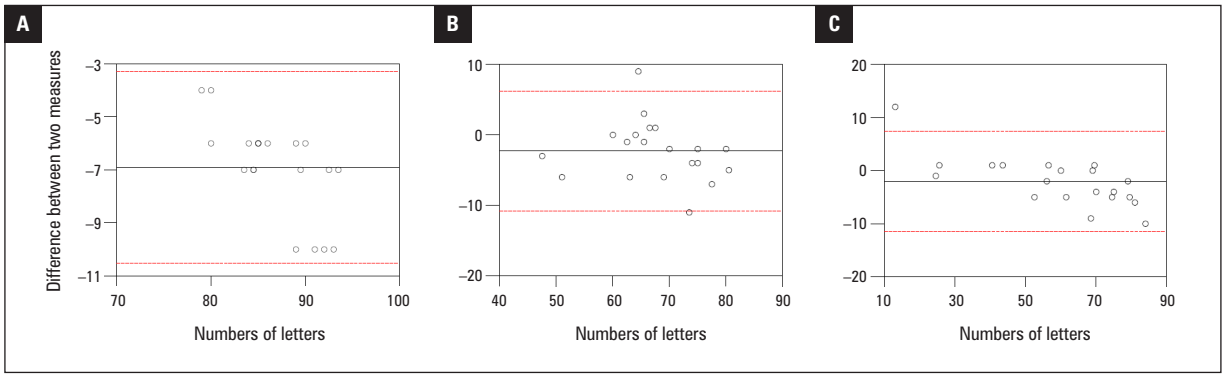

FIGURE 2. Bland-Altmann plots of visual acuity (VA) measurements expressed in letters for group A (**A**), B (**B**) and C (**C**). In the scatter plot the Y axis shows the difference between the two paired measurements and the X axis represents the average of these measures. Solid line shows the mean difference, doted lines represent the confidence interval (from –1.96s to +1.96s)

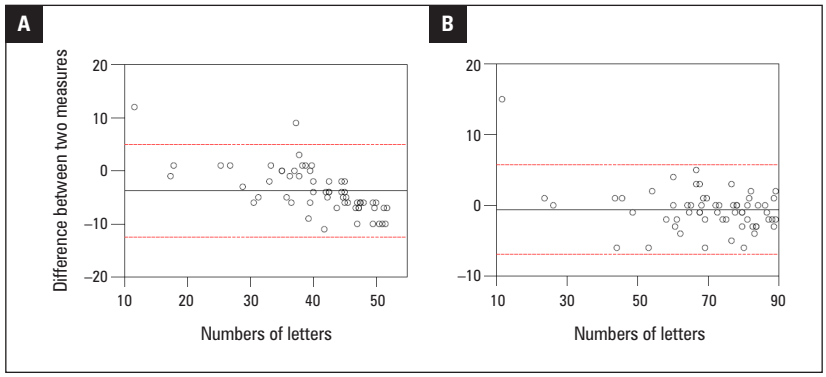

FIGURE 3. Bland-Altmann plots of test-retest reliability expressed in letters for S-ETDRS (**A**) and E-ETDRS (**B**). The plot illustrates the agreement between time 1 and time 2 and identifies possible outliers. Reference lines shows mean difference between time 1 and time 2 (solid line), and 95% limits of agreement for the mean difference (doted lines)

more letters is often used as marker of response to anti-VEGF treatment.

It is difficult to explain this difference, but the most obvious reason may be the limited resolution of the screen. Differences in technical specifications such as calibration of sizes, spacing, luminance and contrast levels between the two devices deserve further investigation.

The only other study [2] we found in literature comparing traditional and electronic ETDRS charts showed similar results, with scores of S-ETDRS and of a computerized vision tester called EVA (electronic visual acuity) differing by ≤ 0.1 logMAR and by ≤ 0.2 logMAR on 74% and 94% of patients tested, respectively. In that study the difference was at least in part ascribed to the effect of using single-letter presentations with the E-ETDRS and line presentations with the S-ETDRS [2].

In our study both ETDRS had a line presentation procedure; however, a relevant difference between the 2 charts was that S-ETDRS were used at 4 meters while E-ETDRS at 2 meters (as per indication of the company). This difference could be a reason for the discrepancy in VA we recorded. For instance, Kaiser [5] has demonstrated, by using S-ETDRS charts at 2 and 4 meters, a statistically significant difference in the VA measurements at the two distances. Moreover other authors [6] have found an improvement in visual acuity as observation distance is reduced from six meters to approximately three meters, followed by a decrease in acuity as the distance is further reduced to 0.75 meter.

Both S-ETDRS and E-ETDRS in our study showed high test-retest reliability across the range of VA, with a slight lower reliability for S-ETDRS. Several other studies have demonstrated analogues results with ETDRS testing and similar optotype testing with letter scoring [1, 7–9].

CONCLUSIONS

In summary, the E-ETDRS provided by TOPCON CP-24 has high test-retest reliability and good concordance with S-ETDRS testing, at least for medium and low VA. However, since small discrepancies between the 2 devices have been detected, especially at highest VA, caution must be taken if the 2 devices are used interchangeably during the follow-up of patients undergone a particular ocular treatment. Future work is indicated to determine whether the E-ETDRS testing algorithm can be modified to further reduce the above mentioned letter discrepancy with S-ETDRS.

Conflict of interest and funding

None.

REFERENCES

1. Ferris F, Kassoff A, Bresnick G, et al. New Visual Acuity Charts for Clinical Research. Am J Ophthalmol. 1982; 94(1): 91–96, doi: 10.1016/0002-9394(82)90197-0.
2. Beck RW, Moke PS, Turpin AH, et al. A computerized method of visual acuity testing: adaptation of the early treatment of diabetic retinopathy study testing protocol. Am J Ophthalmol. 2003; 135(2): 194–205, doi: 10.1016/s0002-9394(02)01825-1, indexed in Pubmed: 12566024.
3. Rosser DA, Murdoch IE, Cousens SN. The effect of optical defocus on the test-retest variability of visual acuity measurements. Invest Ophthalmol Vis Sci. 2004; 45(4): 1076–1079, doi: 10.1167/iovs.03-1320, indexed in Pubmed: 15037571.
4. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: one-year results of 2 randomized clinical trials — TAP report. Treatment of

age-related macular degeneration with photodynamic therapy (TAP) Study Group. Arch Ophthalmol. 1999; 117(10): 1329, doi: 10.1001/archopht.117.10.1329, indexed in Pubmed: 10532441.
5. Kaiser PK. Prospective evaluation of visual acuity assessment: a comparison of snellen versus ETDRS charts in clinical practice (An AOS Thesis). Trans Am Ophthalmol Soc. 2009; 107: 311–324, indexed in Pubmed: 20126505.
6. Geddes M, McLean J, McMonnies C, et al. The variation of visual acuity with observation distance. Austral J Optometry. 1966; 49(6): 164–9, doi: 10.1111/j.1444-0938.1966.tb04527.x.
7. Lovie-Kitchin JE. Validity and reliability of visual acuity measurements. Ophthalmic Physiol Opt. 1988; 8(4): 363–370, doi: 10.1111/j.1475-1313.1988.tb01170.x, indexed in Pubmed: 3253626.
8. Arditi A, Cagenello R. On the statistical reliability of letter-chart visual acuity measurements. Invest Ophthalmol Vis Sci. 1993; 34(1): 120–129, indexed in Pubmed: 8425819.
9. Blackhurst DW, Maguire MG. Reproducibility of refraction and visual acuity measurement under a standard protocol. The Macular Photocoagulation Study Group. Retina. 1989; 9(3): 163–169, indexed in Pubmed: 2480626.

CASE REPORT
DOI: 10.5603/OJ.2020.0008

Intraorbital wooden foreign body — a case report

Piotr Kanclerz[1], Agnieszka Chrząszcz-Włodarczyk[2], Andrzej Grzybowski[3, 4]

[1]Hygeia Clinic, Department of Ophthalmology, Gdansk, Poland
[2]Department of Ophthalmology, Medical University of Gdansk, Poland
[3]Institute for Research in Ophthalmology, Foundation for Ophthalmology Development, Poznan, Poland
[4]Department of Ophthalmology, Medical University of Warmia i Mazury, Olsztyn, Poland

ABSTRACT

BACKGROUND: Wood as an intraorbital foreign body (IOFB) is infrequent, and as it is organic matter patients represent an increased risk of infection. The aim of this study is to report the complexity of treatment of patient with a wooden IOFB. We describe a case of a 67-year-old male with a wooden IOFB.

CASE REPORT: On referral, the patient presented with exophthalmos, pain, blurry vision and discharge from his left eye was admitted to the Department of Ophthalmology, Medical University of Gdańsk. The previous evening, he fell with his face down. Computed tomography revealed a low-density IOFB of approximately -980 Hounsfield Units, sized 62 × 8 mm, in the area of left orbit, ethmoid and sphenoid sinus. Subsequently, the IOFB was removed under general anaesthesia. After three days of empirical antibiotic therapy, the patient was discharged with a switch to oral antibiotics. Shortly after the conversion to oral therapy, he developed an orbital inflammatory syndrome and was readmitted to the hospital. His condition improved after readministration of parenteral antibiotics.

CONCLUSION: This case demonstrates that wooden IOFBs should be treated with caution. Parenteral antibiotic delivery leads to higher serum levels than with oral intake, and in this case, was essential in preventing infection after IOFB removal.

KEY WORDS: foreign body; wood; orbit; computed tomography

Ophthalmol J 2020; Vol. 5, 51–54

INTRODUCTION

One out of every six cases of penetrating orbital trauma is associated with an intraorbital foreign body (IOFB) [1]. Intraorbital foreign bodies might present a wide range of imaging manifestation, and the entry wound may often be small and self-sealing, resulting in diagnostic difficulties. The aim of this study is to report the complexity of treatment of a patient with a wooden IOFB.

CASE REPORT

A 67-year-old Caucasian male presented to the Department of Ophthalmology of the Medical University of Gdańsk with decreased to hand movements visual acuity in the left eye, along with diplopia, exophthalmos and severe limitation of eye movements in all directions (Fig. 1A). The previous evening, he fell with his face down. He did not report any general diseases or prior antibiotic

CORRESPONDING AUTHOR:
Piotr Kanclerz, Hygeia Clinic, ul. Jaśkowa Dolina 57, 80–286 Gdańsk, Poland, tel: (+48) 661 61 04 61; e-mail: p.kanclerz@gumed.edu.pl

Copyright © 2020 Via Medica, ISSN 2450–7873

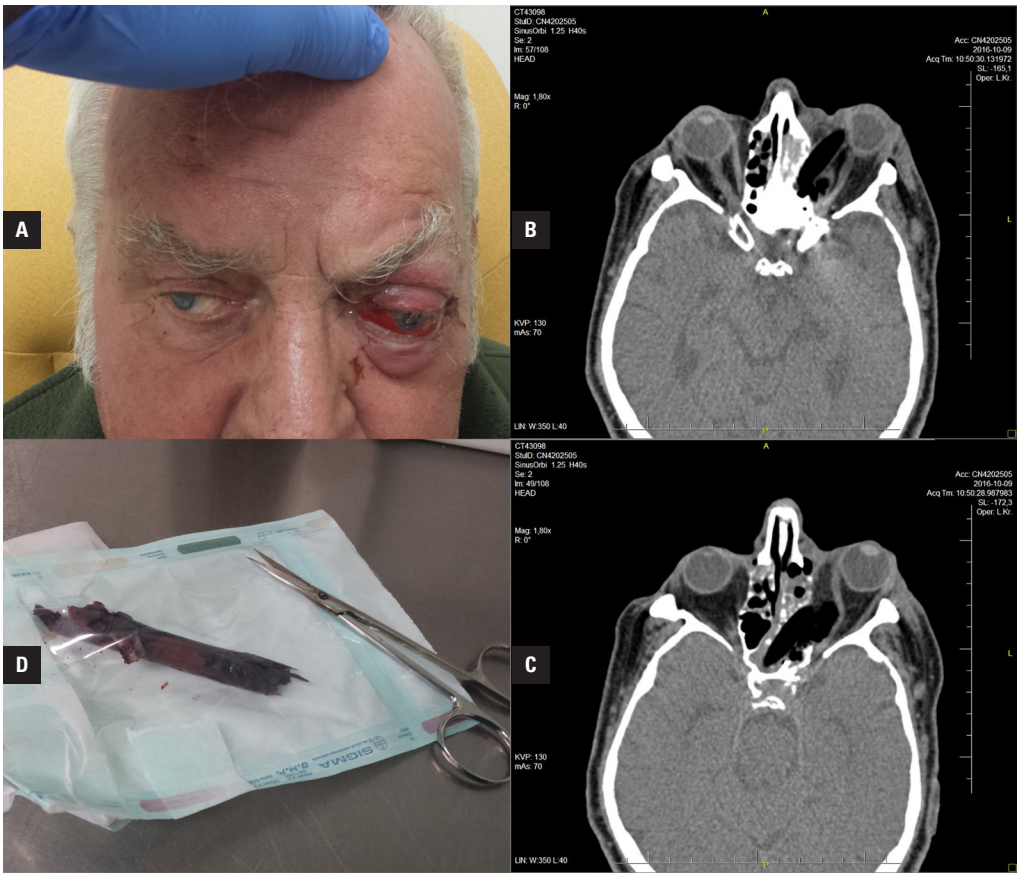

FIGURE 1. A. The patient preoperatively. He was asked to look right; a significant limitation in eye movements, pain, severe exophthalmos and discharge from the left eye is noted. **B–C**. Computed tomography revealed a low-density foreign body of approximately –980 Hounsfield Units (HU), sized 62 × 8 mm in the area of left orbit, ethmoid and sphenoid sinus. **D.** A macroscopic image of the foreign body just after removal. For size comparison, iris scissors are presented

use. Computed tomography revealed a low-density foreign body of approximately –980 Hounsfield Units (HU), sized 62 x 8 mm in the area of left orbit, ethmoid and sphenoid sinus (Fig. 1B, C). The intraocular pressure of the left eye was palpably increased, the pupil was large and poorly reactive, no entry wound was found. Systemic therapy with intravenous cefuroxime 750 mg three times daily (TID), metronidazole 500 mg TID and topical tobramycin 0.3% and dexamethasone 0.1% was prescribed. The patient received enoxaparin 80 mg/0.8 mL subcutaneously and a tetanus immune globulin 250 U IM. As magnetic resonance imaging (MRI) was not available in a reasonable timespan, a surgical intervention in general anesthesia was carried out.

The surgery was performed by the ENT specialist; after anesthetization, a 1.5 cm-long wound was noted in the medial angle of the upper left eyelid with the edge of the IOFB visible in it. An anterior orbitotomy was performed in the extension of laceration, and after scrupulous tissue dissection around the IOFB the wooden piece was removed (Fig. 1D). Swabs were taken and several additional splinters were removed with copious irrigation of the cavity using a 3% hydrogen peroxide solution [2]. The eye was reviewed showing no signs of discontinuity of the sclera. Intraoperative tonometry revealed a pressure of 3 mm Hg in the left eye, with no signs of scleral discontinuity.

In the postoperative MRI, the medial rectus muscle (MRM) was thickened with the suspicion of a small 10-mm splinter within the muscle. Nevertheless, the local condition improved. Two days after surgery the patient demonstrated the visual acuity in his left eye of 0.1, minor exophthalmos and eyelid edema, and was discharged on empirical antibiotic therapy. A sequential switch to cefuroxime acetyl 500 mg twice daily and metronidazole 250 mg TID orally was recommended. Topical tobramycin 0.3% and dexamethasone 0.1% four times daily was to be continued.

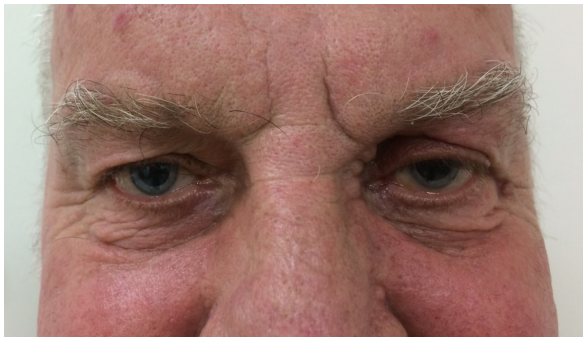

FIGURE 2. One month after surgery the patient presented in his left eye minimal exophthalmos and only partial limitation of eye movements medially

The next day he was readmitted to the emergency unit because of increasing exophthalmos and pain in his left eye and orbital region. In contrast-enhanced MRI MRM remained thickened with no signs of a splinter. Cavernous sinus thrombosis was excluded. The results of intraoperative swabs revealed *Escherichia coli, Lecleria adecarboxylata, Bacillus cereus* and coagulase-negative *staphylococcus* (CNS). All of the microbes were found to be susceptible to cefuroxime; however, the susceptibility of *B. cereus* was not assessed. As no anaerobic bacteria were found, susceptibility to metronidazole was not analyzed. Intravenous treatment including dexamethasone 12 mg once daily was administered, while cefuroxime with metronidazole was reintroduced. Additionally, intramuscular galantamine hydrobromide 2.5 mg and combined 100 mg thiamine, 100 mg pyridoxine and 1 mg cyanocobalamin were recommended in order to relieve the pain and enhance nerve regeneration. The patient improved over the following seven days.

One month after surgery he presented minimal exophthalmos and partial limitation of eye movement medially (Fig. 2). Since it was attributed to the medial rectus muscle injury no additional treatment was recommended.

DISCUSSION

The current literature reports that the diagnosis and management of IOFBs might be contentious. Particularly wooden IOFBs can be occult due to late presentation and the lack of external signs of injury [1]. In the study by Shelsta et al., the time from injury to the presentation was highly variable, with a mean of 62 days from the injury to the presentation (range 1–17 months; median 3 days and only 43% of cases presented within 24 hours of injury) [1]. In other studies, the time from injury to admission was up to 22 months [1, 3–5]. One study found that the time from injury to the presentation was negatively correlated with the size of the wooden IOFB [4]. As wood presents a wide range of CT densities, the imaging findings in these cases are diverse [3]; in a single study, an orbital foreign body after the CT scan was suggested only in six out of eleven cases [6]. The CT densities vary between –984 HU for dry porous wood, –70 HU for wet wood, and up to +156 HU for tree bark encapsulated with soft tissue [7–9]. Performing MRI scans is beneficial when the wood is surrounded by fat or extracellular fluid, although MRI was not proven to be more useful than CT in wooden IOFBs [10]. In the study by Li et al. the IOFB was not found during surgery in three out of 11 cases, while in two cases fistula tracts have developed due to late removal [6]. Due to its fragile structure, complete removal of a wooden foreign body might be impossible, and the remaining splinters are a potential source of infection. Complications include abscess formation, local infection, development of a fistula or granuloma, and these problems might develop several months or years after successful IOFB removal [1, 4, 11].

Infections associated with organic foreign bodies occur in up to 64% of IOFBs, even if antibiotics are applied [1]. The porous structure of wood and its characteristics of organic matter support bacterial ingrowth. Pathogens commonly cultured such foreign bodies include *Streptococcus* sp., *E. coli*, CNS and anaerobes [1]. In our case, four types of bacteria were isolated from the wound. Two ubiquitous species, which are susceptible to several antimicrobials including cefuroxime were the CNS and *Leclercia adecarboxylata.* The former is a gram-negative bacteria, a member of the family *Enterobacteriaceae*, and has a role in infections mainly in immunocompetent patients [12]. The third species, *B. cereus* is a soil bacterium and can be found on plants; it could an incidental finding. On the other hand, *B. cereus* manifest resistance to β-lactam antibiotics [13]; in our case, it was not possible to determine its susceptibility. Finally, *E. coli* is commonly resistant against routinely used antibiotics; one of the most important determinant for resistance is the recent antibiotic use [14]. In this subject, the strain was susceptible to cefuroxime. Additional therapy with ciprofloxacin to which *B. cereus* is highly susceptible could have been considered [13].

In general, intravenous administration of antibiotics leads to higher serum levels than with oral intake [15]. However, conversion to oral therapy has many advantages, including less healthcare costs, fewer complications associated with parenteral therapy and earlier hospital discharge [16]. The poor outcome of oral therapy in the described case could be presumably attributed to insufficient therapeutic levels of oral treatment. This report demonstrates that wooden IOFBs should be treated with caution; in this case, parenteral antibiotic delivery was essential in preventing a local infection after IOFB removal.

Acknowledgements

Nothing to acknowledge.

Conflict of interests and funding

No conflicting relationship exists for any author. P.K. reports non-financial support from Visim. A.Ch.W. has nothing to disclose. A.G. reports grants, personal fees and non-financial support from Bayer; grants, non-financial support from Novartis; non-financial support from Alcon, personal fees and non-financial support from Valeant, grants and non-financial support from Allergan, grants and non-financial support from Pfizer, grants, and financial support from Santen.

REFERENCES

1. Shelsta HN, Bilyk JR, Rubin PAD, et al. Wooden intraorbital foreign body injuries: clinical characteristics and outcomes of 23 patients. Ophthalmic Plast Reconstr Surg. 2010; 26(4): 238–244, doi: 10.1097/IOP.0b013e3181bd7509, indexed in Pubmed: 20523259.
2. Malik N. Benign Tumors of the Jaw Bones. In: Malik N. ed. Textbook of Oral and Maxillofacial Surgery. Jaypee Brothers Medical Pub 2016: 674–734.
3. Zhou L, Li SY, Cui JP, et al. Analysis of missed diagnosis of orbital foreign bodies. Exp Ther Med. 2017; 13(4): 1275–1278, doi: 10.3892/etm.2017.4146, indexed in Pubmed: 28413466.
4. Taş S, Top H. Intraorbital wooden foreign body: clinical analysis of 32 cases, a 10-year experience. Ulus Travma Acil Cerrahi Derg. 2014; 20(1): 51–55, doi: 10.5505/tjtes.2014.93876, indexed in Pubmed: 24639316.
5. John SS, Rehman TA, John D, et al. Missed diagnosis of a wooden intra-orbital foreign body. Indian J Ophthalmol. 2008; 56(4): 322–324, doi: 10.4103/0301-4738.41416, indexed in Pubmed: 18579994.
6. Li J, Zhou LP, Jin J, et al. Clinical diagnosis and treatment of intraorbital wooden foreign bodies. Chin J Traumatol. 2016; 19(6): 322–325, doi: 10.1016/j.cjtee.2016.04.006, indexed in Pubmed: 28088934.
7. van der Wal KG, Boukes RJ. Intraorbital bamboo foreign body in a chronic stage: case report. Int J Oral Maxillofac Surg. 2000; 29(6): 428–429, doi: 10.1034/j.1399-0020.2000.290606.x, indexed in Pubmed: 11202322.
8. Glatt H, custer p, Barrett L. Magnetic Resonance Imaging and COmputead Tomography in a Model of wooden Foreign Bodies in the orbit. Ophthal Plast Reconstruct Surg. 1990; 6(4): 290, doi: 10.1097/00002341-199012000-00036.
9. Krimmel M, Cornelius CP, Stojadinovic S, et al. Wooden foreign bodies in facial injury: a radiological pitfall. Int J Oral Maxillofac Surg. 2001; 30(5): 445–447, doi: 10.1054/ijom.2001.0109, indexed in Pubmed: 11720049.
10. McGuckin JF, Akhtar N, Ho VT, et al. CT and MR evaluation of a wooden foreign body in an in vitro model of the orbit. AJNR Am J Neuroradiol. 1996 Jan; 17(1): 129–33, indexed in Pubmed: 8770263.
11. Nishio Y, Hayashi N, Hamada H, et al. A case of delayed brain abscess due to a retained intracranial wooden foreign body: a case report and review of the last 20 years. Acta Neurochir (Wien). 2004; 146(8): 847–850, doi: 10.1007/s00701-004-0283-7, indexed in Pubmed: 15254807.
12. Spiegelhauer MR, Andersen PF, Frandsen TH, et al. Leclercia adecarboxylata: a case report and literature review of 74 cases demonstrating its pathogenicity in immunocompromised patients. Infect Dis (Lond). 2019; 51(3): 179–188, doi: 10.1080/23744235.2018.1536830, indexed in Pubmed: 30488747.
13. Fiedler G, Schneider C, Igbinosa EO, et al. Antibiotics resistance and toxin profiles of Bacillus cereus-group isolates from fresh vegetables from German retail markets. BMC Microbiol. 2019; 19(1): 250, doi: 10.1186/s12866-019-1632-2, indexed in Pubmed: 31706266.
14. Duerink DO, Lestari ES, Hadi U, et al. Study Group Antimicrobial Resistance in Indonesia: Prevalence and Prevention (AMRIN). Determinants of carriage of resistant Escherichia coli in the Indonesian population inside and outside hospitals. J Antimicrob Chemother. 2007; 60(2): 377–384, doi: 10.1093/jac/dkm197, indexed in Pubmed: 17595290.
15. Enenkel S, Stille W. Administration of AntiBiotics. Antibiotics in the Tropics. 1988: 39–40, doi: 10.1007/978-3-642-73276-8_5.
16. Shrayteh ZM, Rahal MK, Malaeb DN. Practice of switch from intravenous to oral antibiotics. Springerplus. 2014; 3: 717, doi: 10.1186/2193-1801-3-717, indexed in Pubmed: 25674457.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0011

The frequency and costs of intravitreal therapy agents in retinal diseases

Mahmut Atum, Burçin Çakır, İsa Yuvacı, Erkan Çelik, Gürsoy Alagöz

Department of Ophthalmology, Sakarya University Education and Research Hospital, Sakarya, Turkey

ABSTRACT

BACKGROUND: The aim of this study is to analyze the numbers and the economic burden of intravitreal anti-VEGF agents and intravitreal dexamethasone (IVD) implants administered to patients with diabetic retinopathy (DR), age-related macular degeneration (AMD) and retinal vein occlusion (RVO).

MATERIAL AND METHODS: The retrospective case-control study included 1525 patients diagnosed with DME, neovascular AMD and RVO, and received intravitreal anti-VEGF and IVD between January 2016 and December 2018. Intravitreal anti-VEGF administration was performed within the framework of the Pro Re Nata (PRN) regimen. The prices of anti-VEGF agents and IVDs were calculated on the average of the prices in the relevant year.

RESULTS: The total number of intravitreal injections in 3 years was 5864. During the 3-year follow-up, on average, ranibizumab (Lucentis) was applied 3.56 ± 2.25 times, alfibercept (Eylea) was applied 3.31 ± 2.16 times, and IVD (Ozurdex) was applied 1.70 ± 0.83 times. The anti-VEGF numbers in 2016, 2017 and 2018 were 1997, 1801, 2066, respectively. In total, the 3-year drug cost was 3,587,812.44 USD.

CONCLUSIONS: The economic burden of intravitreal anti-VEGF and IVD treatment for retinal diseases is so important to developing countries such as Turkey. The economic burden created by anti-VEGF agents and IVDs in Turkey will reduce in a serious sense, and the legal concerns of physicians will decrease thanks to the decision taken by the Turkish Medicines and Medical Devices Agency (TMMDA).

KEY WORDS: retinal diseases; anti-VEGF; economic burden; diabetic retinopathy; age-related macular degeneration; retinal vein occlusion

Ophthalmol J 2020; Vol. 5, 55–59

INTRODUCTION

Diabetic retinopathy (DR), age-related macular degeneration (AMD) and retinal vein occlusion (RVO) are the most important causes of vision loss [1]. It is estimated that these three retinal diseases will gradually increase all over the world [2]. Diabetic macular edema (DME) due to DR, neovascular AMD and RVO-induced macular edema (ME) are the main reasons for decreased vision. In recent years, intravitreal anti-vascular endothelial growth factor (anti-VEGF) agents have been used frequently in the treatment of ME due to these three retinal diseases [3–5]. The most commonly used anti-VEGF agents are aflibercept (Eylea, Regeneron Pharmaceuticals, Tarrytown, New York, USA and Bayer Healthcare Pharmaceuticals, Berlin, Germany), bevacizumab (Avastin, Genentech, Inc., South San Francisco, CA, USA) and ranibizumab (Lucentis; Genentech, South San Francisco, CA, USA). Intravitreal dexamethasone implant (IVD; Ozurdex; Allergan Inc, Irvine, CA, USA) is also used for treatment of ME. The efficiencies of all these agents were similar in the studies conducted [5–7].

CORRESPONDING AUTHOR:
Mahmut Atum, Department of Ophthalmology, Sakarya University Education and Research Hospital, Korucuk Mah. 54100 Sakarya, Turkey, tel: +90 555 809 62 75; e-mail: mahmutatum@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

The widespread use of anti-VEGF agents causes a serious economic burden. In a study, it was reported that 2.1 million anti-VEGFs were used in the United States in 2013 and the approximate cost of this amount was more than 2.3 billion dollars [8]. Studies have shown that bevacizumab is 30–40 times cheaper than other agents and it is cost-effective [9–11]. As in many countries, there is no indication for intraocular use of bevacizumab in Turkey. Legal and ethical problems related to this issue limit the use of bevacizumab by ophthalmologists. Turkish Medicines and Medical Devices Agency (TMMDA) took a new decision on December 28, 2018, and according to this decision, it is stated that 3 dose bevacizumab should be used in patients who need anti-VEGF, and then other anti-VEGF agents can be used only in resistant and/or unresponsive cases [12]. It is estimated that this application aims to reduce the economic burden of anti-VEGF agents.

The aim of this study is to analyze the numbers and the economic burden of intravitreal anti-VEGF agents and IVD implants administered to patients with DME, AMD and RVO between January 2016 and December 2018.

MATERIAL AND METHODS

This retrospective study included 1525 patients who were diagnosed with DME, neovascular AMD and RVO, and received intravitreal anti-VEGF between January 2016 and December 2018. The study was conducted in the Retina Clinic of Sakarya University Education and Research Hospital. Approval for the study was obtained from the local ethics committee (Sakarya University Medical Faculty Ethics Committee, 15.02.2019/38). A detailed ophthalmologic examination was performed in all patients who were referred to the ophthalmology clinic, referred to the retinal unit, and followed up. In all patients, the best corrected visual acuity with Snellen chart, intraocular pressure measurement with Goldmann applanation tonometer, and anterior and posterior segment examination with a slit-lamp bio microscopy were performed. In addition, in all patients, a central foveal thickness with optical coherence tomography device (OCT, Cirrus HD OCT, Carl Zeiss Meditec, Dublin, CA, USA) and a fundus photograph and fluorescein angiography with fundus fluorescein angiography device (FFA, Canon Sales Co., Inc., Chiba, Japan) were performed. As a result of these measurements, intravitreal anti-VEGF treatment was applied to the patients in need of anti-VEGF by the ophthalmologist in the operating room conditions. Intravitreal anti-VEGF administration was performed within the framework of the PRN protocol adopted in EURETINA guidelines [13]. According to this protocol, all naive patients were given monthly injections in OCT until the intraretinal/subretinal fluid passed and anti-VEGF was administered when needed. In addition, anti-VEGF changes were performed or dexamethasone implants were used in patients who did not respond to treatment.

The prices of anti-VEGF agents and IVDs were calculated on the average of the prices in the relevant year (the year anti-VEGF administered). The calculations made over Turkish Lira (TL) were converted to US dollar (USD) by basing on the average dollar exchange rate of the Central Bank of the Republic of Turkey in the relevant year. The average price of Lucentis in 2016, 2017, 2018 was 704.16 USD (2128.97 TL), 644.58 USD (2352.72 TL), 505.75 USD (2437.83 TL), respectively. In the same years, the price of Eylea was 592.54 USD (1791.5 TL), 496.45 USD (1812.05 TL) and 415.99 USD (2005.16 TL), respectively. Furthermore, the price of Ozurdex was 665.96 USD (2013.48 TL), 609.57 USD (2224.93 TL), 529.92 USD (2554.34 TL), respectively. The decrease in drug prices in dollar terms between 2016 and 2018 is due to the depreciation of TL against USD. (USD / TL average rate was 3.02, 3.65, and 4.82 in 2016, 2017, 2018, respectively.)

This study was conducted at the Department of Ophthalmology of Sakarya University Medical Education and Research Hospital. Prior approval from the Institutional Review Board was taken and written informed consent was obtained from each subject. The study was performed in adherence to the Declaration of Helsinki.

STATISTICAL ANALYSIS

Data were analyzed using SPSS (version 17.0, SPSS Inc., Chicago, IL, USA) and Microsoft Excel (Microsoft Corp., Redmond, WA, USA). Descriptive analysis was used to analyze the data and the numerical data were given as mean and standard deviation (SD). The Kolmogorov-Smirnov test was used for the analysis of the distribution of the normality, and while the parametric Student's t-test was used for the analysis of the normally distributed parameters, non-parametric ANOVA test and Post Hoc Tests (Tamhane) were used to analyze abnor-

mally distributed data. $p < 0.05$ was considered statistically significant.

RESULTS

In total, data of 1525 patients were analyzed: 742 (48.7%) of the patients were male and 783 (51.3%) were female. The mean age of the patients was 66.17 ± 10.36 years in males and 65.36 ± 9.95 years in females, and there was not a statistically significant difference between them ($p = 0.118$). 801 patients (52.5%) had DME, 395 (25.9%) had neovascular AMD, and 329 (21.6%) had RVO. The total number of intravitreal anti-VEGFs in 3 years was 5864. The anti-VEGF numbers in 2016, 2017 and 2018 were 1997, 1801, 2066, respectively (Tab. 1). In total, 3-year drug cost was 3,587,812.44 USD, and the distribution of drugs by years and drug type is summarized in Table 1.

During the 3-year follow-up, on average annually, ranibizumab (Lucentis) was applied 3.56 ± 2.25 times (range 1–13), alfibercept (Eylea) was applied 3.31 ± 2.16 times (1–19), and IVD (Ozurdex) was applied 1.70 ± 0.83 times (range 1–4) There was no significant difference between the number of ranibizumab administered in DME and the number applied in AMD, but it was significantly higher than RVO. In addition, the average number of ranibizumab applied in AMD was significantly higher than RVO ($p = 0.249$, $p < 0.05$, $p = 0.045$). There was no significant difference between the mean alfibercept number applied in DME and AMD, but DME was significantly higher than RVO. However, no significant difference was found between the mean alfibercept number applied in AMD and those applied in RVO ($p = 0.858$, $p = 0.004$, $p = 0.069$). Intravitreal dexamethasone implant was used in patients with DME and RVO, and its use was significantly higher in patients with DME than in patients with RVO ($p < 0.05$) (Tab. 2).

DISCUSSION

Vision loss due to retinal diseases such as DME, AMD, and RVO is increasing day by day and these diseases are a major part of visual loss [14–16]. Intravitreal anti-VEGF is one of the proven treatment modalities for reducing visual loss [17, 18]. However, the high cost of anti-VEGF agents and their frequent repetition constitute a serious economic burden [9]. In this study, we aimed to investigate the economic burden of intravitreal anti-VEGF and IVD treatment for DME, AMD and RVO.

There are several studies analyzing the frequency and cost of anti-VEGF use in retinal diseases. In his study, Turpcu et al. compared the number and cost of intravitreal injections applied in DME, RVO and AMD. In AMD, an annual average of 5.6 times alfibercept and 5.3 times ranibizumab were performed while 4.5 times aflibercept and 5 times ranibizumab were performed in RVO, and there was no significant difference in anti-VEGF usage numbers and prices. On average, 4.4 ± 2.9 times

Table 1. Distribution and cost of intravitreal drugs by years

	2016 (n)	2017 (n)	2018 (n)	Total (n)	2016 (USD)	2017 (USD)	2018 (USD)	Total (USD)
Lucentis	1096	712	1056	2864	772,632.82	458,941.54	534,097.20	1,765,671.56
Eylea	901	1089	1010	3000	534,483.94	540,636.28	420,168.40	1,495,288.61
Ozurdex	121	150	292	563	80,672.54	91,435.47	154,744.20	326,852.27
Total	1997	1801	2066	5864	1,387,789.30	1,091,013.31	1,109,009.80	3,587,812.44

Table 2. Comparison of intravitreal agents in diabetic macular edema (DME), age-related macular degeneration (AMD), retinal vein occlusion (RVO) diseases (average of 3 years)

	DME (Mean)	AMD (Mean)	RVO (Mean)	Total (Mean)	p (DME-AMD)	p (DME-RVO)	p (AMD-RVO)
Lucentis (n = 805)	3.79 ± 2.30	3.46 ± 2.303	2.91 ± 1.84	3.56 ± 2.25	0.249	< 0.05	0.045
Eylea (n = 907)	3.46 ± 2.12	3.34 ± 2.31	2.90 ± 1.94	3.31 ± 2.16	0.858	< 0.05	0.069
Ozurdex (n = 331)	1.80 ± 0.82	-	1.53 ± 0.82	1.70 ± 0.83	–	< 0.05	–

ranibizumab was administered to DME patients in a year. The annual cost of treatment with ranibizumab in DME patients was lower than in RVO and AMD patients [11]. In our study, it was observed that the mean number of injections was lower and it is thought that this was due to long follow-up periods (3 years) and treatment protocol In their study, Johnson et al. found that the total direct health care cost per patient in patients treated with anti-VEGF was 14,725 euros in France, 10,927 euros in Spain and 9,647–13,759 pounds in the UK and 50–80% of this cost was the drug cost. They also reported that the most commonly used anti-VEGF agent was ranibizumab [19]. Drug prices in Turkey are cheaper than in Europe and anti-VEGF annual costs are significantly lower than the European countries. However, Turkey is a developing country and despite being cheaper in dollar, anti-VEGF agents are estimated to have a higher economic burden in the country.

In a study conducted by Hollingworth et al., the use of anti-VEGF agents (ranibizumab, bevacizumab) in various retinal diseases in the UK has been found to increase by 215% over a 5-year period (2010/2011 to 2014/2015). In addition, it is estimated that there will be a 447 million pounds drug spending during the 2015/2016 period due to the intravitreal use of anti-VEGF agents [20]. Moreover, these expenditures are expected to increase with each passing day. In a study by Dakin et al., it was reported that the replacement of ranibizumab treatment for AMD patients with bevacizumab would save around 102 million pounds annually [21]. In another study, Hutton et al. reported that in the 10-year period (2010–2020), approximately 18 billion dollars could be saved if all other anti-VEGF agents were replaced with bevacizumab [22]. In our study, it is seen that the number of patients with a sudden-VEGF need has increased over the years and the economic burden created by this situation also increases. We believe that the transition to bevacizumab will provide significant savings.

Bevacizumab is an anti-VEGF agent with proven efficacy in retinal diseases such as DME, AMD, RVO, despite the lack of FDA approval for intravitreal use (indication in colon cancer) [6, 23, 24]. In addition, the cost of the intravitreal use of bevacizumab is quite inexpensive compared to other drugs [25]. In addition, many studies have proven that bevacizumab is more cost-effective in various retinal diseases than other anti-VEGF agents on the market [10, 21, 26]. Turkish Medicines and Medical Devices Agency has confirmed the intravitreal use of bevacizumab since 2019 in Turkey. In light of this information, considering that there will be a significant increase in the use of bevacizumab from 2019 with the recent decision by TMMDA, we think that the economic burden created by anti-VEGF drugs will significantly decrease.

Legal and ethical issues are also important in anti-VEGF preferences of ophthalmologists. Hollingworth et al. reported that physicians had to choose expensive agents because of the lack of legal basis [20]. With the decision taken by the TMMDA, we think that the legal problems ophthalmologists in Turkey go through will reduce, and they may feel more comfortable in their anti-VEGF preferences.

CONCLUSION

As a result, we think the financial burden created by anti-VEGF in Turkey will reduce in a serious sense, and the legal concerns of physicians will decrease thanks to the decision taken by the TMMDA. We intend to continue our current work in the following years. Thus, we will have the opportunity to evaluate the amount of money spent on anti-VEGF drugs and the savings provided.

Acknowledgments

We are grateful to Atilla Akgül, one of the staff of the Sakarya Provincial Health Directorate, for his contributions to the data collection.

REFERENCES

1. Bourne R, Stevens G, White R, et al. Causes of vision loss worldwide, 1990–2010: a systematic analysis. Lancet Glob Health. 2013; 1(6): e339–e349, doi: 10.1016/s2214-109x(13)70113-x, indexed in Pubmed: 25104599.
2. Li JQ, Welchowski T, Schmid M et al. Retinal Diseases in Europe 2017. https://www.euretina.org/downloads/EURETINA_Retinal_Diseases.pdf (2017).
3. Cai S, Bressler NM. Aflibercept, bevacizumab or ranibizumab for diabetic macular oedema: recent clinically relevant findings from DRCR.net Protocol T. Curr Opin Ophthalmol. 2017; 28(6): 636–643, doi: 10.1097/ICU.0000000000000424, indexed in Pubmed: 28837425.
4. Hanhart J, Rozenman Y. Comparison of Intravitreal Ranibizumab, Aflibercept, and Dexamethasone Implant after Bevacizumab Failure in Macular Edema Secondary to Retinal Vascular Occlusions. Ophthalmologica. 2017; 238(1-2): 110–118, doi: 10.1159/000473864, indexed in Pubmed: 28535531.
5. Kovach JL, Schwartz SG, Flynn HW, et al. Anti-VEGF Treatment Strategies for Wet AMD. J Ophthalmol. 2012; 2012: 786870, doi: 10.1155/2012/786870, indexed in Pubmed: 22523653.
6. Cai S, Bressler N. Aflibercept, bevacizumab or ranibizumab for diabetic macular oedema. Current Opinion in Ophthalmology. 2017; 28(6): 636–643, doi: 10.1097/icu.0000000000000424.

7. Chakravarthy U, Harding SP, Rogers CA, et al. IVAN Study Investigators. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration: one-year findings from the IVAN randomized trial. Ophthalmology. 2012; 119(7): 1399–1411, doi: 10.1016/j.ophtha.2012.04.015, indexed in Pubmed: 22578446.
8. Erie JC, Barkmeier AJ, Hodge DO, et al. High Variation of Intravitreal Injection Rates and Medicare Anti-Vascular Endothelial Growth Factor Payments per Injection in the United States. Ophthalmology. 2016; 123(6): 1257–1262, doi: 10.1016/j.ophtha.2016.02.015, indexed in Pubmed: 26976701.
9. Baker-Schena L. Expensive Drugs. Eye Net Mag. 2017: 39–44.
10. Ross EL, Hutton DW, Stein JD, et al. Diabetic Retinopathy Clinical Research Network. Cost-effectiveness of Aflibercept, Bevacizumab, and Ranibizumab for Diabetic Macular Edema Treatment: Analysis From the Diabetic Retinopathy Clinical Research Network Comparative Effectiveness Trial. JAMA Ophthalmol. 2016; 134(8): 888–896, doi: 10.1001/jamaophthalmol.2016.1669, indexed in Pubmed: 27280850.
11. Turpcu A, Wilson K, Huang A et al. Injection frequency and costs of anti-vegf treatments for neovascular age-related macular degeneration, retinal vein occlusion, and diabetic macular Eedema. Value Heal 2015; 18(3): A180. http://linkinghub.elsevier.com/retrieve/pii/S1098301515011018.
12. Sosyal Güvenlik Kurumu. Sosyal Güvenlik Kurumu Sağlık Uygulama Tebliği. Sosyal Güvenlik Kurumu Sağlık Uygulama Tebliği. 2018. http://www.sgk.gov.tr/wps/portal/sgk/tr/kurumsal/merkez-teskilati/ana_hizmet_birimleri/gss_genel_mudurlugu/anasayfa_duyurular/guncel_sut_28122018.
13. Schmidt-Erfurth U, Chong V, Loewenstein A, et al. European Society of Retina Specialists. Guidelines for the management of neovascular age-related macular degeneration by the European Society of Retina Specialists (EURETINA). Br J Ophthalmol. 2014; 98(9): 1144–1167, doi: 10.1136/bjophthalmol-2014-305702, indexed in Pubmed: 25136079.
14. Lee R, Wong TY, Sabanayagam C. Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. Eye Vis (Lond). 2015; 2: 17, doi: 10.1186/s40662-015-0026-2, indexed in Pubmed: 26605370.
15. Wong WL, Su X, Li X, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. Lancet Glob Health. 2014; 2(2): e106–e116, doi: 10.1016/S2214-109X(13)70145-1, indexed in Pubmed: 25104651.
16. Flaxman S, Bourne R, Resnikoff S, et al. Global causes of blindness and distance vision impairment 1990–2020: a systematic review and meta-analysis. The Lancet Global Health. 2017; 5(12): e1221–e1234, doi: 10.1016/s2214-109x(17)30393-5, indexed in Pubmed: 29032195.
17. Wecker T, Ehlken C, Bühler A, et al. Five-year visual acuity outcomes and injection patterns in patients with pro-re-nata treatments for AMD, DME, RVO and myopic CNV. Br J Ophthalmol. 2017; 101(3): 353–359, doi: 10.1136/bjophthalmol-2016-308668, indexed in Pubmed: 27215744.
18. Ou WC, Brown DM, Payne JF, et al. Relationship Between Visual Acuity and Retinal Thickness During Anti-Vascular Endothelial Growth Factor Therapy for Retinal Diseases. Am J Ophthalmol. 2017; 180: 8–17, doi: 10.1016/j.ajo.2017.05.014, indexed in Pubmed: 28549848.
19. Johnson MK, Lara N. PSS18 Direct Economic Burden of Regular Intravitreal Injections for the Treatment of Retina Diseases in Three European Countries. Value Heal. Elsevier Inc. 2011; 14(7): A505. https://linkinghub.elsevier.com/retrieve/pii/S1098301511030452.
20. Hollingworth W, Jones T, Reeves BC, et al. A longitudinal study to assess the frequency and cost of antivascular endothelial therapy, and inequalities in access, in England between 2005 and 2015. BMJ Open. 2017; 7(10): e018289, doi: 10.1136/bmjopen-2017-018289, indexed in Pubmed: 29061629.
21. Dakin HA, Wordsworth S, Rogers CA, et al. IVAN Study Investigators. Cost-effectiveness of ranibizumab and bevacizumab for age-related macular degeneration: 2-year findings from the IVAN randomised trial. BMJ Open. 2014; 4(7): e005094, doi: 10.1136/bmjopen-2014-005094, indexed in Pubmed: 25079928.
22. Hutton D, Newman-Casey PA, Tavag M, et al. Switching to less expensive blindness drug could save medicare part B $18 billion over a ten-year period. Health Aff (Millwood). 2014; 33(6): 931–939, doi: 10.1377/hlthaff.2013.0832, indexed in Pubmed: 24889941.
23. Narayanan R, Panchal B, Das T, et al. MARVEL study group. A randomised, double-masked, controlled study of the efficacy and safety of intravitreal bevacizumab versus ranibizumab in the treatment of macular oedema due to branch retinal vein occlusion: MARVEL Report No. 1. Br J Ophthalmol. 2015; 99(7): 954–959, doi: 10.1136/bjophthalmol-2014-306543, indexed in Pubmed: 25631483.
24. Martin DF, Maguire MG, Fine SL, et al. Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. Ophthalmology. 2012; 119(7): 1388–1398, doi: 10.1016/j.ophtha.2012.03.053, indexed in Pubmed: 22555112.
25. Raftery J, Clegg A, Jones J, et al. Ranibizumab (Lucentis) versus bevacizumab (Avastin): modelling cost effectiveness. Br J Ophthalmol. 2007; 91(9): 1244–1246, doi: 10.1136/bjo.2007.116616, indexed in Pubmed: 17431015.
26. van Asten F, Michels CTJ, Hoyng CB, et al. The cost-effectiveness of bevacizumab, ranibizumab and aflibercept for the treatment of age-related macular degeneration-A cost-effectiveness analysis from a societal perspective. PLoS One. 2018; 13(5): e0197670, doi: 10.1371/journal.pone.0197670, indexed in Pubmed: 29772018.

CASE REPORT
DOI: 10.5603/OJ.2020.0011

Successful management of a large traumatic iris cyst

Imane Chabbar, Louai Serghini, Amina Berraho

Ophthalmology B Department, Ibn Sina University Hospital, Rabat, Morocco

ABSTRACT

BACKGROUND: Iris cysts are rare lesions of the anterior segment of the eye, they can be congenital or acquired. The management of acquired post-traumatic iris cysts remains difficult.

CASE REPORT: We report the case of a 24-year-old girl who presented with a progressive decrease in vision in the left eye with pain and redness for the past few months. She had a history of penetrating injury in the same eye 14 years ago. The slit lamp examination identified a corneal scar at 7' o'clock and a large iris cyst deforming the pupillary area. Ultrasound biomicroscopy (UBM) has confirmed the benign nature of the cyst. Anterior segment optical coherence tomography (AS-OCT) has shown the contact of the external layer of the cyst with the corneal endothelium. Surgical management consisted of soft viscodissection to separate the cyst from the corneal endothelium followed by complete excision of the external layer of the cyst.

CONCLUSION: The postoperative course was simple with good visual outcome.

KEY WORDS: large traumatic iris cyst; UBM; AS-OCT; surgical management

Ophthalmol J 2020; Vol. 5, 60–63

INTRODUCTION

Post-traumatic iris cysts are rare. They result from the inclusion of epithelial cells, of corneal or conjunctival origin, in the anterior chamber through a traumatic corneoscleral perforation [1]. The management of post-traumatic iris cysts is delicate involving various therapies and the results depend on associated ocular morbidity and postoperative complications [2]. The aim of our work is to report a case of a large traumatic iris cyst treated by surgical excision with a good anatomical and functional result.

CASE REPORT

A 24-year-old young woman presented to the ophthalmic consultation for a decrease in visual acuity in the left eye associated with pain and redness that had progressively worsened over the last few months. The interrogation revealed a history of penetrating injury in the same eye going back 10 years resulting in a corneal wound at 7h parallel to the corneoscleral limbus. The patient received a wound toilet and surgical suturing under a microscope. On admission, his visual acuity was reduced to 2/10 in the left eye and 10/10 in the right eye. The slit lamp examination revealed a corneal scar at 7 o'clock, a giant iris cyst extending from 7 to 11 o'clock, making contact with the corneal endothelium and deforming the pupillary area (Fig. 1AB). We noted also an opacification of the crystalline lens facing the cyst. The intraocular pressure was 14 mm Hg and the fundus examination was without particularity.

Ultrasound biomicroscopy (UBM) examination confirmed the benign nature of the cyst by showing thin hyperechoic wall and hypoechoic internal con-

CORRESPONDING AUTHOR:
Imane Chabbar, Ophthalmology B department, Ibn Sina University Hospital, Rabat, Morocco; e-mail: imana1chab@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

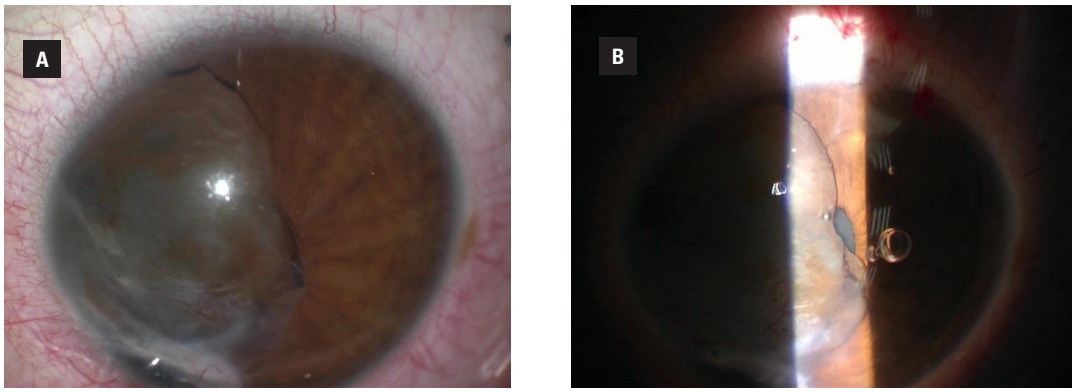

FIGURE 1. Large iris cyst of the left eye (**A**) obstructing the pupil (**B**) with corneal contact

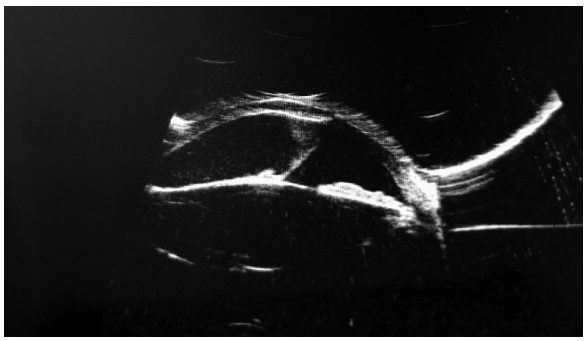

FIGURE 2. Ultrasound biomicroscopy (UBM) showing hyperechoic wall and hypoechoic internal content of the iris cyst

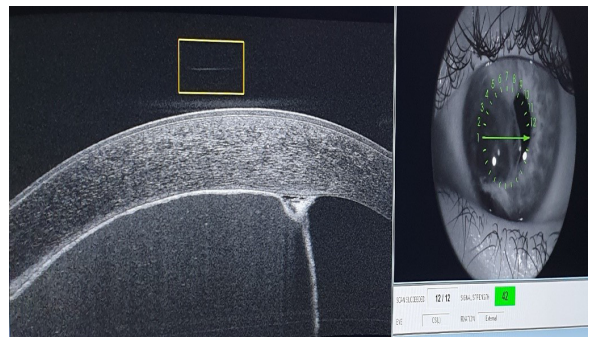

FIGURE 3. Anterior segment optical coherence tomography (AS-OCT) showing the contact of cyst external layer with corneal endothelium

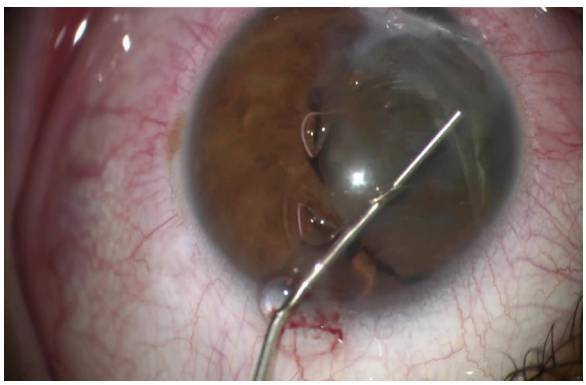

FIGURE 4. Intraoperative appearance showing viscodissection of the cyst and its gentle separation from the corneal endothelium

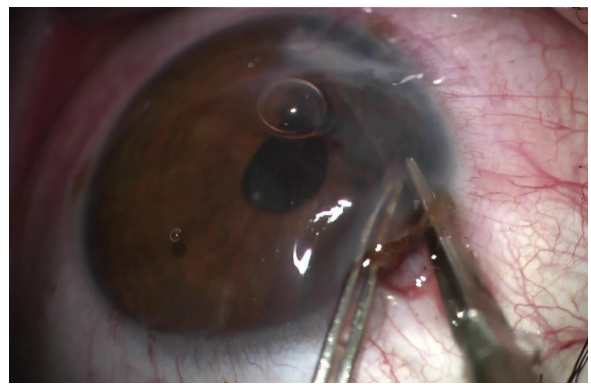

FIGURE 5. Intraoperative appearance showing excision and removal of the external layer with Vannas scissors

tent without involvement of the posterior segment (Fig. 2). Anterior segment optical coherence tomography (AS-OCT) showed close contact of cyst external layer with corneal endothelium without an increase in corneal thickness (Fig. 3).

The patient underwent surgical management of the iris cyst to prevent endothelial and hypertensive decompensation. The operative technique consisted, under general anesthesia and through a 2.5 mm calibrated corneal incision located at 12 o'clock, of intracameral injection of viscoelastic in order to gently separate the external layer of the iris cyst from the corneal endothelium (Fig. 4). A second corneal incision was then made at 9 o'clock allowing Vannas scissors to remove the external layer of the cyst and to extract it with forceps (Fig. 5). Finally, corneal

incisions were closed by sutures with buried knots using 10/0 monofilament. The immediate postoperative course was marked by minimal corneal edema and moderate hypertonia controlled by local treatment. After a week, the examination found a visual acuity at 8/10 with a minimal corectopia.

DISCUSSION

Iris cysts are rare. They can be of primitive or acquired origin [1, 2]. Acquired iris cysts are secondary to perforating trauma, anterior segment surgery, chronic eye inflammation, prolonged use of miotic eye drops or, more rarely, presence of a melanocytic tumor of the anterior segment [3]. Post-traumatic iris cysts result from the inclusion of epithelial cells, of corneal or conjunctival origin, in the anterior chamber through a traumatic corneoscleral perforation [3]. These cells transplanted into the anterior chamber are subsequently involved in the formation of the cyst walls [4]. Post-traumatic iris cysts can vary in size. Small cysts can remain asymptomatic and incidentally discovered. However, large cysts can cause local complications due to their extension. They can cause angle-closure glaucoma, cataract, corneal edema by endothelial decompensation, pupillary deformation and intraocular inflammation [5]. The diagnosis of iris cysts is initially clinical, supported by imaging techniques to confirm the diagnosis and guide treatment. It is necessary to differentiate iris cysts from iris tumors. Iris cysts are fluid, thin-walled with regular contours while iris tumors are solid, thick-walled with irregular contours and frequently associated with local complications [6]. Ultrasound biomicroscopy is currently offering decisive help in the diagnosis of iris cysts, allowing to measure the cyst dimensions, to study its extension and its contact with neighboring structures and to differentiate it from solid tumors [7–9]. Anterior segment optical coherence tomography compared to UBM is unable to visualize the posterior wall of the iris cyst. Anterior segment optical coherence tomography is especially efficient for analyzing small iris tumors and assessing corneal repercussions [8–9]. The management of iris cysts is variable. Non-invasive treatment modalities are based on needle aspiration, intracystic injections of sclerosing agents, Argon laser photocoagulation and Nd:YAG laser iridocystotomy [10–12]. Surgical treatment should be indicated as a last resort, given the risk of serious complications, particularly in cases where non-invasive treatments are insufficient. The surgical modality must be chosen according to the extension and complications of the cyst. Viscodissection helps to separate the cyst from the corneal endothelium without traumatizing it and then facilitate the excision of the cyst [13]. Surgical excision can range from a resection of the external layer to a resection of the iris cyst in toto, or a partial iridectomy or even an extensive corneoscleral iridocyclectomy involving corneoscleral grafts [14, 15]. According to some authors, surgery can be associated with endocoagulation or limbus cryotherapy facing the cyst, which allows treating cystic cells disseminated in the iridocorneal angle.

CONCLUSION

In our case, complete excision of the cyst by iridectomy was not possible due to the large size of the lesion. We performed a viscodissection to softly separate the cyst from the cornea then surgical removal of its external layer. However, surgical treatment is not trivial, exposing particularly to the risk of induced astigmatism and endophthalmitis.

REFERENCES

1. Zografos L, Uffer S. Tumeurs du complexe iridociliaire. EMC — Ophtalmol. 2004; 1(2): 1–12, doi: 10.1016/s0246-0343(04)40183-x.
2. Shields CL, Kancherla S, Patel J, et al. Clinical survey of 3680 iris tumors based on patient age at presentation. Ophthalmology. 2012; 119(2): 407–414, doi: 10.1016/j.ophtha.2011.07.059, indexed in Pubmed: 22035581.
3. Gupta V, Rao A, Sinha A, et al. Post-traumatic inclusion cysts of the iris: a longterm prospective case series. Acta Ophthalmol Scand. 2007; 85(8): 893–896, doi: 10.1111/j.1600-0420.2007.00975.x, indexed in Pubmed: 17822446.
4. Moreno-López M, Arruabarrena C, Regueras A, et al. [Conservative surgical management of a post-traumatic iris cyst]. Arch Soc Esp Oftalmol. 2007; 82(7): 455–457, doi: 10.4321/s0365-66912007000700012, indexed in Pubmed: 17647123.
5. Regis A, Roussat B, Ullern M, et al. Kyste congénital du stroma irien. J Franç Ophtalmol. 2004; 27(4): 379–382, doi: 10.1016/s0181-5512(04)96144-x.
6. Rao A, Gupta V, Bhadange Y, et al. Iris cysts: a review. Semin Ophthalmol. 2011; 26(1): 11–22, doi: 10.3109/08820538.2010.541319, indexed in Pubmed: 21275599.
7. Roche O, Orssaud C, Beby F, et al. Ultrabiomicroscopie et physiopathologie des kystes iriens congénitaux. J Franç Ophtalmol. 2007; 30(1): 25–30, doi: 10.1016/s0181-5512(07)89546-5.
8. Bianciotto C, Shields CL, Guzman JM, et al. Assessment of anterior segment tumors with ultrasound biomicroscopy versus anterior segment optical coherence tomography in 200 cases. Ophthalmology. 2011; 118(7): 1297–1302, doi: 10.1016/j.ophtha.2010.11.011, indexed in Pubmed: 21377736.
9. Hau SC, Papastefanou V, Shah S, et al. Evaluation of iris and iridociliary body lesions with anterior segment optical coherence tomography versus ultrasound B-scan. Br J Ophthalmol. 2015; 99(1): 81–86, doi: 10.1136/bjophthalmol-2014-305218, indexed in Pubmed: 25091953.
10. Tsai J, Arrindell E, O'Day D. Needle aspiration and endodiathermy treatment of epithelial inclusion cyst of the iris. Am J Ophthalmol. 2001; 131(2): 263–265, doi: 10.1016/s0002-9394(00)00707-8, indexed in Pubmed: 11228309.

11. Shields CL, Arepalli S, Lally EB, et al. Iris stromal cyst management with absolute alcohol-induced sclerosis in 16 patients. JAMA Ophthalmol. 2014; 132(6): 703–708, doi: 10.1001/jamaophthalmol.2014.160, indexed in Pubmed: 24723076.
12. Xiao Y, Wang Y, Niu G, et al. Transpupillary argon laser photocoagulation and Nd:YAG laser cystotomy for peripheral iris pigment epithelium cyst. Am J Ophthalmol. 2006; 142(4): 691–693, doi: 10.1016/j.ajo.2006.04.050, indexed in Pubmed: 17011872.
13. Al-Ghadeer H, Al-Towerki AE, Al-Rajhi A, et al. Long-term follow-up and visual outcome after excision of a traumatic iris cyst by viscoelastic dissection. Int Ophthalmol. 2011; 31(6): 529–531, doi: 10.1007/s10792-011-9498-9, indexed in Pubmed: 22222716.
14. Dorecka M, Miniewicz-Kurkowska J, Michalska-Małecka K, et al. Needle aspiration with surgical excision of an epithelial post traumatic iris cyst – a case report. Med Sci Monit. 2011; 17(5): CS60–CS2, doi: 10.12659/msm.881754 Free PMC article, indexed in Pubmed: 21525817.
15. Georgalas I, Petrou P, Papaconstantinou D, et al. Iris cysts: A comprehensive review on diagnosis and treatment. Surv Ophthalmol. 2018; 63(3): 347–364, doi: 10.1016/j.survophthal.2017.08.009, indexed in Pubmed: 28882598.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0015

Prevalence of myopia and its socio-demographic distribution amongst secondary school going adolescents in Lurambi Sub-County, Kakamega, Kenya

Alfred Ragot[1], Mustafa Baraza[2], Peter Clarke-Farr[3]

[1]Department of Optometry and Vision Science, School of Public Health and Biomedical Sciences, Masinde Muliro University of Science and Technology, Kakamega, Kenya
[2]Department of Medical Laboratory and Biotechnology, School of Public Health and Biomedical Sciences, Masinde Muliro University of Science and Technology, Kakamega, Kenya
[3]Department of Ophthalmic Sciences, Faculty of Health and Wellness Sciences, Cape Peninsula University of Technology, Cape Town, South Africa

ABSTRACT

BACKGROUND: Globally the prevalence of myopia has increased alarmingly and is expected to affect an estimated 2.56 billion people in the world by the end of 2020. It is believed to be the leading cause of visual impairment in Kenya, contributing 59.5% of all causes of visual impairment. Still, agreement on the exact prevalence in Kenya and whether socio-demographic factors have an influence on myopia is unknown.
This study was aimed at evaluating the prevalence of myopia and its socio-demographic distribution amongst randomly selected school-going adolescent.
This study was conducted in Lurambi Sub-County in Kakamega, Kenya.
MATERIAL AND METHODS: The study adopted a school-based cross-sectional descriptive study design. Using a multi -stage sampling technique, 733 participants from a population of 7,400 secondary school students within Lurambi Sub-County were randomly selected. A standard optometric vision-assessment protocol was applied to those who met the inclusion criteria and cycloplegic refraction was conducted to elicit those who had myopia.
RESULTS: The prevalence of myopia was found to be 7.5% of which 29 (52.7%) were male while 26 (47.3%) were female and there was no association between gender and myopia (p = 0.572). Myopia was found to be more prevalent in urban 49 (87.3%) as compared to rural 7 (12.7%) areas and there was no association between place of residences and myopia (p = 0.381). Similarly, 15–18 years was the dominant age group 39 (70.9%) and there was no association between age and having myopia (p = 0.926). The study also found that there was no association (p = 0.207) between school class of the participants and having myopia, although most myopic cases were in the form four class 15 (27.3%).
CONCLUSION: Myopia was found to be mostly prevalent in the urban setting and upper classes as compared to rural and lower classes. This may link myopia to other risk factors such as near work and outdoor activities, but more research needs to be done in these areas.

KEY WORDS: myopia; Kenya; prevalence; socio-demographic

Ophthalmol J 2020; Vol. 5, 64–70

CORRESPONDING AUTHOR:
Alfred Ragot, P.O. BOX 190-50100, Masinde Muliro University of Science and Technology, Kakamega, Kenya, 0716584698;
e-mail: aragot@mmust.ac.ke

Copyright © 2020 Via Medica, ISSN 2450–7873

INTRODUCTION

Myopia is estimated to be the leading cause of visual impairment (VI) of all Uncorrected Refractive Error (URE) and it is believed to be the most common eye condition worldwide [1]. Nearly 1.89 billion people are myopic in the world [2], and this number is projected to rise to 2.56 billion by 2020 if nothing is done to address the situation [3]. Myopia is a public health problem worldwide [4], and it is one of the five ocular problems that have been identified by the World Health Organization as an immediate priority for the global initiative of preventable blindness [5]. Myopia and high myopia can result in other vision-threatening conditions like myopic macular degeneration, retinal detachment, cataract as well as choroid degenerative conditions [6]. The risk is comparable to the risk of smoking and hypertension to cardiovascular health [7]. Myopia has also been associated with poor socioeconomic status and quality of life [The prevalence of URE in Africa has been estimated to be 2.3%, and that of myopia is not well documented [9]. In Kenya, studies on the prevalence of myopia and its risk factors are scarce. It is, however, believed to be the leading cause of visual impairment in Kenya and it contributes to 59.5% of refractive errors in Kenya [10]. Despite this, its exact prevalence is not well known.

MATERIAL AND METHODS

This study was conducted in secondary schools around Lurambi Sub-County, Kenya. Lurambi Sub-County is one of the most cosmopolitan sub-counties which is located in the western part of the country (Kenya), and it is inhabited by people from different parts of the country and different ethnic groups. A school-based cross-sectional study design was adopted. All participants that were selected were aged between 10 to 19 years. Significant myopia in this study was defined as myopia ≥ –0.50D. In addition, the participant with defined myopia must present with Snellen Visual Acuity (VA) of 6/9 or worse for distance VA in any eye, equivalent to 0.1 or worse logarithm of the minimum angle of resolution (logMAR). The multistage sampling technique took place in two stages as follows:

- stage one — this involved purposive sampling of two clusters. The 22 schools in Lurambi Sub-County were classified into two; urban schools and rural schools. The urban schools were identified by their locality. Those schools that were found within Kakamega Municipality of Lurambi Sub-County were classified as urban schools and those that were found in the rural part of Lurambi Sub-County formed the second cluster which were rural schools. This was to ensure maximum coverage of all levels of socio-demographic and socio-economic features of the study area. The two clusters had a total of 22 secondary schools with students' enrolment having been estimated to be 7,400 in 2020;
- stage two — this involved a computer-generated random system in order to sample the schools. Since there was a disproportionate number of students in the schools, a proportionate sampling technique was employed to ensure that all the schools and every student in each cluster had an equal chance of being selected. To achieve this and considering that some schools had student populations as low as 25 while others had student population as high as 1500, all the schools in the two clusters were shared into groups of near-equal student numbers. The grouping was based on an increasing additive order, and each of the groups were serially numbered. Using the computer-generated random system (http://www.random.org/integers/), two groups were selected for screening, one in the rural group and one in the urban group. The purpose of eye screening was to identify children with myopia and those with normal sight.

Free eye screening was conducted in each of the schools that formed part of the study in both rural and urban areas. The study population was subjected to visual acuity screening and all those who had visual acuity of 6/9 or worse in any of the two eyes qualified for the next stage of the examination. To avoid loss of school-time during the screening sessions, pre-arrangement was agreed upon with the school headteacher or principal for a make-up class for the children that were to be included in the study. Also, lunch plans to cater for extended hours for the children was provided in the study budget.

Permission was sought from the different authorities, namely the legal guardians of the children through the different school heads for each of the selected schools in the selected groups, the Sub-County education officers, and the county education officer before the commencement of the study. The final years optometry students were briefed on the research and they assisted in assessments and examination of the participants. Written informed consent/assent was obtained for all the adolescents

or from the legal guardians. For minors, permission was sought through the headteacher before conducting a detailed assessment. Ethical approval was granted by the ethical review committee of Masinde Muliro University of Science and Technology and the approval letter is available upon request. The consent had the full content of the study. The assessment included the steps below.

STEP 1

Visual acuity testing was done with all participants that formed part of the study. Those having a visual acuity of 6/9 or worse were subjected to the pinhole test to elicit if the refractive error was the reason for the reduced visual acuity. Those with visual acuity better than 6/6 were classified as normal. The children and their teachers (for minors) presenting as their legal proxies were counselled on their identified visual condition. The children were also informed of the importance of their continued participation in the study. Those with minor allergies or infections were dispensed free of charge (on the study budget).

STEP 2

Children presenting with Snellen VA of 6/9 or worse in any of the eyes underwent direct ophthalmoscopy using Keeler professional direct ophthalmoscope, to rule out any non-refractive ocular pathology. If any pathology was found, these children were excluded from the study. However, the children were referred to either the Academic Vision Centre or Sabatia Eye Hospital (SEH) which is the only eye hospital in the western part of Kenya. If no pathology was found, children underwent cycloplegic refraction, and where cycloplegia was not possible, non-cycloplegic Mohindra retinoscopy was performed, using a Keeler streak retinoscope, to elicit if the refractive error was myopia, while controlling for accommodation. If the participants had any other refractive error apart from myopia and myopic astigmatism in which the spherical equivalent was calculated, the participants or their legal guardians were counselled on the need for spectacle correction. They were also then excluded from the study and were referred to MMUST Academic Vision Centre (AVC) for spectacle correction that was subsidized.

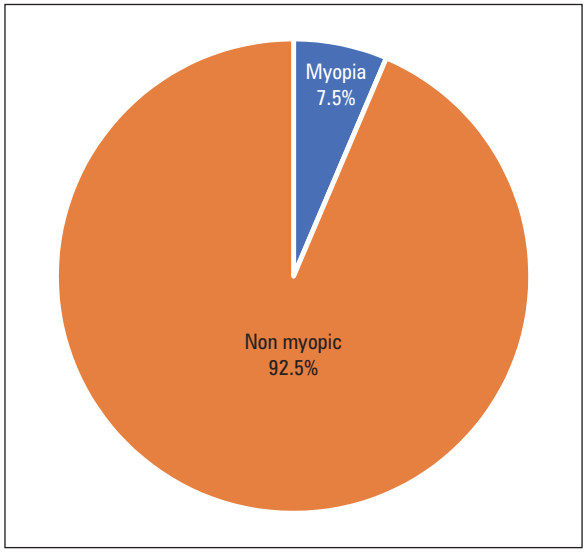

FIGURE 1. Prevalence of myopia

STEP 3

The basic socio-demographic data and contact details of the participants and their legal guardians were collected.

RESULTS

The current study sampled a total of 733 students, of whom 55 were found to be myopic giving an overall prevalence of 7.5% (Fig. 1). Of these students, 29 (52.7%) were male while 26 (47.3%) were female. Further details of the gender, domicile and age are presented in Table 1.

This study found the prevalence of myopia in males to be 29 (4.0%) while that of females was found to be 26 (3.5%). Myopia was found to be more prevalent in urban 49 (6.7%) as compared to the rural 6 (0.8%) schools (Tab. 4).

AGE AND MYOPIA

Myopia was found to occur in the range from 14 to 19 years while the most dominant age of

Table 1. Descriptive statistics for students

		Frequency	Percent
Gender	Female	326	44.5
	Male	407	55.5
Domicile	Rural	383	52.3
	Urban	349	47.6
Age	11–14 years	60	8.2
	15–18 years	520	70.9
	Above 18 years	153	20.9

Table 2. Distribution of myopia in terms of age

		Age							Total
		13.0	14.0	15.0	16.0	17.0	18.0	19.0	
Myopia	Count	0	3	7	15	12	9	9	55
	Percentage of total	0.0%	0.4%	1.0%	2.1%	1.6%	1.2%	1.2%	7.5%

Table 3. Magnitude of myopia distribution

Magnitude of myopia		Right eye n (%)	Left eye n (%)
Myopia values	–10.00	1 (1.8%)	2 (3.6%)
	–4.00	1 (1.8%)	1 (1.8%)
	–3.75	1 (1.8%)	1 (1.8%)
	–3.50	2 (3.6%)	3 (5.5%)
	–3.25	2 (3.6%)	1 (1.8%)
	–2.50	1 (1.8%)	1 (1.8%)
	–2.25	1 (1.8%)	1 (1.8%)
	–2.00	3 (5.5%)	3 (5.5%)
	–1.75	1 (1.8%)	2 (3.6%)
	–1.25	4 (7.3%)	3 (5.5%)
	–1.00	5 (9.1%)	5 (9.1%)
	–0.75	16 (29.1%)	16 (29.1%)
	–0.50	16 (29.1%)	16 (29.1%)
	–0.25	1 (1.8%)	0 (0%)
	Total	55 (100%)	

those who had myopia was found to be 16 years 15 (2.1%).

MAGNITUDE OF MYOPIA

About one third 16 (29.1%), of the participants, had mild (–0.50D) myopia while 16 (29.1%) had moderate myopia (–0.75D). One participant (1.8%) had –10.00DS.

SOCIAL-DEMOGRAPHIC DISTRIBUTION OF STUDY PARTICIPANTS

The socio-demographic characteristics, as shown in Table 1 found no association between gender and myopia ($p = 0.572$). Males constituted just over half of the study participants 29 (52.7%). The 15–18-year group was the dominant age group and there was no association between age and myopia ($p = 0.926$). In addition, most of the participants came from an urban setting 49 (87.3%) although there was no association between place of residence and myopia ($p = 0.381$).

There was no association between the school class group of the participants and having myopia ($p = 0.207$). Most of the participants who were myopic, were form four 15 (27.3%) although there was an equal distribution of myopia in terms of the class of the respondents. A significant number of the parents of the respondents 24 (43.6%) were unemployed and 39 (70.9%) were married. While 23 (41.8%) of the parents of the participants had primary and 22 (40.0%) had secondary education qualifications, there were no significant differences between the highest level of education and myopia ($p = 0.283$).

DISCUSSION

The overall prevalence of myopia in this study was found to be 7.5%, which is a higher value compared to previous studies [11] of 1.7%, [12] 5.6% and 1.7% of [13]. This can be attributed to the study population in this study as compared to other studies. It is well established that myopia is highly prevalent in adolescents as compared to other age groups (14). The high prevalence has been attributed to the eyeball elongation due to environmental factors such as near work and reduced outdoor activities [15].

Females and males in the study constituted 45% and 55% respectively of the total of 733 students who participated in the study. Myopia was found to be only slightly more prevalent in males 29 (52.7%) compared to females, 26 (47.3%). The difference in prevalence among male and female was not significant ($p = 0.576$). The study was concurrent with [11] that found that there was no statistically significant difference in the prevalence of myopia among females and males. Although a study by [13] found myopia to be slightly more prevalent in females compared to males at 1.8% and 1.7% respectively, the difference not to be statistically significant.

This study found that myopia was mostly prevalent in the age group of 15–18 years and the mean age of participants who were myopic was 16 years. This can be because of the eyeball elongation due to hereditary/familial or due to environmental or other causes that are related to the growth of the eye, specifical overgrowth of the eye and dis-correlation between axial length and cor-

Table 4. Cross-tabulation of socio-demographic factors with myopia				
Socio-demographic variable		**Myopia n (%)**	**Myopia percentage of total sample (n = 733)**	**p value**
Gender	Male	29 (52.7%)	29 (4.0%)	0.576
	Female	26 (47.3%)	26 (3.6%)	
Age	11–14 Years	5 (9.1%)	5 (0.6%)	0.926
	15–18 Years	39 (70.9%)	39 (5.3%)	
	Above 18 years	11 (20.0%)	11 (1.5%)	
Residence of the client	Urban	49 (89.0%)	49 (6.7%)	0.381
	Rural	6 (11.0%)	6 (0.8%)	
Current Class of The Respondent	Form One	15 (27.3%)	15 (2.0%)	0.207
	Form Two	15 (27.3%)	15 (2.0%)	
	Form Three	10 (18.1%)	10 (1.4%)	
	Form Four	15 (27.3%)	15 (2.0%)	
Parents'/Caregivers' occupation	Self-Employed	10 (18.2%)	10 (1.4%)	0.750
	Employed	13 (23.6%)	13 (1.8%)	
	Unemployed	24 (43.6%)	24 (3.2%)	
	Farming	8 (14.5%)	8 (1.1%)	
Parents' marital status	Married	39 (70.9%)	39 (5.3%)	0.507
	Divorced	6 (10.0%)	6 (0.8%)	
	Separated	10 (18.2%)	10 (1.4%)	
Fathers' education level	Primary	23 (41.8%)	23 (3.1%)	0.283
	Secondary	22 (40.0%)	22(3.0%)	
	Tertiary	10 (18.2%)	10(1.4%)	
Mothers' education level	Primary	22 (40.0%)	22(3.0%)	0.283
	Secondary	22 (40.0%)	22(3.0%)	
	Tertiary	11(10.0%)	11(1.5%)	

Data are presented as frequencies (n) and percentages (%), categorical variables were compared using Chi-square test. Significance set at $p < 0.05$

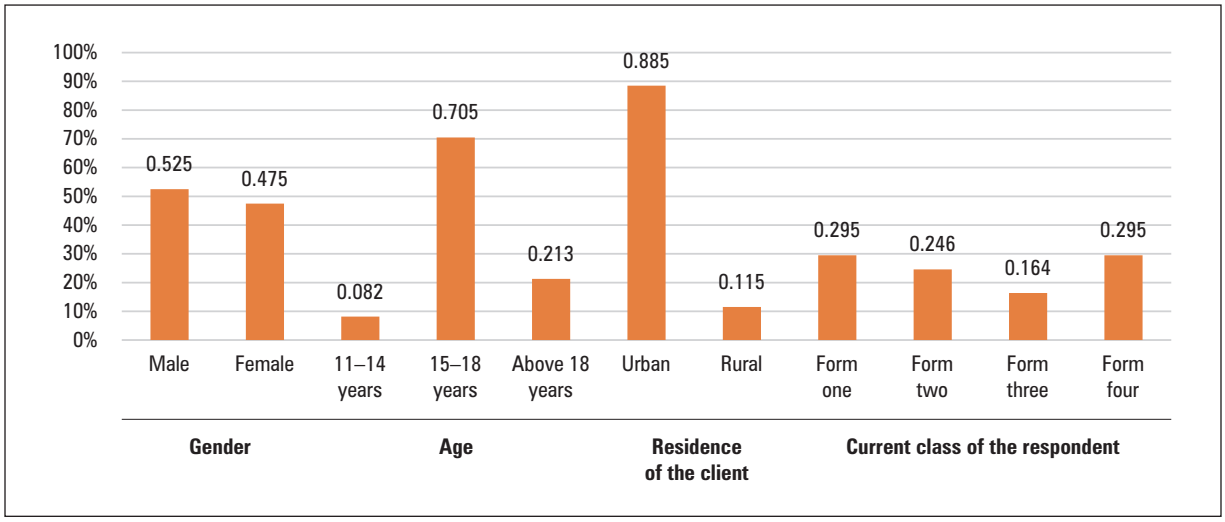

FIGURE 2. Student's socio-demographic factors cross-tabulation with myopia

neal curvature soon after puberty [16]. The finding of this study is slightly different to [3] study that was conducted in Uganda of myopia being highly prevalent in 11–14 yearsMost of the study population came from the rural area since the Kakamega county setting is mostly rural. The urban setting is located in the square radius of 10 kilometers from the town center. Most secondary schools are also found in a rural area with few schools found in the urban area. This study found that myopia was mostly prevalent in students that come from urban areas 49 (6.7%) compared to the students that come from rural areas 6 (0.8%) even though the most domiciled area was a rural area. These results are similar to a recent study [17], that found a higher prevalence of myopia in urban areas compared to the rural areas. Another study by [18] found that the prevalence of childhood myopia was lowest (6.9%) in the outer suburban region and highest (17.8%) in the inner-city region. Although the comparison of the prevalence of myopia in the two settings is difficult due to the impact of other confounding factors such as education, schooling and outdoor activities, these factors make it difficult to entirely associate the difference with the urban or rural environments alone. One suggestion for the reason for the high prevalence of myopia in urban setting has been attributed to the rise in technology and the increased usage of mobile phones, tablets, computers and televisions, especially among children and youths. This and the reduction in outdoor activities have been found to have some influence on the onset, development and progression of myopia [19]. Children in urban settings, in this era, spend less time with outdoor activities unlike children in the 1980's and early 1990's. This is due to the lack of playing grounds since most of the areas that were set aside in urban areas as children playing grounds are now high rise buildings. This has made children prefer indoor activities and indoor games instead of the outdoor games and activities [20].

The prevalence of myopia was found to increase with the older class of the respondents, from being least prevalent in lower forms to the higher prevalence in Form Four class. This can be attributed to the educational pressures in upper classes that are Forms Three and Four [21]. This can be equated to the global trends that have found myopia to be highly prevalent in those that are involved with intensive near work activities [22]. Educational pressure has been shown to have a significant relationship with myopia [23], since in order to get good grades one has to study hard which involves a lot of near related activities that have been found to sometimes have an influence on myopia [24].

CONCLUSION AND RECOMMENDATIONS

The prevalence of myopia in this study was found to be 7.5% and was higher in males as compared to females. It was also found to be more prevalent in those aged 11–15 years of age. Most of those who were found to be affected were those from urban areas and the prevalence was higher in the upper school level classes compared to those in lower classes. Although there was no association between socio-demographic (gender, age, class of respondent and place of residence) with myopia the prevalence tends to demonstrate a clear increase with age.

It is recommended that further studies be conducted on other risk factors such as near work activities, the use of new technologies and increasing time spent indoors and how they may influence myopia

Acknowledgements

I take this opportunity to pass my appreciation to Masinde Muliro University of Science and Technology, particularly, the Department of Optometry and Vision Science — I am very grateful for the logistical support and opportunity given to me to undertake this academic endeavour. I acknowledge the contribution of research assistants.

Authors' contributions

This research was undertaken for the MSc in Optometry and Vision Science degree. A.R. was the project leader responsible for the experimental and project design under the supervision of M.B. and P.C.F. AR conducted the clinical research while M.B. and P.C.F. provided guidance on study design, methodology and research procedures. A.R. was responsible for the writing of this paper with support and editorial input from M.B. and P.C.F.

Disclosures about a potential conflict of interests

I declare that there is no conflict of interest in this study.

REFERENCES

1. Naidoo KS, Fricke TR, Frick KD, et al. Potential Lost Productivity Resulting from the Global Burden of Myopia: Systematic Review, Meta-analysis, and Modeling. Ophthalmology. 2019; 126(3): 338–346, doi: 10.1016/j.ophtha.2018.10.029, indexed in Pubmed: 30342076.

2. Bourne R, Flaxman SR, Braithwaite TB, et al. Vision Loss Expert Group of the Global Burden of Disease Study. Magnitude, temporal trends, and projections of the global prevalence of blindness and distance and near vision impairment: a systematic review and meta-analysis. Lancet Glob Health. 2017; 5(9): e888–e897, doi: 10.1016/S2214-109X(17)30293-0, indexed in Pubmed: 28779882.
3. Bourne RRA, Stevens GA, White RA, et al. Vision Loss Expert Group. Causes of vision loss worldwide, 1990-2010: a systematic analysis. Lancet Glob Health. 2013; 1(6): e339–e349, doi: 10.1016/S2214-109X(13)70113-X, indexed in Pubmed: 25104599.
4. Holden BA, Fricke TR, Wilson DA, et al. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016; 123(5): 1036–1042, doi: 10.1016/j.ophtha.2016.01.006, indexed in Pubmed: 26875007.
5. Holden B, Sankaridurg P, Smith E, et al. Myopia, an underrated global challenge to vision: where the current data takes us on myopia control. Eye (Lond). 2014; 28(2): 142–146, doi: 10.1038/eye.2013.256, indexed in Pubmed: 24357836.
6. Pan CW, Ramamurthy D, Saw SM. Worldwide prevalence and risk factors for myopia. Ophthalmic Physiol Opt. 2012; 32(1): 3–16, doi: 10.1111/j.1475-1313.2011.00884.x, indexed in Pubmed: 22150586.
7. Morgan PB, Efron N, Woods CA, et al. International Contact Lens Prescribing Survey Consortium. International survey of orthokeratology contact lens fitting. Cont Lens Anterior Eye. 2019; 42(4): 450–454, doi: 10.1016/j.clae.2018.11.005, indexed in Pubmed: 30448008.
8. Wong HB, Machin D, Tan SB, et al. Visual impairment and its impact on health-related quality of life in adolescents. Am J Ophthalmol. 2009; 147(3): 505–511.e1, doi: 10.1016/j.ajo.2008.09.025, indexed in Pubmed: 19056077.
9. Barasa E, Otieno S, Karimurio J. The prevalence and pattern of visual impairment and blindness among Primary School pupils in Kitale Municipality, Kenya. J Ophthalmol East Cent South African. 2013; October: 66–70.
10. Nyamai LA. Prevalence, Knowledge, Attitude and Practice on Refractive error among Students attending Public High Schools in Nairobi County. Dep Ophthalmol. 2016; October: 109.
11. Bastawrous A, Mathenge W, Foster A, et al. Prevalence and predictors of refractive error and spectacle coverage in Nakuru, Kenya: a cross-sectional, population-based study. Int Ophthalmol. 2013; 33(5): 541–548, doi: 10.1007/s10792-013-9742-6, indexed in Pubmed: 23440405.
12. Wedner SH, Ross DA, Balira R, et al. Prevalence of eye diseases in primary school children in a rural area of Tanzania. Br J Ophthalmol. 2000; 84(11): 1291–1297, doi: 10.1136/bjo.84.11.1291, indexed in Pubmed: 11049957.
13. Nzuki HN. Significant refractive errors as seen in standard eight pupils attending public schools in Langata division. Nairobi 2004.
14. Rey-Rodríguez D, Álvarez-Peregrina C, Moreno-Montoya J. Prevalencia y factores asociados a miopía en jóvenes. Rev Mexic Oftalmol. 2017; 91(5): 223–228, doi: 10.1016/j.mexoft.2016.06.007.
15. Ho T, Nallasamy S. Myoia: Eidemiology and Strategies for Intervention. Vol. 2, Advances in Ohthalmology and Otometry. Elsevier Inc 2017: 63–74.
16. Morgan IG, Rose KA. Myopia: is the nature-nurture debate finally over? Clin Exp Optom. 2019; 102(1): 3–17, doi: 10.1111/cxo.12845, indexed in Pubmed: 30380590.
17. Ip J, Saw SM, Rose K, et al. Role of Near Work in Myopia: Findings in a Sample of Australian School Children. Invest Opthalmol Vis Sci. 2008; 49(7): 2903, doi: 10.1167/iovs.07-0804, indexed in Pubmed: 18579757.
18. Ip JM, Rose KA, Morgan IG, et al. Myopia and the urban environment: findings in a sample of 12-year-old Australian school children. Invest Ophthalmol Vis Sci. 2008; 49(9): 3858–3863, doi: 10.1167/iovs.07-1451, indexed in Pubmed: 18469186.
19. Hsu CC, Huang N, Lin PY, et al. Prevalence and risk factors for myopia in second-grade primary school children in Taipei: A population-based study. J Chin Med Assoc. 2016; 79(11): 625–632, doi: 10.1016/j.jcma.2016.02.011, indexed in Pubmed: 27349942.
20. You QiS, Wu LiJ, Duan JLi, et al. Factors associated with myopia in school children in China: the Beijing childhood eye study. PLoS One. 2012; 7(12): e52668, doi: 10.1371/journal.pone.0052668, indexed in Pubmed: 23300738.
21. Li SM, Li He, Li SY, et al. Anyang Childhood Eye Study Group. Time Outdoors and Myopia Progression Over 2 Years in Chinese Children: The Anyang Childhood Eye Study. Invest Ophthalmol Vis Sci. 2015; 56(8): 4734–4740, doi: 10.1167/iovs.14-15474, indexed in Pubmed: 26207310.
22. Sun JT, An M, Yan XBo, et al. Prevalence and Related Factors for Myopia in School-Aged Children in Qingdao. J Ophthalmol. 2018; 2018: 9781987, doi: 10.1155/2018/9781987, indexed in Pubmed: 29507811.
23. Bez D, Megreli J, Bez M, et al. Association Between Type of Educational System and Prevalence and Severity of Myopia Among Male Adolescents in Israel. JAMA Ophthalmol. 2019 [Epub ahead of print], doi: 10.1001/jamaophthalmol.2019.1415, indexed in Pubmed: 31145422.
24. Wu LJ, Wang YX, You QS, et al. Risk Factors of Myopic Shift among Primary School Children in Beijing, China: A Prospective Study. Int J Med Sci. 2015; 12(8): 633–638, doi: 10.7150/ijms.12133, indexed in Pubmed: 26283882.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0016

Microbiology of the conjunctival sac before and after cataract surgery

Patrycja Kuklo[1], Andrzej Grzybowski[2]

[1]Department of Ophthalmology, University of Warmia and Mazury, Olsztyn, Poland
[2]Institute for Research in Ophthalmology, Poznan, Poland

ABSTRACT

BACKGROUND: The aim of the study was to evaluate the bacterial flora and antibiotic susceptibility profile of bacterial isolates taken from the conjunctival sacs of patients undergoing phacoemulsification cataract surgery, and to compare them.

MATERIAL AND METHODS: In total, 200 conjunctival swabs were collected from 50 patients between June and December of 2017.

RESULTS: The most common pathogen collected from the conjunctival sacs before surgery was coagulase-negative *staphylococci* (CoNS) (65% of swabs); 45 of them (45%) were methicillin-sensitive *staphylococci* (MS-CoNS) and 25 (25%) were methicillin-resistant *staphylococcus* (MR-CoNS). Following the surgeries, CoNS were collected from 34 swabs (34%), 16% of which were taken from the eye on which the operation had been performed. Twenty-three swabs (23%) were MS-CoNS and 11 (11%) were MR-CoNS. The number of CoNS-positive swabs after pharmacotherapy decreased by 52%. The possibility of obtaining sterile swabs was statistically and significantly higher in eyes in which chemoprophylaxis was used [(OR = 4.58, 95% CI: 2.91–7.21), $p < 0.001$)]. The possibility of obtaining sterile swabs was not correlated with gender ($p = 0.866$) or diabetes ($p = 0.712$), but was observed more frequently in younger patients ($p = 0.001$). Multi-drug resistant bacteria were detected in 34 swabs before surgery (34%) and in 26 samples after operations (26%).

CONCLUSION: It is probably impossible to sterilise the conjunctival sac. There is a risk of multi-drug resistant bacterial flora colonising the conjunctival sac.

KEY WORDS: conjunctival sac; cataract surgery; antibiotic susceptibility profile

Ophthalmol J 2020; Vol. 5, 71–75

INTRODUCTION

Endophthalmitis is rare, but it is one of the most devastating complications following cataract surgery, with a recorded frequency of 0.087% in 1990 and 0.265% after 2000 [1]. It can have heterogeneous etiologies and variable clinical manifestations, with a high risk of blindness, irreversible changes in the anatomy of the eye or even the loss of the eyeball. It is known that post-cataract endophthalmitis is caused by bacteria being transferred into the eyeball from the conjunctival sac, the eyelids, the eyelashes or the periorbital skin [2]. All these areas are colonised physiologically by bacteria. During operation, they are transferred to the normally sterile anterior chamber, which can be a risk factor for endophthalmitis [3]. The aim of this study was to describe the microbiological profile of the conjunctival sac before and after cataract surgery and to assess how perioperative prophylaxis affects changes in the bacterial flora.

MATERIAL AND METHODS

From June to December 2017, 200 conjunctival swabs were collected from 50 patients undergoing

CORRESPONDING AUTHOR:
Patrycja Kuklo, MD, Department of Ophthalmology, University of Warmia and Mazury, ul. Żołnierska 18, 10–900 Olsztyn, Poland, tel: (+48) 89 538 64 05; e-mail: patrycjakuklo@uwm.edu.pl

Copyright © 2020 Via Medica, ISSN 2450–7873

phacoemulsification cataract surgery. Four swabs were obtained from each patient. The first two swabs from each eye were collected on admission to the hospital before any eye-drops were administered. The second two samples were taken from each eye 20 minutes after the cataract surgery. Each patient received either four drops of topical 0.3% ofloxacin every 15 minutes one hour before surgery in the eye to be operated upon, or two drops of antibiotic on the day of admission and another two drops the next day, 30 and 15 minutes before surgery, respectively. Concomitant medications to the operated eye contained one drop of 1% tropicamide, one drop of 10% phenylephrine and one drop of diclofenac. Routine prophylaxis in the operating theatre included a 5% povidone-iodine solution for surface disinfection of the eyelids and skin around the orbit, 5% povidone-iodine for three minutes administered to the conjunctival sac before operation, and intracameral injection of 1 mg 0.1 mL cefuroxime at the end of the procedure. On the day of admission, one drop of 1% tropicamide was administered to the eye that was not to be operated upon as part of the routine examination. The exclusion criteria included topical and systemic antibiotic therapy one month prior to the surgery, glaucoma that was being treated with eye-drops, keratoconjunctivitis sicca, and orbital or ocular inflammation one month prior to the surgery. The same examiner collected all the samples in this study, thus ensuring that the collecting procedure was consistent for all the samples taken. All the tests were analysed in the same microbiological laboratory. All the patients signed an informed consent form approved by the local ethics committee.

Table 1. Descriptive characteristics of the study cohort (n = 49)

Trait	Statistics
Sex	
Females, n (%)	31 (62.0)
Males, n (%)	19 (38,0)
Age (years)	
Overall, mean (SD)	71.81 (8.86)
Females, mean (SD)	73.91 (7.69)
Males, mean (SD)	68.05 (9.76)
Diabetes mellitus, n (%)	15 (30.0)
Eye operated	
Left, n (%)	28 (56.0)
Right, n (%)	22 (44.0)

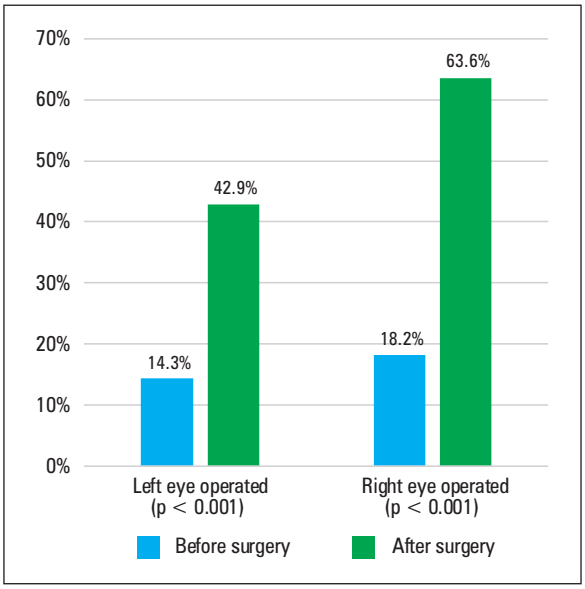

FIGURE 1. Sterility of conjunctival sac before and after cataract surgery in the examined patient who had undergone chemoprophylaxis by operated eye ($p < 0.001$)

RESULTS

Forty-nine patients were included in the study. Thirty one were female (61.0%) and 19 were male (38.0%). The mean age of the patients was 71.81 (SD = 8.86 years). The female group was statistically significantly older than was the male group. The mean age of the female group was 73.91 (SD = 7.69), while it was 68.05 (± 9.76) for the male group ($p = 0.031$). Thirty per cent of the patients were diabetic. Twenty-seven patients (19 females and eight males) operation to the left eye, and 22 patients (12 females and 10 males) to the right eye, ($p = 0.389$). Two hundred conjunctival swabs were collected. Sterile samples were collected from 14 eyes (14%) prior to the operations. Following the surgeries, sterile samples were obtained from 26 (52.0%) that had been operated upon and from 20 (40%) that had not. The possibility of obtaining sterile swabs was statistically significantly higher for eyes in which chemoprophylaxis had been used (OR = 4.58, 95% CI: 2.91–7.21; $p < 0.001$). A multifactor analysis with repeatable measurements showed that the possibility of obtaining sterile swabs was not correlated with gender ($p = 0.866$) or diabetes ($p = 0.712$), but was observed statistically more frequently in younger patients ($p = 0.001$). No patient developed endophthalmitis after surgery (Tab. 1, Fig. 1).

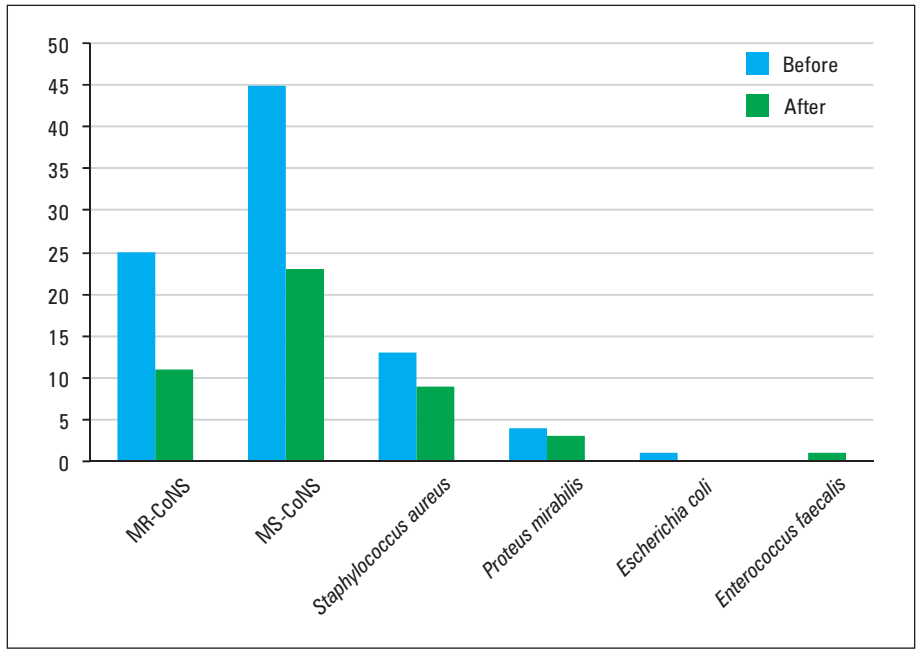

FIGURE 2. Percentage of bacteria cultured from the operated eye before and after cataract surgery. MR-CoNS — methicillin-resistant coagulase negative *Staphylococci*; MS-CoNS — methicillin-sensitive coagulase negative *Staphylococci*

Prior to the operations, CoNS were cultured from 65 samples (65% of the swabs collected before the surgeries). Of them, 45 (45%) were methicillin-sensitive (MS-CoNS) and 25 (25%) were methicillin-resistant *Staphylococci* (MR-CoNS). After the surgeries, CoNS were obtained from 16 eyes that had been operated upon (16%) and from 18 (18%) that had not. Twenty-three (23%) were MS-CoNS and 11 (11%) were MR-CoNS. The number of CoNS-positive swabs after pharmacotherapy decreased by 52%. *Staphylococcus aureus* was cultured from 13 (13%) swabs obtained prior to the operations (five from the eyes that would be operated upon and eight from the eyes that would not) and in nine (9%) samples following the surgeries. Three (3%) positive samples were obtained from eyes that had received operations. Other pathogens cultivated before the surgeries included *Proteus mirabilis* from four (4%) swabs and *Escherichia coli* from one swab (1%). After the operations, *Proteus mirabilis* was cultured from three (3%) samples and *Enterococcus faecalis* from one (1%) sample taken from the eyes that had been operated upon. *Proteus mirabilis* was cultured from one (1%) swab, Klebsiella spp. from one (1%) swab, and Enterobacter cloacae from one (1%) swab taken from the eyes that had not been operated upon. The patient with *Klebsiella spp*. was hospitalised for one day prior to the surgery, and the patient with *Enterobacter cloacae* was operated upon on the day of admission. Multi-drug resistant bacterial flora was detected in 34 (34%) of the swabs taken before the surgeries, and in 26 (26%) of the swabs taken following the operations from both the eyes that had been operated upon and those that had not. Multi-drug resistant CoNS were detected in 18 (18%) swabs. Amongst the diabetic patients, the bacterial flora contained CoNS in 23 swabs (47% of the samples from the diabetic patients versus 53% from the non-diabetic patients), *Staphylococcus aureus* in eight swabs (16% versus 8%) and *Escherichia coli* in one swab taken from a diabetic patient (Fig.2).

Sensitivity testing was performed for all the swabs. Prior to the surgeries, bacteria sensitive to all antibiotics were collected from 35 swabs (35% samples taken before the operations); resistance to erythromycin was detected in 28 (28%) swabs, to cloxacillin in 21 (21%), to tobramycin in 19 (19%), to gentamicin in 12 (12%), to tetracycline in 12 (12%), to ciprofloxacin in seven (7%), to levofloxacin in six (6%), to moxifloxacin in four (4%), and to ofloxacin in seven (7%) swabs. After the operations, bacteria sensitive to all antibiotics were collected from 23 eyes (23%). Resistance to tobramycin was found in 20 swabs (20%), to erythromycin in 16 (16%), to cloxacylin in 15 (15%), to gentamicin in 13 (13%), to ciprofloxacin in nine (9%), to tetracycline in

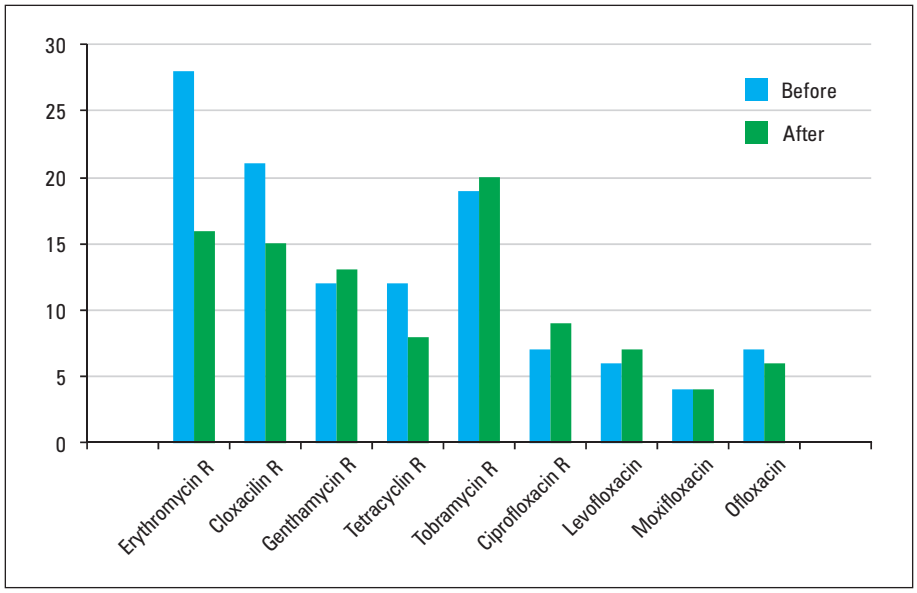

FIGURE 3. Bacteria susceptibility before and after the operation

eight (8%), to levofloxacin in seven (7%), to amikacin in six (6%), to ofloxacin in six (6%), and to moxifloxacin in four (4%) swabs. The number of bacteria resistant to gentamicin, tobramycin, ciprofloxacin and levofloxacin increased after the operations (12% *vs.* 13%, 19% *vs.* 20%, 7% *vs.* 9%, and 6% *vs.* 7%, respectively). The number of bacteria resistant to moxifloxacin was the same before and after the operations. A lower number of pathogens resistant to erythromycin, cloxacilline and tetracycline was observed. Multi-drug resistant bacteria were detected in 34 (34%) swabs prior to the surgeries and in 26 (26%) of the samples after the operations (Fig. 3).

DISCUSSION

In our study, the possibility of obtaining sterile swabs was statistically significantly higher from eyes in which chemoprophylaxis had been used. The possibility of obtaining sterile swabs was not linked to gender or diabetes, but was observed more frequently in younger patients. The most common bacterium collected from the conjunctival sacs before and after the operations was CoNS (65% before the operation versus 34% after the surgery). The other pathogens were *Staphylococcus aureus*, *Proteus mirabilis*, *Escherichia coli*, *Enterococcus faecalis*, *Klebsiella spp.*, and *Enterobacter cloacae*. The profiles of the collected microorganisms changed after the operations, which also led to changes in the antibiograms, with higher antibiotic resistance following the operations. Multi-drug resistant bacteria were detected in 34 (34%) swabs before surgery and in 26 (26%) samples after operation. Gram-positive CoNS (particularly *Staphylococcus epidermidis*) were the most common bacterial flora isolated from eyes with post-cataract endophthalmitis [4, 5]. The EVS study showed that the percentage of Gram-positive coagulase-negative bacteria isolated from postoperative endophthalmitis was 46.9% [6]. In our study, the most frequently isolated microorganism taken from the conjunctival sac before and after cataract surgery was coagulase-negative staphylococcus. This type of bacteria occurs naturally in the conjunctival sac and on the surrounding skin and lashes [5] and does not cause infection in these areas. Other Gram-positive microorganisms isolated from the conjunctiva constituted 15% [6]. In our study, they were collected from 13 (13%) swabs prior to the operations and from nine (9%) swabs after the surgeries. The frequency of isolated microorganisms in our analysis is comparable to the frequency of pathogens isolated from eyes after endophthalmitis [6]. Hori et al. [7] noted the appearance of multi-drug resistant CoNS in conjunctival swabs taken prior to surgery. In our study, these pathogens were found in a high percentage of swabs taken both before (34% samples) and after surgery (26%). This is potentially a serious problem because most of the antibiotics used in ophthalmology are useless in the treatment of infections based on this aetiology. Moreover, perioperative antibiotherapy is a potential risk factor for increased antibiotic resistance [8].

A correlation between diabetes mellitus and a greater risk of positive conjunctival swabs was confirmed in previous studies [9, 10]. An increased prevalence of specific conjunctival bacterial flora, such as *Staphylococcus aureus*, *Enterococci* and *Klebsiella spp*., was also observed in diabetic patients. A greater incidence of positive cultured swabs was not confirmed in our study; however, the diabetic patients' bacterial flora contained CoNS in 23 swabs (47% of the samples taken from diabetic patients), *Staphylococcus aureus* in swabs (16%) and *Escherichia coli* in one swab. The ages and genders of the patients were identified as risk factors contributing to the cultured swabs that were positive in the previous studies [11, 12], but only younger patients had a lower risk of positive swabs taken from the conjunctiva in our study.

The intracameral concentration of topical preoperative antibiotics is too low to decrease the number of the most common microorganisms [13], and the ability of the most common conjunctival bacteria to form a biofilm [14] can reduce the effectiveness of perioperative antibiotherapy significantly.

In our study, sterile swabs were collected from 19% of the eyes before and 47% of the eyes after the operations. This does not necessarily imply sterility in those eyes. No treatment was administered and the patients did not receive any eye-drops in 19% of the sterile swabs that were collected before the operations. Considering the types of bacteria, some of the positive swabs that were taken after the operations could have been contaminated by the surrounding skin during the collection of the samples and could have been the result of the patient having poor hygiene.

Although a limitation of this study was the small sample size, the sample size is comparable to sample sizes in previous publications [7, 9–12].

CONCLUSION

Perioperative chemotherapy changes the profile of conjunctival bacteria and their susceptibility to antibiotics. Chemoprophylaxis increases the possibility of obtaining sterile swabs after an operation, but it also changes the profile of the bacteria in the conjunctival sac. It is probably impossible to sterilise the conjunctival sac. There is a risk that the conjunctival sac will be colonised by multi-drug resistant bacterial flora.

Conflict of interests

The authors declare that there is no conflict of interest.

REFERENCES

1. Taban M, Behrens A, Newcomb RL, et al. Acute endophthalmitis following cataract surgery: a systematic review of the literature. Arch Ophthalmol. 2005; 123(5): 613–620, doi: 10.1001/archopht.123.5.613, indexed in Pubmed: 15883279.
2. Bannerman TL, Rhoden DL, McAllister SK, et al. The source of coagulase-negative staphylococci in the Endophthalmitis Vitrectomy Study. A comparison of eyelid and intraocular isolates using pulsed-field gel electrophoresis. Arch Ophthalmol. 1997; 115(3): 357–361, doi: 10.1001/archopht.1997.01100150359008, indexed in Pubmed: 9076208.
3. Leong J, Shah R, McCluskey P, et al. Bacterial contamination of the anterior chamber during phacoemulsification cataract surgery. J Cataract Refract Surg. 2002; 28(5): 826–833, doi: 10.1016/s0886-3350(01)01160-9, indexed in Pubmed: 11978463.
4. Keynan Y, Finkelman Y, Lagacé-Wiens P. The microbiology of endophthalmitis: global trends and a local perspective. Eur J Clin Microbiol Infect Dis. 2012; 31(11): 2879–2886, doi: 10.1007/s10096-012-1659-x, indexed in Pubmed: 22664925.
5. HAN D, WISNIEWSKI S, WILSON L, et al. Spectrum and Susceptibilities of Microbiologic Isolates in the Endophthalmitis Vitrectomy Study. Am J Ophthalmol. 1996; 122(1): 1–17, doi: 10.1016/s0002-9394(14)71959-2, indexed in Pubmed: 8659579.
6. Results of the Endophthalmitis Vitrectomy Study. Arch Ophthalmol. 1995; 113(12): 1479, doi: 10.1001/archopht.1995.01100120009001, indexed in Pubmed: 7487614.
7. Hori Y, Nakazawa T, Maeda N, et al. Susceptibility comparisons of normal preoperative conjunctival bacteria to fluoroquinolones. J Cataract Refract Surg. 2009; 35(3): 475–479, doi: 10.1016/j.jcrs.2008.11.049, indexed in Pubmed: 19251140.
8. Simunovic MP, Rush RB, Hunyor AP, et al. Endophthalmitis following intravitreal injection versus endophthalmitis following cataract surgery: clinical features, causative organisms and post-treatment outcomes. Br J Ophthalmol. 2012; 96(6): 862–866, doi: 10.1136/bjophthalmol-2011-301439, indexed in Pubmed: 22446145.
9. Fernández-Rubio ME, Rebolledo-Lara L, Martinez-García M, et al. The conjunctival bacterial pattern of diabetics undergoing cataract surgery. Eye (Lond). 2010; 24(5): 825–834, doi: 10.1038/eye.2009.218, indexed in Pubmed: 19713978.
10. Hoshi S, Hashida M, Urabe K. Risk factors for aerobic bacterial conjunctival flora in preoperative cataract patients. Eye (Lond). 2016; 30(11): 1439–1446, doi: 10.1038/eye.2016.143, indexed in Pubmed: 27419840.
11. Rubio EF. Climatic influence on conjunctival bacteria of patients undergoing cataract surgery. Eye (Lond). 2004; 18(8): 778–784, doi: 10.1038/sj.eye.6701352, indexed in Pubmed: 15002018.
12. Hoshi S, Hashida M, Urabe K. Risk factors for aerobic bacterial conjunctival flora in preoperative cataract patients. Eye (Lond). 2016; 30(11): 1439–1446, doi: 10.1038/eye.2016.143, indexed in Pubmed: 27419840.
13. Donnenfeld ED, Comstock TL, Proksch JW. Human aqueous humor concentrations of besifloxacin, moxifloxacin, and gatifloxacin after topical ocular application. J Cataract Refract Surg. 2011; 37(6): 1082–1089, doi: 10.1016/j.jcrs.2010.12.046, indexed in Pubmed: 21596251.
14. Kıvanç SA, Kıvanç M, Bayramlar H. Microbiology of corneal wounds after cataract surgery: biofilm formation and antibiotic resistance patterns. J Wound Care. 2016; 25(1): 12, 14–9, doi: 10.12968/jowc.2016.25.1.12, indexed in Pubmed: 26762493.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0017

Blood cell ratios in patients with primary acquired nasolacrimal duct obstruction

Mahmut Atum, Gürsoy Alagöz

Department of Ophthalmology, Sakarya University Education and Research Hospital, Sakarya, Turkey

ABSTRACT

BACKGROUND: In this study, we aimed to measure neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and mean platelet volume (MPV) levels in primary acquired nasolacrimal duct obstruction (PANDO) patients and to determine whether there it could be used as a marker for PANDO.

MATERIAL AND METHODS: This retrospective study included 61 patients with PANDO and 65 healthy controls. Data were excluded from the file records of patients who underwent external dacryocystorhinostomy (DCR). Blood samples were obtained from venous blood and serum neutrophil, lymphocyte, and platelet data of all patients were recorded and also, NLR-PLR values were calculated.

RESULTS: There was no significant difference between PANDOs and controls in terms of gender and age ($p > 0.05$). Neutrophil-to-lymphocyte was significantly increased in PANDOs compared to the controls ($p < 0.05$). There was no statistically significant difference between PANDOs and controls in term of PLR ($p > 0.05$). The average MPV in the PANDOs was found to be significantly lower than controls ($p < 0.05$)

CONCLUSION: Neutrophil-to-lymphocyte ratio and MPV counts were associated with PANDO.

KEY WORDS: neutrophil-to-lymphocyte ratio; platelet-to-lymphocyte ratio; mean platelet volume; primary acquired nasolacrimal duct obstruction

Ophthalmol J 2020; Vol. 5, 76–80

INTRODUCTION

Epiphora develops after obstruction of nasolacrimal canal and this condition is common in society. Acquired nasolacrimal duct obstructions are divided into two; primary and secondary. Primary acquired nasolacrimal duct obstruction (PANDO) is the most common type and especially seems after the age of 50 years. Primary acquired nasolacrimal duct obstruction is known to be more common in women than men (3-fold) [1]. Pathological studies showed that PANDO develops as a result of fibrous obstruction secondary to chronic inflammation [2–4].

Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), calculated from hemogram are systemic inflammatory responses. Many different studies published before have shown that NLR and PLR are indicative of systemic inflammation [5–10].

Mean platelet volume (MPV) is a parameter that indicates the status of platelets, and MPV is associated with inflammation [11].

According to our literature review, there are different studies researched the association between NLR, MPV, PLR and many diseases but, there was no study to measure/examine NLR, MPV, PLR levels in PANDO disease. In this study, we purposed to measure NLR, PLR and MPV levels in PANDO patients and to determine whether there is a significant change.

CORRESPONDING AUTHOR:
Mahmut Atum, Department of Ophthalmology, Sakarya University Education and Research Hospital, Korucuk Mah. 54100 Sakarya, Turkey, tel: (+90) 555 809 62 75; e-mail: mahmutatum@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

MATERIAL AND METHODS

This retrospective case-control study was conducted at Sakarya University Training and Research Hospital, Ophthalmology Clinic between January and November 2019. Data were excluded from the file records of patients who underwent external dacryocystorhinostomy (DCR) between January 2017 and November 2018. Our study was carried out according to the ethical principles set out in the Helsinki Declaration and the consent was obtained from Sakarya University Medical School Ethics Committee. The study included 61 patients with PANDO and 65 healthy controls. Healthy control patients consisted of persons with senile cataract or refractive error in ophthalmology outpatient clinic. Age and sex-matched in two groups.

Criteria for inclusion were: patients with PANDO and operated by standard external DCR technique. Criteria for exclusion were: traumatic etiology, cancer history, systemic diseases (such as cardiovascular diseases and diabetes), history of cerebrovascular disease, blood diseases, acute/chronic kidney failure.

Hemogram parameters of all cases were measured by Cell-DYN 3700 (Cell-DYN 3700, Abbott Diagnostics, Abbott Park, IL, USA) automated hematology analyzer. According to the results of hemogram; neutrophil, lymphocyte, MPV and platelet counts of all the cases were recorded and NLR-PLR values were calculated.

STATISTICAL ANALYSIS

Data analyzed due to the SPSS software (version 17.0, SPSS Inc., Chicago, IL, USA) program. Data were also reported as mean and standard deviation (± SD). Comparison of the independent groups was done by parametric Student t-test. The cut-off point between PANDOs and controls determined due to receiver operating characteristic (ROC) curve analysis. According to the cut-off value, sensitivity and specificity values were calculated. $P < 0.05$ was considered significant.

RESULTS

Our study consisted of a total of 126 people, including 61 patients with PANDO and 65 healthy controls. The gender distribution of patients in PANDOs and controls was 17 male/44 female and 23 male/42 female, respectively. The mean age of the PANDOs was 53.21 ± 14.23 years and the controls were 55.29 ± 8.60 years. Primary acquired nasolacrimal duct obstruction group and controls were similar in terms of gender, age, and systemic diseases (diabetes, hypertension) ($p > 0.05$) (Tab. 1).

The mean WBC count was 7.44 ± 2.07 10^9/L in the PANDOs and 7.28 ± 2.18 10^9/L in the controls and the difference between the groups was not significant ($p = 0.678$). The mean neutrophil count was 4.34 ± 1.60 10^9/L in the PANDOs and 3.94 ± 1.44 10^9/L in the controls and the difference between the groups was not significant ($p = 0.146$). The mean lymphocyte count was 2.34 ± 0.74 10^9/L in the PANDOs and 2.54 ± 1.05 10^9/L in the controls and the difference between the groups was not significant ($p = 0.232$).

The mean platelet count was 245.72 ± 57.04 10^9/L in the PANDOs and 246.27 ± 56.42 10^9/L in the controls and the difference between the groups was not significant ($p = 0.956$). The mean NLR was 1.99 ± 0.89 in the PANDOs and 1.69 ± 0.66 in the controls. NLR was significantly higher in the PANDOs than in the controls ($p = 0.032$). The mean PLR was 112.74 ± 35.93 in the PANDOs and 108.77 ± 40.05 in the controls and the difference between the groups was not significant ($p = 0.560$). The mean MPV was 8.00 ± 1.55 fL in the PANDOs and 9.01 ± 1.77 fL in the controls. MPV was signifi-

Table 1. Demographic features in the primary acquired nasolacrimal duct obstruction (PANDO) and control groups

	PANDO (n = 61)	Control (n = 65)	p*
Age (years)	53.21 ± 14.23	55.29 ± 8.60	0.320
Sex			0.369
Male	17	23	
Female	44	42	
DM	6	10	0.354
HT	7	10	0.525

DM — diabetes mellitus; HT — hypertension; *independent samples t-test

Table 2. Laboratory findings in the primary acquired nasolacrimal duct obstruction (PANDO) and control groups

	PANDO (n = 61)	Control (n = 65)	p*
WBC [10^9/L]	7.44 ± 2.07	7.28 ± 2.18	0.678
Neutrophil [10^9/L]	4.34 ± 1.60	3.94 ± 1.44	0.146
Lymphocyte [10^9/L]	2.34 ± 0.74	2.54 ± 1.05	0.232
Platelet [10^9/L]	245.72 ± 57.04	246.27 ± 56.42	0.956
NLR	1.99 ± 0.89	1.69 ± 0.66	0.032
PLR	112.74 ± 35.93	108.77 ± 40.05	0.560
MPV [fL]	8.00 ± 1.55	9.01 ± 1.77	0.001

WBC — white blood cell; NLR — neutrophil-to-lymphocyte ratio; PLR — platelet-to-lymphocyte ratio; MPV — mean platelet volume; *independent samples t test

Table 3. Receiver operating characteristic (ROC) curve analyses of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and mean platelet volume (MPV) in primary acquired nasolacrimal duct obstruction (PANDO)

	AUC	Cut off	Sensitivity	Specificity
NLR	0.597	1.77	0.57	0.62
PLR	0.536	107.99	0.55	0.53
MPV	0.735	8.22	0.70	0.72

AUC — area under curve

cantly decreased in the PANDOs than the controls (p = 0.001) (Tab. 2).

In the ROC analysis, area under curve (AUC) for NLR was 0.597, the cut-off value was 1.77, the sensitivity was 57%, and the specificity was 62% (95% CI: 0.498–0.696). The area under curve for PLR was 0.536, the cut-off value was 107.99, the sensitivity was 55%, and the specificity was 53% (95% CI: 0.434–0.637). The AUC for MPV was 0.735, the cut-off value was 8.22, the sensitivity was 70%, and the specificity was 72% (95% CI: 0,645–0,824) (Tab. 3).

DISCUSSION

According to studies in the literature, this is the first study investigating the relationship between NLR, PLR, MPV and PANDO. The present study showed us that NLR and MPV were associated with PANDO; however, the relationship between PLR and PANDO was not seen in this study.

Primary acquired nasolacrimal duct obstruction is the main cause of nasolacrimal duct obstruction in adult humans. Previous studies have shown that PANDO develops secondary to chronic inflammation [2–4]. In addition, some studies in different diseases indicate that NLR, PLR and MPV can be used to predict inflammation [5, 7–11].

The neutrophil-lymphocyte ratio is considered an easy and practical indicator of systemic inflammation. Some studies have shown that NLR can be used as a prognostic indicator in coronary artery disease, Behçet's disease, rheumatoid arthritis and some malignancies [5, 12–16]. Systemic inflammation typically involves lymphopenia and neutrophilia [17]. Alan et al. reported that the NLR levels was increased in patients with Behçet's syndrome than controls [15]. In our study, NLR was significantly increased in PANDOs compared to control patients, and we think this might be used to predict the development of nasolacrimal duct obstruction.

The PLR is cheap, and giving some information about condition of platelets and white cells. Platelet-to-lymphocyte ratio is a predictor that has been studied in recent years and has shown the systematic inflammation (presence and severity) [18]. The relationship between PLR and various cancer types and acute coronary syndrome has been reported in previous [19, 20]. There are studies reporting that PLR is a negative prognostic factor in some inflammatory conditions [21, 22] Azab et al. reported a relationship between increased PLR and long-term mortality in patients with myocardial infarction [10]. In another study, it was found that elevation in PLR was associated with non-dipper status in hypertensive patients [23]. In our study,

there was no increase or decrease in PLR levels in the patient group because there was no significant change in platelet and lymphocyte counts in both groups.

Mean platelet volume is being used as a new indicator of inflammation. Inagaki et al. found that MPV levels were significantly decreased in the advanced non-small cell lung cancer group than the controls [24]. In addition, Kisacik et al. showed that MPV was significantly decreased in patients with ankylosing spondylitis and rheumatoid arthritis as compared to controls [25]. In our study, we found that in MPV levels were significantly decreased in PANDOs than the controls. The best-known effects of inflammatory disorders on hematopoiesis are anemia and thrombocytosis [26, 27]. It has been demonstrated in previous studies that MPV reflects platelet activation [28–31]. These studies suggest that there is a relationship between inflammatory diseases and MPV. In our study, we can link the statistically significant low occurrence of MPV to this mechanism.

The limitations of the study are the small patient number and retrospective design of the study. New studies involving more patients are needed to analyze the relationship between serum blood ratios and PANDO. However, further prospective studies are needed.

Acknowledgements

We are grateful to Atilla Akgül, one of the staff of the Sakarya Provincial Health Directorate, for his contributions to the data collection.

REFERENCES

1. Bartley G. Acquired Lacrimal Drainage Obstruction. Ophthal Plast Reconstr Surg. 1993; 9(1): 11–26, doi: 10.1097/00002341-199303000-00002, indexed in Pubmed: 1476972.
2. Busse H, Müller KM. [Development of idiopathic dacryostenosis (clinical and pathologico-anatomical findings)]. Klin Monbl Augenheilkd. 1977; 170(4): 627–632, indexed in Pubmed: 886804.
3. Linberg JV, McCormick SA. Primary acquired nasolacrimal duct obstruction. A clinicopathologic report and biopsy technique. Ophthalmology. 1986; 93(8): 1055–1063, doi: 10.1016/s0161-6420(86)33620-0, indexed in Pubmed: 3763155.
4. Mauriello JA, Palydowycz S, DeLuca J. Clinicopathologic study of lacrimal sac and nasal mucosa in 44 patients with complete acquired nasolacrimal duct obstruction. Ophthalmic Plast Reconstr Surg. 1992; 8(1): 13–21, doi: 10.1097/00002341-199203000-00002, indexed in Pubmed: 1554647.
5. Tamhane UU, Aneja S, Montgomery D, et al. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol. 2008; 102(6): 653–657, doi: 10.1016/j.amjcard.2008.05.006, indexed in Pubmed: 18773982.
6. Akdag S, Akyol A, Asker M, et al. Platelet-to-Lymphocyte Ratio May Predict the Severity of Calcific Aortic Stenosis. Med Sci Monit. 2015; 21: 3395–3400, doi: 10.12659/msm.894774, indexed in Pubmed: 26544152.
7. Akboga MK, Canpolat U, Yuksel M, et al. Platelet to lymphocyte ratio as a novel indicator of inflammation is correlated with the severity of metabolic syndrome: A single center large-scale study. Platelets. 2016; 27(2): 178–183, doi: 10.3109/09537104.2015.1064518, indexed in Pubmed: 26196312.
8. Tsiara S, Elisaf M, Jagroop IA, et al. Platelets as predictors of vascular risk: is there a practical index of platelet activity? Clin Appl Thromb Hemost. 2003; 9(3): 177–190, doi: 10.1177/107602960300900301, indexed in Pubmed: 14507105.
9. Azab B, Daoud J, Naeem FB, et al. Neutrophil-to-lymphocyte ratio as a predictor of worsening renal function in diabetic patients (3-year follow-up study). Ren Fail. 2012; 34(5): 571–576, doi: 10.3109/0886022X.2012.668741, indexed in Pubmed: 22452450.
10. Azab B, Shah N, Akerman M, et al. Value of platelet/lymphocyte ratio as a predictor of all-cause mortality after non-ST-elevation myocardial infarction. J Thromb Thrombolysis. 2012; 34(3): 326–334, doi: 10.1007/s11239-012-0718-6, indexed in Pubmed: 22466812.
11. Ryu HJ, Seo MiR, Choi HJ, et al. Mean platelet volume as a marker for differentiating disease flare from infection in Behçet's disease. Int J Rheum Dis. 2018; 21(8): 1640–1645, doi: 10.1111/1756-185X.13008, indexed in Pubmed: 27886446.
12. Yayla Ç, Açikgöz SK, Yayla KG, et al. The association between platelet-to-lymphocyte ratio and inflammatory markers with the severity of aortic stenosis. Biomark Med. 2016; 10(4): 367–373, doi: 10.2217/bmm-2015-0016, indexed in Pubmed: 26974393.
13. Racz JM, Cleghorn MC, Jimenez MC, et al. Predictive Ability of Blood Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios in Gastrointestinal Stromal Tumors. Ann Surg Oncol. 2015; 22(7): 2343–2350, doi: 10.1245/s10434-014-4265-6, indexed in Pubmed: 25472648.
14. Yin Y, Wang J, Wang X, et al. Prognostic value of the neutrophil to lymphocyte ratio in lung cancer: A meta-analysis. Clinics (Sao Paulo). 2015; 70(7): 524–530, doi: 10.6061/clinics/2015(07)10, indexed in Pubmed: 26222823.
15. Alan S, Tuna S, Türkoğlu EB. The relation of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and mean platelet volume with the presence and severity of Behçet's syndrome. Kaohsiung J Med Sci. 2015; 31(12): 626–631, doi: 10.1016/j.kjms.2015.10.010, indexed in Pubmed: 26709224.
16. Mercan R, Bitik B, Tufan A, et al. The Association Between Neutrophil/Lymphocyte Ratio and Disease Activity in Rheumatoid Arthritis and Ankylosing Spondylitis. J Clin Lab Anal. 2016; 30(5): 597–601, doi: 10.1002/jcla.21908, indexed in Pubmed: 26666737.
17. Zahorec R. Ratio of neutrophil to lymphocyte counts--rapid and simple parameter of systemic inflammation and stress in critically ill. Bratisl Lek Listy. 2001; 102(1): 5–14, indexed in Pubmed: 11723675.
18. Koseoglu HI, Altunkas F, Kanbay A, et al. Platelet-lymphocyte ratio is an independent predictor for cardiovascular disease in obstructive sleep apnea syndrome. J Thromb Thrombolysis. 2015; 39(2): 179–185, doi: 10.1007/s11239-014-1103-4, indexed in Pubmed: 25002338.
19. Unal D, Eroglu C, Kurtul N, et al. Are neutrophil/lymphocyte and platelet/lymphocyte rates in patients with non-small cell lung cancer associated with treatment response and prognosis? Asian Pac J Cancer Prev. 2013; 14(9): 5237–5242, doi: 10.7314/apjcp.2013.14.9.5237, indexed in Pubmed: 24175807.
20. Akkaya E, Gul M, Ugur M. Platelet to lymphocyte ratio: a simple and valuable prognostic marker for acute coronary syndrome. Int J Cardiol. 2014; 177(2): 597–598, doi: 10.1016/j.ijcard.2014.08.143, indexed in Pubmed: 25220175.
21. Akboga MK, Canpolat U, Yayla C, et al. Association of Platelet to Lymphocyte Ratio With Inflammation and Severity of Coronary Atherosclerosis in Patients With Stable Coronary Artery Disease. Angiology. 2016; 67(1): 89–95, doi: 10.1177/0003319715583186, indexed in Pubmed: 25922197.
22. Lian L, Xia YY, Zhou C, et al. Application of platelet/lymphocyte and neutrophil/lymphocyte ratios in early diagnosis and prognostic prediction in patients with resectable gastric cancer. Cancer Biomark. 2015; 15(6): 899–907, doi: 10.3233/CBM-150534, indexed in Pubmed: 26444485.
23. Sunbul M, Gerin F, Durmus E, et al. Neutrophil to lymphocyte and platelet to lymphocyte ratio in patients with dipper versus non-dipper

hypertension. Clin Exp Hypertens. 2014; 36(4): 217–221, doi: 10.3109/10641963.2013.804547, indexed in Pubmed: 23786430.
24. Inagaki N, Kibata K, Tamaki T, et al. Prognostic impact of the mean platelet volume/platelet count ratio in terms of survival in advanced non-small cell lung cancer. Lung Cancer. 2014; 83(1): 97–101, doi: 10.1016/j.lungcan.2013.08.020, indexed in Pubmed: 24189108.
25. Kisacik B, Tufan A, Kalyoncu U, et al. Mean platelet volume (MPV) as an inflammatory marker in ankylosing spondylitis and rheumatoid arthritis. Joint Bone Spine. 2008; 75(3): 291–294, doi: 10.1016/j.jbspin.2007.06.016, indexed in Pubmed: 18403245.
26. Bowman SJ. Hematological manifestations of rheumatoid arthritis. Scand J Rheumatol. 2002; 31(5): 251–259, doi: 10.1080/03009742760375124, indexed in Pubmed: 12455813.
27. Bertero MT, Caligaris-Cappio F. Anemia of chronic disorders in systemic autoimmune diseases. Haematologica. 1997; 82(3): 375–381, indexed in Pubmed: 9234597.
28. Bath P, Algert C, Chapman N, et al. PROGRESS Collaborative Group. Platelet size: measurement, physiology and vascular disease. Blood Coagul Fibrinolysis. 1996; 7(2): 157–161, indexed in Pubmed: 8735807.
29. Bath P, Algert C, Chapman N, et al. PROGRESS Collaborative Group. Association of mean platelet volume with risk of stroke among 3134 individuals with history of cerebrovascular disease. Stroke. 2004; 35(3): 622–626, doi: 10.1161/01.STR.0000116105.26237.EC, indexed in Pubmed: 14976328.
30. Endler G, Klimesch A, Sunder-Plassmann H, et al. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. Br J Haematol. 2002; 117(2): 399–404, doi: 10.1046/j.1365-2141.2002.03441.x, indexed in Pubmed: 11972524.
31. Kapsoritakis AN, Koukourakis MI, Sfiridaki A, et al. Mean platelet volume: a useful marker of inflammatory bowel disease activity. Am J Gastroenterol. 2001; 96(3): 776–781, doi: 10.1111/j.1572-0241.2001.03621.x, indexed in Pubmed: 11280550.

REVIEW PAPER
DOI: 10.5603/OJ.2020.0018

Antioxidants in the retina and vitreous — current state of knowledge

Agata Pietras-Baczewska[1], Katarzyna Nowomiejska[1], Małgorzata Sztanke[2], Mario Damiano Toro[1, 3], Robert Rejdak[1]

[1]Department of General Ophthalmology, Medical University of Lublin, Lublin, Poland
[2]Chair and Department of Medical Chemistry, Medical University of Lublin, Lublin, Poland
[3]Faculty of Medicine, Collegium Medicum Cardinal Stefan Wyszynski University, Warsaw, Poland

ABSTRACT

In the healthy organism, there is a constant balance between the formation and neutralization of free radicals. Oxidative stress is a result of free radicals' production and naturalization imbalance, in favor of the free radicals' high concentration. Literature suggests the existence of the relationship between decreased intraocular antioxidant capacity and ocular diseases. Retina and the photoreceptors in particularl, are susceptible to oxygen deficiency due to their great oxygen consumption. The aim of this review was to describe the relationship between oxidative stress and the most common vitreoretinal disorders. The authors focused on four ocular diseases such as vitreous degeneration, rhegmatogenous retinal detachment, age-related macular degeneration and diabetic retinopathy. It was widely proven that high oxidative stress damages retina by the acceleration of photoreceptors and ganglion cells apoptosis. Available data suggesting that substances scavenging oxidative stress may be effective in slowing down the progression of these degenerative ocular diseases. However, the effects of antioxidants treatment are ambiguous, successful results of experimental studies lead straight to clinical use in human in the future.

KEY WORDS: antioxidants; antioxidant capacity; oxidative stress; vitreous degeneration; retinal detachment; diabetic retinopathy; age-related macular degeneration

Ophthalmol J 2020; Vol. 5, 81–86

INTRODUCTION

Oxygen is the essential vital chemical element. It can be either consumed by the cells remaining in its molecular form or be transformed into insoluble reactive oxygen species (ROS). Reactive oxygen derivatives such as superoxide aions (O2–), hydrogen peroxide (H2O2), hydroxyl radical (OH–), peroxyl radical and singlet oxygen are the most common radicals in the organisms [1]. Free radicals are the molecules containing unpaired electrons making them capable of independent existence. The unpaired electron makes the molecules highly reactive. They can either donate an electron or extract an electron from other molecules, behaving as a reductant or oxidant. Vivid reactivity of radicals is the cause of their short half-life (10-4 seconds or less) in any biological environment [2]. In the healthy organism, there is a constant balance between the formation and neutralization of free radicals. Free radicals' formation is a natural consequence of cellular functioning, but one has to remember that exogenous factors can trigger radicals' overproduction. Any substance or molecule with the capacity of delaying or inhibiting oxidation of other substance is generally defined as an antioxidant. There are different types of antioxidants, they can be both exogenous and endogenous, but they are all responsible for the prevention of radicals' induced cell damage and death. All antioxi-

CORRESPONDING AUTHOR:
Agata Pietras-Baczewska, Department of General Ophthalmology, Medical University of Lublin, Chmielna 1, 20-079 Lublin, Poland; e-mail: agatapie@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

dants can by divided into three main groups — antioxidant enzymes, chain-breaking antioxidants and metal bonding proteins [2].

Oxidative stress is a result of free radicals' production and naturalization imbalance, in favor of the free radicals' high concentration. The imbalance can be either due to overproduction of endogenous ROS by mitochondrial respiration or decreased antioxidant capacity [3]. ROS damage range of molecular elements including proteins, lipids and nucleic acids (DNA and/or RNA). These cellular structures destruction contributes to cell aging, acceleration of genetically programmed cell death or apoptosis [1]. There are suggestions in the literature concerning the relationship between decreased intraocular antioxidant capacity and the ocular diseases. Several age-related ocular diseases have been described as associated with oxidative stress, such as Fuch's dystrophy, nuclear cataract, age-related macular degeneration (AMD), diabetic retinopathy (DR) [4].

The aim of this review was to describe the relationship between oxidative stress and vitreoretinal disorders.

VITREOUS DEGENERATION

Vitreous body is the biggest structural component of the eye, being roughly 80% of the total globe size. Vitreous cavity is the space between the posterior lens surface and the inner limiting membrane (ILM) of the retina. Vitreous has approximately 4ml of volume and it is built of water (99%), collagen fibres, non-collagen proteins, glucosaminoglycans (e.g. hyaluronic acid) [5]. It is relatively acellular with only one layer of mononuclear phagocytes and hyalocytes in the posterior part of its cortex [6]. Due to its clarity vitreous enables the photons to freely penetrate to posterior eye elements, such as retina. It also takes part in maintaining intraocular pressure and intraocular oxygen tension. As vitreous body is an avascular structure it has no capacity of regeneration once it is damaged [7].

Vitreous degeneration is a physiological age-related process resulting from gel liquefaction and concurrent dehiscence of vitreoretinal adhesion [8]. As the gel liquefies the adhesion of vitreal body to retina weakens. In consequence vitreal cortex separates totally form the ILM of the retina, which literature refers as posterior vitreous detachment (PVD). Although it is said that vitreous degeneration is a physiological phenomemnon, there are factors which can facilitate the process. Increased oxidative stress biomarkers and increased activity of proteolytic enzymes are said to be positively correlated with the vitreous degeneration [9]. A high concentration of ROS induced by light was presented as the liquefication factor to be age-related by Uneo and collegues [10]. It was also proven that free radicals, such as hydroxyl radical (OH–) and superoxide anion (02–), generated by visible light irradiation, contribute to vitreous liquefaction [11]. Berra and associates found that the antioxidative potential of human vitreous decrease with age which contribute to subsequent oxidative-stress-induced retinal pathologies [12].

RETINAL DETACHMENT

Rhegmatogenous retinal detachment (RRD) is one of the ophthalmological emergencies. The epidemiology of RRD varies. Different studies show there is 1 person per 10.000 yearly [13] while others estimate the incidence of approximately 6–18 cases for every 100.000 people a year [14]. Following the definition retinal detachment occurs when the neurosensory retina (NSR) separates from the retinal pigment epithelium (RPE). There are four types of retinal detachment distinguished on the basis of the underlying cause. The majority of RRD cases derives from the retinal break which becomes an entrance to subretinal space. Leakage of the vitreous cavity fluid leads to separation of the NSR [15]. Detached sensory retina is deprived of oxygen and nutrients, thus leading to stress conations and ROS overproduction in photoreceptors [16]. Both photoreceptors and RPE are very susceptible to ROS formation due to their high proportion of fatty acids, high oxygen consumption and permanent exposure to sunlight.

Study shows that biological antioxidative potential (BAP) was significantly deceased in the vitreous fluid of patients with RRD. Oxidative stress was elevated as the result of retinal cells damage. What is more, authors imply that the level of BAP seems to be correlated only with the extent of retinal detachment, with no proved correlation with duration, presence of proliferative vitreoretinopathy (PVD), vitreous hemorrhage (HV), macular status or patients' age [17]. Photoreceptors are very susceptible to oxygen deficiency due to their great oxygen consumption. They have a large number of mitochondria to fulfil their metabolic demand. A detachment of neurosensory retina form under-

lying retinal segments leads to hypoxic stress and other nutrients deprivation. The exact mechanism of cell death is not yet clearly known. It was found that oxidative stress causes mitochondrial and extra-mitochondrial aerobic ATP synthesis leading to ROS overproduction. Elevated ROS concentration, however, is proven to accelerate cell apoptosis. The experimental study questioned whether decrease of oxidative stress would have an effect on mitochondrial dynamics in photoreceptors after retinal detachment. The outcomes showed inhibition of essential mitochondrial fission mediator and decreased photoreceptor death [18]. A different study, conducted on the experimental retinal detachment, proved successfull photoreceptors protection by antioxidative substances as edaravone or tauroursodeoxycholic acid [19]. Another antioxidant factor — N-acetylocysteine (NAC) was specifically examined for its possible use in preventing retinal detachment, secondary do PVR. N-acetylcysteine, a ROS scavenger, was introduced subretinally at the time of RD induction. The experiment was conducted on rabbit eyes and cell models. The outcome showed that N-acetylcysteine (NAC) effectively decreased the accumulation of ROS. Although NAC therapy prevented rabbits from retinal detachment itself, the majority of the animals treated still developed PVR membranes. This study makes one consider the future therapeutic use and clinical application of N-acetylocysteine in prevention of RD [20].

AGE-RELATED MACULAR DEGENERATION

Age-related macular degeneration (AMD) is listed as one of the XXI-century diseases [21]. It is macular pathology of the elderly. Its incidence increases with age however it usually does not affect people before 50 years of age. The course of the disease may have different rates of development. Any type causes irreversible visual impairment, gradually leading to blindness if left untreated. Researchers estimate that the number of individuals with AMD to be 196 million in 2020 with the tendency to increase to 288 million in 2040 [22]. AMD is generally characterized as drusen, pathologies of pigment epithelium (RPE) or pathological vessels formation in the central retina. Literature classifies AMD into two types — "dry" and "wet". The first type called 'dry-type AMD' is the great majority of cases, being approximately 90% of the population suffering from AMD. It is described as the formation of drusen — deposits of metabolism products localized between RPE and Bruch's membrane. RPE is very susceptible to ROS influence mostly due to its high oxygen consumption and exposure to light. As the AMD progresses, the degeneration of RPE spreads through resulting in "geographical atrophy" (GA), well visible in fundus examination. Approximately 10–15% of patients suffer from "wet-type AMD". Vision impairment in this AMD type is greater and the course of the disease is more rapid in comparison to dry-type. Clinically it is characterized as the choroidal neovascularization (CNV) or pigment epithelium detachment (PED). Newly formed sub-RPE vessels are very weak which leads to vascular leakages or hemorrhage causing further retina destruction and vision loss [23]. The only advantage of the rapidly progressing wet-type AMD over the dry-type AMD is the treatment method. Currently, there is no targeted treatment for early-stage drusen formation nor advanced geographic atrophy in dry AMD. On the contrary, patients suffering from wet AMD can be successfully treated with intraocular anti-VEGF injections (anti-vascular endothelial growth factor). It has been widely proven that antioxidant activity decreases with age. Moreover, the level of ROS increases, and thus the total antioxidant capacity of any tissue [24]. Age-related macular degeneration is still being tested for genetical inheritance. Studies had shown individuals with the complement factor H (CFH) polymorphism of Y402H are at greater risk of suffering from AMD. This type of polymorphism reduces the CHF's ability to neutralize the effect of oxidized photoreceptor phospholipids, which later triggers RPE cells' apoptosis [25]. Retinal pigment epithelium damage is observed even in the early stages of AMD, however, the correlation between the damage extent with the OS and disease progression has not been found [26]. Retinal pigment epithelium cells are known to have high metabolic activity. The two-compound pigment of macula (zeaxantin and lutein) is the barrier, which protects the cells form oxidative stress [27]. The cells themselves have their own antioxidant system. The NRF-2/ARE (nuclear factor-erythroid 2-related factor-2/antioxidant response element) complex plays great role in the oxidative stress regulation [28]. In the oxidative stress environment, the NRF-2 has released the complex and is tan moved from cytostol to cell nucleus allowing antioxidant system to be activated [29]. The experimental study on mice models, proved that the loos of NRF-2 gene caused more intensive oxidative stress and what is more the

RPE became more susceptible to oxidative damage [30]. On the contrary to inheritance, AMD RPE damage can be also caused by environmental factors. These modifiable external factors; they are cigarettes smoking or high fat consumption. The exact correlation between cigarette smoking and AMD progression is not yet clearly known. However, data shows substances from cigarette smoke diminish tissues from ascorbic acid and protein sulphyrdyl groups, leading to DNA, lipids and proteins oxidation and damage.

The molecular changes, like these caused by cigarette smoke, have been described in AMD. This fact could lead to assumption that oxidative damage is one of the factors in the mechanism of AMD disease development or progression. The same observations had been made in the multiple studies concluding that smoking is the strongest environmental risk factor for AMD [31].

DIABETIC RETINOPATHY

Diabetes is a major cause of secondary blindness in developed countries in people of working age. It is a civilization disease and a great epidemiological problem. It is estimated that over 420 million people with diabetes currently live in the world. World Health Organisation predicts that diabetes will become the seventh death cause by 2030 [32]. The vast majority of diabetics, reaching even 90%, are people with type 2 diabetes. It is now believed that in the next 15–20 years the number of diabetics in Poland will double. All patients with diagnosed diabetes and those with pre-diabetes are at risk of complications. The most important concern blood vessels (angiopathies) in the kidneys, brain, heart and eyes. Diabetic retinopathy is a complication associated with retinal vascular remodelling resulting from chronic hyperglycemia. Unfavorably for the patients, complications occur regardless of the type of diabetes. On the other hand, numerous studies had confirmed that the duration of the underlying disease has the greatest impact on the development of retinopathy. Treatment of complications is often difficult, sometimes unsatisfactory for the patient and an ophthalmologist. good glycemic control is still the most important Among all the methods of treating diabetes and its complication.

Glucose is known to be the main source of energy in organisms. Its metabolism in the cells involves redox reactions to produce energy by transport, storage or extraction of electrons. [33]. In the conditions of normal glycemic level, glucose undergoes the glycolysis pathway to produce ATP in the Kreb's cycle in the mitochondria, where electrons are being stored in form reduced form of Nicotinamide adenine dinucleotide (NADH) and flavin adenine dinucleotide (FADH2 [34]. ROS production takes place in mitochondria by two processes, one is the mitochondrial oxidative phosphorylation and the second NADH oxidase system (Nox). It had been described that over 95% of oxygen transformations take place in the mitochondria. Approximately 1–5% of these reactions result in ROS production. In the environment of hyperglycemia, increased level of ROS stabilizes hypoxia-inducible factor 1α (HIF-1α) leading to upregulation of angiogenic genes e.g. VEGF [35]. Data form the experiment had shown an increased level of VEGF in vitreous body of patients with proliferative diabetic retinopathy. Eye fundus examination revealed pathological neovascularization in retina, secondary to VEGF increased concentration [36].

Another study described the evidence for the correlation between oxidative stress and the severity of diabetic retinopathy. Retinal vessels' damage is caused by four major metabolic mechanisms-increases polyol pathway flux, activation of the protein kinase C (PKC) pathway, increased intracellular formation of advanced glycation end-proteins (AGEs) and expression of their receptors, and hexosamine activation pathway. All of these mechanisms have been positively correlated with increased oxidative stress and ROD overproduction [37]. On the other hand, obesity and dyslipidemia are different external factors leading to ROS overproduction, by fatty acids oxidation with NADPH oxidase. Experimental data showed that degeneration of retinal vessels could be reduced by antioxidant agents by activation of caspase-3 and nuclear factor-κB (NF-κB), which lead to the assumption that oxidative stress is one of the factors causing capillary apoptosis [38].

Longtime clinical observations suggest that decreasing oxidative stress may become part of DR treatment, as they delay or inhibit pathological metabolic pathways producing ROS [39].

CONCLUSIONS

It is proven that high oxidative stress damages retina, by the acceleration of photoreceptors and ganglion cells apoptosis. The denegation of retina, irrespective of the type, especially in macular dis-

eases, causes vision impaired. In great majority of retinal diseases improvement prognosis is very poor. Oxidative stress agents, their influence on particular tissues, the oxidant-antioxidant balance is being still explored. Treatment is being aimed to cure the disease in its asymptomatic stage, to prevent vision impairment. Available data suggest that substances scavenging oxidative stress may be effective slowing down the progression of these degenerative ocular diseases. Therefore, inhibition of the metabolic pathways, producing a high concentration of ROS, may become protective for retinal cells. Currently, there are only cell or animal models studies proving beneficial use of antioxidants in the prevention of retinal damage. Development of the treatment for retinal degeneration still faces great challenges and further investigation is needed. However, predicted effects of antioxidant treatment are ambiguous, successful results of experimental studies lead straight to clinical use in human in the future.

REFERENCES

1. Siegfried CJ, Shui YB. Intraocular Oxygen and Antioxidant Status: New Insights on the Effect of Vitrectomy and Glaucoma Pathogenesis. Am J Ophthalmol. 2019; 203: 12–25, doi: 10.1016/j.ajo.2019.02.008, indexed in Pubmed: 30772349.
2. Young IS, Woodside JV. Antioxidants in health and disease. J Clin Pathol. 2001; 54(3): 176–186, doi: 10.1136/jcp.54.3.176, indexed in Pubmed: 11253127.
3. Saccà SC, Izzotti A. Oxidative stress and glaucoma: injury in the anterior segment of the eye. Prog Brain Res. 2008; 173: 385–407, doi: 10.1016/S0079-6123(08)01127-8, indexed in Pubmed: 18929123.
4. Saccà SC, Roszkowska AM, Izzotti A. Environmental light and endogenous antioxidants as the main determinants of non-cancer ocular diseases. Mutat Res. 2013; 752(2): 153–171, doi: 10.1016/j.mrrev.2013.01.001, indexed in Pubmed: 23337404.
5. Bishop P. The biochemical structure of mammalian vitreous. Eye (Lond). 1996; 10 (Pt 6): 664–670, doi: 10.1038/eye.1996.159, indexed in Pubmed: 9091361.
6. Kita T, Sakamoto T, Ishibashi T. Hyalocytes: Essential Vitreous Cells in Vitreoretinal Health and Disease. In: Vitreous. Springer, Berlin/Heidelberg 2014: 151–164.
7. Kański J. Okulistyka kliniczna. Elsevier Urban & Partner, Wrocław 2013: 716.
8. Sebag J. Posterior Vitreous Detachment. Ophthalmology. 2018; 125(9): 1384–1385, doi: 10.1016/j.ophtha.2018.05.018, indexed in Pubmed: 30143091.
9. Nuzzi R, Marchese A, Gulino GR, et al. Influence of posterior vitreous detachment and type of intraocular lens on lipid peroxidation in the human vitreous. Mol Vis. 2015; 21: 1106–1112, doi: 10.1038/eye.2016.143, indexed in Pubmed: 26396488.
10. Ueno N, Sebag J, Hirokawa H, et al. Effects of visible-light irradiation on vitreous structure in the presence of a photosensitizer. Exp Eye Res. 1987; 44(6): 863–870, doi: 10.1016/s0014-4835(87)80048-9, indexed in Pubmed: 3653277.
11. Akiba J. [Photodynamically induced vitreous liquefaction in vivo]. Nippon Ganka Gakkai Zasshi. 1992; 96(6): 731–736, indexed in Pubmed: 1626474.
12. Berra A, Ferreira S, Stanga P, et al. Age-related antioxidant capacity of the vitreous and its possible relationship with simultaneous changes in photoreceptors, retinal pigment epithelium and Bruchs' membrane in human donors' eyes. Arch Gerontol Geriatr. 2002; 34(3): 371–377, doi: 10.1016/s0167-4943(02)00013-4, indexed in Pubmed: 14764337.
13. Goldberg H. Retinal Detachment. BMJ. 1959; 2(5144): 153–154, doi: 10.1136/bmj.2.5144.153-c, indexed in Pubmed: 24807890.
14. Bechrakis NE, Dimmer A. Rhegmatogene Netzhautablösung. Der Ophthalmologe. 2018; 115(2): 163–178, doi: 10.1007/s00347-017-0647-z.
15. Kański J, Jacek J. Okulistyka kliniczna. Elsevier Urban & Partner, Wrocław 2013: 674–678.
16. Suzuki Y, Adachi K, Takanashi S, et al. Oxidative Stress in the Vitreous Fluid with Rhegmatogenous Retinal Detachment. J Clin Exp Ophthalmol. 2017; 6(5): 1–5, doi: 10.4172/2155-9570.1000682.
17. Maeno A, Suzuki Y, Adachi K, et al. Characterization of the biological antioxidant potential in the vitreous fluid from patients with rhegmatogenous retinal detachment. Acta Ophthalmol. 2016; 94(6): e515–e516, doi: 10.1111/aos.13002, indexed in Pubmed: 27008980.
18. She X, Lu X, Li T, et al. Inhibition of Mitochondrial Fission Preserves Photoreceptors after Retinal Detachment. Am J Pathol. 2018; 188(7): 1713–1722, doi: 10.1016/j.ajpath.2018.03.013, indexed in Pubmed: 29684364.
19. Roh Miln, Murakami Y, Thanos A, et al. Edaravone, an ROS scavenger, ameliorates photoreceptor cell death after experimental retinal detachment. Invest Ophthalmol Vis Sci. 2011; 52(6): 3825–3831, doi: 10.1167/iovs.10-6797, indexed in Pubmed: 21310909.
20. Lei H, Velez G, Cui J, et al. N-acetylcysteine suppresses retinal detachment in an experimental model of proliferative vitreoretinopathy. Am J Pathol. 2010; 177(1): 132–140, doi: 10.2353/ajpath.2010.090604, indexed in Pubmed: 20489144.
21. Kostrzewa B, Rojek A, Gabryś J. Starcze zwyrodnienie plamki żółtej — choroba cywilizacyjna XXI wieku. Acta Bio-Optica et Informatica Medica Inżynieria Biomedyczna. 2015; 21(2): 77–85.
22. Jonas JB, Cheung CM, Panda-Jonas S. Updates on the Epidemiology of Age-Related Macular Degeneration. Asia Pac J Ophthalmol (Phila). 2017; 6(6): 493–497, doi: 10.22608/APO.2017251, indexed in Pubmed: 28906084.
23. Masuda T, Shimazawa M, Hara H. Retinal Diseases Associated with Oxidative Stress and the Effects of a Free Radical Scavenger (Edaravone). Oxid Med Cell Longev. 2017; 2017: 9208489, doi: 10.1155/2017/9208489, indexed in Pubmed: 28194256.
24. Golden TR, Hinerfeld DA, Melov S. Oxidative stress and aging: beyond correlation. Aging Cell. 2002; 1(2): 117–123, doi: 10.1046/j.1474-9728.2002.00015.x, indexed in Pubmed: 12882341.
25. Katz M, Robison W. What is lipofuscin? Defining characteristics and differentiation from other autofluorescent lysosomal storage bodies. Archives of Gerontology and Geriatrics. 2002; 34(3): 169–184, doi: 10.1016/s0167-4943(02)00005-5, indexed in Pubmed: 14764321.
26. Kaarniranta K, Pawlowska E, Szczepanska J, et al. Role of Mitochondrial DNA Damage in ROS-Mediated Pathogenesis of Age-Related Macular Degeneration (AMD). Int J Mol Sci. 2019; 20(10), doi: 10.3390/ijms20102374, indexed in Pubmed: 31091656.
27. Domènech EB, Marfany G. The Relevance of Oxidative Stress in the Pathogenesis and Therapy of Retinal Dystrophies. Antioxidants (Basel). 2020; 9(4), doi: 10.3390/antiox9040347, indexed in Pubmed: 32340220.
28. Takayama K, Kaneko H, Kataoka K, et al. Nuclear Factor (Erythroid-Derived)-Related Factor 2-Associated Retinal Pigment Epithelial Cell Protection under Blue Light-Induced Oxidative Stress. Oxid Med Cell Longev. 2016; 2016: 8694641, doi: 10.1155/2016/8694641, indexed in Pubmed: 27774118.
29. Kansanen E, Kuosmanen SM, Leinonen H, et al. The Keap1-Nrf2 pathway: Mechanisms of activation and dysregulation in cancer. Redox Biol. 2013; 1: 45–49, doi: 10.1016/j.redox.2012.10.001, indexed in Pubmed: 24024136.
30. Felszeghy S, Viiri J, Paterno JJ, et al. Loss of NRF-2 and PGC-1 genes leads to retinal pigment epithelium damage resembling dry age-related macular degeneration. Redox Biol. 2019; 20: 1–12, doi: 10.1016/j.redox.2018.09.011, indexed in Pubmed: 30253279.
31. Datta S, Cano M, Ebrahimi K, et al. The impact of oxidative stress and inflammation on RPE degeneration in non-neovascular AMD. Prog Retin Eye Res. 2017; 60: 201–218, doi: 10.1016/j.preteyeres.2017.03.002, indexed in Pubmed: 28336424.

32. World Health Organization. Global status report on noncommunicable diseases 2014 (No. WHO/NMH/NVI/15.1). WHO, Geneva 2014.
33. Cecilia OM, José Alberto CG, José NP, et al. Oxidative Stress as the Main Target in Diabetic Retinopathy Pathophysiology. J Diabetes Res. 2019; 2019: 8562408, doi: 10.1155/2019/8562408, indexed in Pubmed: 31511825.
34. Yan LJ. Redox imbalance stress in diabetes mellitus: Role of the polyol pathway. Animal Model Exp Med. 2018; 1(1): 7–13, doi: 10.1002/ame2.12001, indexed in Pubmed: 29863179.
35. Masuda T, Shimazawa M, Hara H. Retinal Diseases Associated with Oxidative Stress and the Effects of a Free Radical Scavenger (Edaravone). Oxid Med Cell Longev. 2017; 2017: 9208489, doi: 10.1155/2017/9208489, indexed in Pubmed: 28194256.
36. Izuta H, Matsunaga N, Shimazawa M, et al. Proliferative diabetic retinopathy and relations among antioxidant activity, oxidative stress, and VEGF in the vitreous body. Mol Vis. 2010; 16: 130–136, indexed in Pubmed: 20142849.
37. Kowluru RA, Chan PS. Oxidative stress and diabetic retinopathy. Exp Diabetes Res. 2007; 2007: 43603, doi: 10.1155/2007/43603, indexed in Pubmed: 17641741.
38. Kowluru RA, Koppolu P. Diabetes-induced activation of caspase-3 in retina: effect of antioxidant therapy. Free Radic Res. 2002; 36(9): 993–999, doi: 10.1080/1071576021000006572, indexed in Pubmed: 12448825.
39. Williams M, Hogg RE, Chakravarthy U. Antioxidants and diabetic retinopathy. Curr Diab Rep. 2013; 13(4): 481–487, doi: 10.1007/s11892-013-0384-x, indexed in Pubmed: 23649947.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0019

Management of orbital cellulitis: a retrospective study

Imane Chabbar, Abdallah Elhassan, Amina Berraho

Ophthalmology B Department, Ibn Sina University Hospital, Rabat, Morocco

ABSTRACT

BACKGROUND: Orbital cellulitis is an infectious involvement of the tissues posterior to the orbital septum causing severe local and general complications.

MATERIAL AND METHODS: The aim of our work was to study the clinical, paraclinical and therapeutic characteristics of orbital cellulitis through a retrospective study of 89 cases collected between 2015 and 2019. The diagnosis of orbital cellulitis was based on clinical and imaging elements.

RESULTS: The average age was 17.5 years. Exophthalmos was noted in 33% of cases, ophthalmoplegia in 18% of cases, diplopia in 4.5% of cases and ocular hypertonia in 11% of cases. Orbital CT scan allowed the diagnosis of subperiosteal abscess in 20% of cases and orbital abscess in 10% of cases. Sinusitis was the main infectious origin in children, while dacryocystitis predominated in adults. All patients received parenteral antibiotherapy combined with corticotherapy after 48 hours. Complications occurred in 10 cases, dominated by exposure keratitis, panophthalmitis and optic atrophy with permanent blindness.

CONCLUSIONS: We emphasize the importance of rapid diagnosis and urgent treatment of orbital cellulitis.

KEY WORDS: orbital cellulitis; management; complications; prognosis

Ophthalmol J 2020; Vol. 5, 87–92

INTRODUCTION

Orbital cellulitis is the most common primary orbital pathology. It is an acute orbital infection usually of bacterial origin. The diagnosis of orbital cellulitis is mainly clinical, confirmed by orbital CT scan. Chandler's classification (Tab. 1) allows to group orbital cellulitis into 2 main categories: preseptal cellulitis which describes the infection located before the orbital septum and "real" orbital cellulitis or postseptal cellulitis which involves the tissues posterior to the orbital septum and which is studied in this work.

Orbital cellulitis is a serious pathology causing severe local and general complications. Its unpredictable progression requires early diagnosis and appropriate and effective treatment. The difficulty of management is mainly seen at the stage of complications.

The aim of our work was to study the clinical, paraclinical, therapeutic and evolutive characteristics of orbital cellulitis through 5-years' experience.

Table 1. Chandler's classification of orbital cellulitis

Stage	Description
I	Pre-septal cellulitis: inflammatory oedema of the eyelids
II	True orbital cellulitis: diffuse oedema of the orbital contents, posterior of the septum
III	Subperiosteal abscess: collection of purulent material between the periorbit and the orbital wall (usually medial or superolateral)
IV	Orbital abscess: abscess collection within the orbital tissues
V	Cavernous sinus thrombosis

CORRESPONDING AUTHOR:
Imane Chabbar, Ophthalmology B Department, Ibn Sina University Hospital, Rabat, Morocco; e-mail: imana1chab@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

MATERIAL AND METHODS

We conducted a retrospective study of patients presenting orbital cellulitis, hospitalized in Ophthalmology B Department at Ibn-Sina University Hospital in Rabat-Morocco, for a period of five years (From January 2015 to December 2019).

For each patient, we noted demographic parameters (age, sex, origin), the patient's medical history, the consultation delay, functional signs on admission and initial visual acuity. The slit-lamp examination specified: the presence of eyelids edema, chemosis, fistulization, exophthalmos, lagophthalmos, ophthalmoplegia, the anterior segment evaluation (degree of corneal transparency, anterior chamber inflammation, intraocular pressure measure) and finally the fundus eye examination. All patients underwent an urgent orbital CT scan. The diagnosis of orbital cellulitis was retained on clinical and imaging arguments.

Blood tests (complete blood count, electrolyte panel, C-reactive protein test) and microbiological examinations of purulent material were carried out during hospitalization.

We noted the medical and/or surgical treatment received by each patient, the modality of administration, the evolution after treatment and the complications.

RESULTS

AGE, SEX

In our case series, 89 patients were treated for orbital cellulitis. There were 45% males and 55% females. The average age was 17.5 years with a range of 24 months to 68 years. The age group < 18 years represented 38%.

IMMUNE STATUS

All patients were immunocompetent, except one patient who received chemotherapy for non-Hodgkin's lymphoma and 2 patients under long-term systemic corticotherapy for chronic rheumatic disease. Unbalanced diabetes was associated with 12 cases.

VISUAL ACUITY ON ADMISSION

Initial visual acuity was > 5/10 in 22% of patients, while 5 patients had a negative light perception on admission (Fig. 1). However, visual acuity was not determined in 33% of cases.

CLINICAL SIGNS

On ophthalmological examination, the clinical signs were (Tab. 2): inflammatory edema limiting eyelids opening with chemosis in all patients, exophthalmos in 33% of cases (Fig. 2), ophthalmoplegia in 18% of cases, diplopia in 4.5% of cases and ocular hypertonia in 11% of cases. Fever with the reduced general condition was particularly objectified in young children.

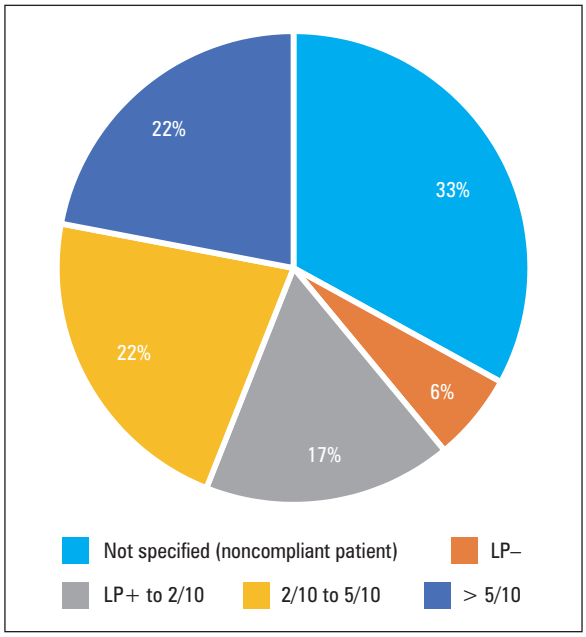

FIGURE 1. Distribution of cases according to initial visual acuity

Table 2. Table showing different clinical signs of orbital cellulitis

Clinical signs	Rate
Fever/reduced general condition	11.2%
Periorbital pain	95.5%
Eyelid edema/chemosis	100%
Exophthalmos	33%
Ophthalmoplegia	18%
Ocular hypertonia	4.5%
Diplopia	11%

ORBITAL CT SCAN SIGNS

Orbital CT scan allowed the diagnosis of orbital cellulitis in all patients, complicated by a subperiosteal abscess in 20% of cases (Fig. 3) and an orbital abscess in 10% of cases (Fig. 4). It also allowed the exophthalmos measurement (Fig. 5) and the diagnosis of related neighbouring infections.

INITIAL INFECTIOUS ORIGIN

Sinusitis was the main infectious origin in children (32 cases) while dacryocystitis was predomi-

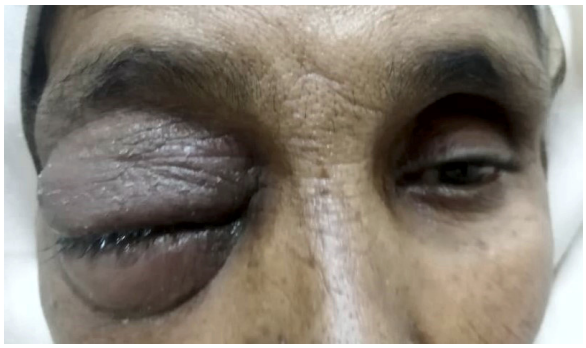

FIGURE 2. Orbital cellulitis in a 62-year-old woman: Photo showing eyelid edema with manifest exophthalmos

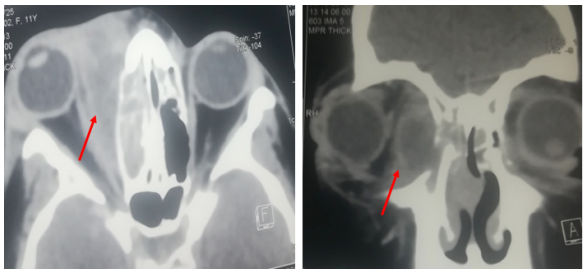

FIGURE 3. Orbital CT scan showing orbital cellulitis with subperiosteal abscess (arrow) in the right orbit complicating pansinusitis

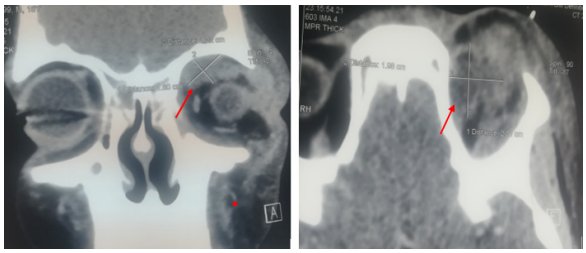

FIGURE 4. Orbital CT scan showing left orbital cellulitis complicated by an orbital abscess (arrow)

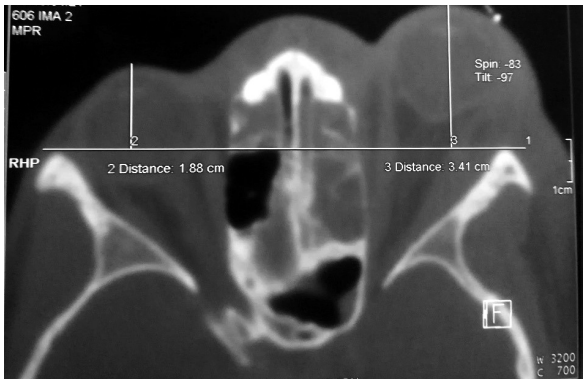

FIGURE 5, Orbital CT scan showing left orbital cellulitis with exophthalmos grade III complicating an acute ethmoiditis

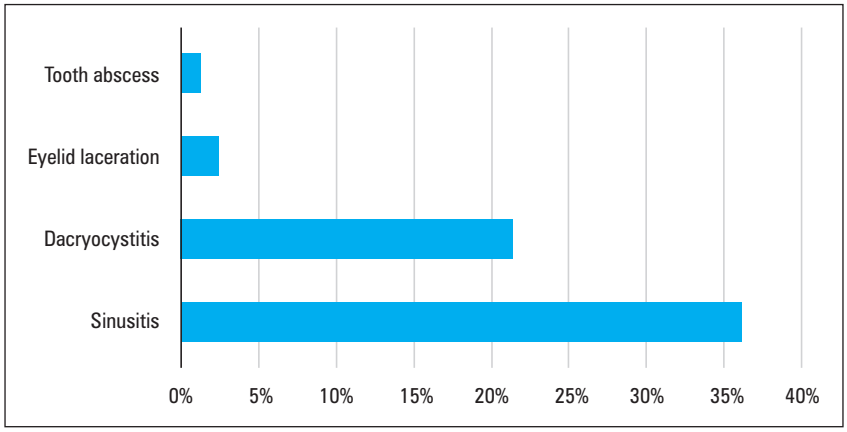

FIGURE 6. Distribution of cases according to initial infectious origin

nant in adults (19 cases) (Fig. 6). Two cases of eyelid laceration with a retained foreign body (Fig. 7) and one case of dental abscess were found.

BACTERIAL IDENTIFICATION

Microbiological examinations of purulent material taken either at the fistulization site or by needle puncture allowed the identification of bacteria in only 13% of cases. Isolated germes were respectively (Fig. 8): *streptococcus pneumoniae*, *staphylococcus aureus*, *haemophilus influenzae* and *streptococcus mitis*.

TREATMENT

Medical treatment required urgent hospitalization and initiation of parenteral antibiotherapy based on amoxicillin/clavulanic acid or ceftriaxone

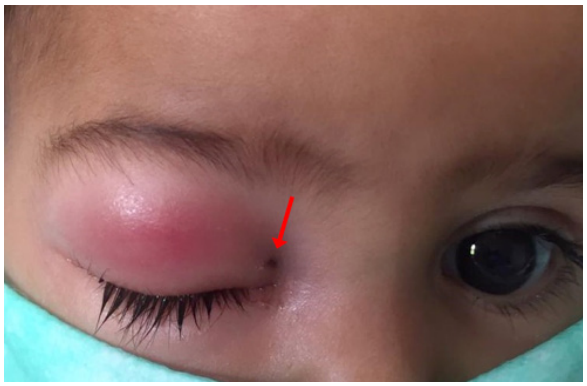

FIGURE 7. Orbital cellulitis in a 24-month old infant; photo showing a punctiform wound with a vegetable foreign body (arrow) at the medial canthus, with inflammatory edema limiting the eyelid opening

associated with aminoglycoside. Metronidazole was added if there was any doubt about the presence of anaerobic germs. Systemic corticotherapy was considered after 48 hours of effective antibiotherapy. Surgical treatment consisted of prefistulated collections drainage or needle puncture when the collection was deep.

COMPLICATIONS

The evolution after treatment was favorable in the majority of cases. Complications were encountered in 11.2% of cases, such as exposure keratitis, panophthalmitis, optic atrophy with permanent blindness and retinal detachment (Tab. 3).

Table 3. Distribution of cases according to orbital cellulitis complications

Complications	Number of cases
Exposure keratitis	5
Optic atrophy	2
Panophthalmitis	2
Retinal detachment	1

DISCUSSION

Orbital cellulitis is an inflammatory process of infectious origin involving the tissues posterior to the orbital septum. The morbidity and mortality associated with orbital cellulitis have greatly decreased thanks to diagnostic and therapeutic advances. However, prompt diagnosis and urgent treatment remain crucial.

Although that can occur at any age, orbital cellulitis is more common in the paediatric population [1]. In our study, the mean age was 17.5 years with a range of 24 months to 65 years and 38% of cases under 18 years. Wane et al. [2] reported an average age of 18 years with a range of 7 months to 50 years. Kaimbo et al. [3] found an average age of 68 years with a significant proportion of patients for more than forty years. In the various published paediatric series [4–6], the age varied between 6 months and 14 years with an average of 5 years. Orbital cellulitis mainly affects young male patients [1]. However, we found a slight female predominance, also objectified in Aidan et al. study [7].

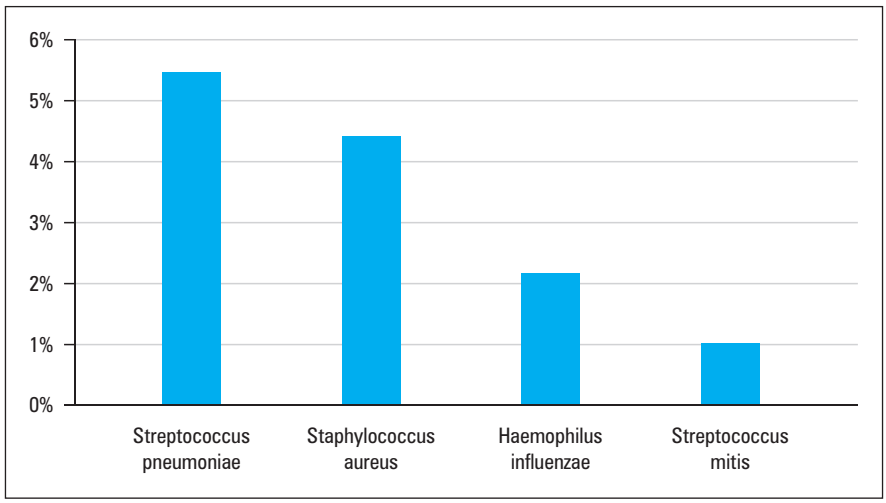

FIGURE 8. Bacterial identification in orbital cellulitis cases

The clinical signs depend on the location of the infection objectified by Chandler's anatomo-clinical classification [8]. The presence of inflammatory eyelids edema with chemosis is characteristic. They were constantly present in all our cases. An inadequate initial treatment, prescribed on an outpatient basis or by self-medication, was the cause of a delayed consultation and a source of complications. The patients presented with a rapidly increasing and irreducible exophthalmos. Visual acuity could be severely decreased or even lost. In our series, 5 patients presented a negative light perception on admission.

Sinusitis is involved in at least two-thirds of orbital cellulitis in adults and 90% of cellulitis in children [1–9]. The second infectious origin described in the literature is skin infections and eye trauma with contaminated wound. In our study, the infectious origins are dominated by sinusitis, especially pansinusitis, which highlights the influence of delayed diagnosis until the spread of infection to other sinuses. Dacryocystitis predominated in adults followed by skin and oral infections [10]. Orbital cellulitis before the age of 5 years is almost always due to ethmoid sinusitis and the germs involved are *Hemophilus influenzea* and *staphylococcus* [11]. In our study, the most common germ was streptococcus, focusing on the severity of neighbouring infections (ENT sphere). However, many microbiological tests returned non-contributory and negative as a result of inappropriate initial treatment and self-medication.

Orbital CT scan is the imaging modality of choice in orbital cellulitis. It allows good visualization of orbital contents, sinus cavities, the surrounding structures and makes it possible to determine the stage of the cellulitis [1, 9–12]. All of our patients received an urgent orbital CT scan confirming the diagnosis.

Once the diagnosis of orbital cellulitis is confirmed, the hospitalization with the institution of probabilistic broad-spectrum parenteral antibiotherapy is indicated without waiting for the paraclinical investigations results. The aim of treatment is to avoid the abscesses formation and to prevent their rupture and their spread to neighbouring structures. In this study, streptococcus was the main germ found, so we associated amoxicillin/clavulanic acid or ceftriaxone with aminoglycoside, metronidazole was added if there was any doubt about the presence of anaerobic germs. The addition of systemic corticotherapy helped relieve inflammation, improve antibiotics spread, and decrease pressure in the orbit in order to protect the optic nerve. Antibiotics and lubricating eye drops protected the cornea from ulceration and superinfection. Subperiosteal abscesses can be treated with parenteral antibiotics alone, especially in young patients, if the collection is < 10 mm with no mass effect on the medial rectus and in the absence of air bubbles suggesting an anaerobic infection [13]. In all other cases, particularly in the presence of severity signs such as a significant decrease in visual acuity, an afferent pupillary deficit (reflecting optic neuropathy), an ophthalmoplegia, a diplopia, an elderly patient, a collected orbital abscess or a clinical aggravation under medical treatment, surgery is recommended [1]. In the case of an accessible abscess, it can be evacuated by puncture drainage. However, if the abscess is deep, the surgical drainage guided by imagery is ensured by orbitotomy or by endonasal surgical technique.

The evolution of orbital cellulitis is unpredictable. In some cases, the eyeball can be spared for a long time, while in other cases, despite appropriate treatment, visual function may be threatened and lead to blindness [14]. This blindness can be secondary to an optic neuropathy of mechanical origin by intraorbital pressure elevation, or of vascular origin by ischemia, central retinal artery occlusion or thrombophlebitis, or of inflammatory origin (infectious neuritis). Retinal and choroidal vascular occlusions, retinal detachments and phthisis of the globe have also been described. Finally, a poor functional result can be linked to exposure keratitis or more exceptionally to retinal haemorrhages and retinal exudates [15].

CONCLUSION

Orbital cellulitis is a serious infection that can affect the visual prognosis, especially when the diagnosis is late and the treatment is inadequate. Sinus infections are mainly involved in this condition. Faced with the significant rate of functional complications, the ophthalmologist must make a rapid diagnosis, assess the ocular repercussions and initiate urgent medical treatment. Surgery will remain reserved for complications.

Conflict of interest

The authors do not declare any conflict of interest.

REFERENCES

1. Mouriaux F, Rysanek B, Babin E, et al. Les cellulites orbitaires. J Fr Ophtalmol. 2012; 35(1): 52–57, doi: 10.1016/j.jfo.2011.08.004.
2. Wane AM, Ba EA, Ndoye-Roth PA, et al. Une expérience sénégalaise des cellulites orbitaires. J Fr Ophtalmol. 2005; 28(10): 1089–1094, doi: 10.1016/s0181-5512(05)81143-x.
3. Kaimbo DK, Kiangalanga J, Missotten L. L'étude des exophtalmies au Zaïre. Bull Soc Belge Ophtalmol. 1995; 259: 199–204.
4. Fanella S, Singer A, Embree J. Presentation and management of pediatric orbital cellulitis. Can J Infect Dis Med Microbiol. 2011; 22(3): 97–100, doi: 10.1155/2011/626809, indexed in Pubmed: 22942886.
5. Boivin L, Adenis JP. Infections orbitaires de l'enfant : clinique, imagerie et traitement. J Fr Ophtalmol. 2009; 32(5): 368–373, doi: 10.1016/j.jfo.2008.10.005.
6. Basraoui D, Elhajjami A, Jalal H. [Imaging of orbital cellulitis in children: about 56 cases]. Pan Afr Med J. 2018; 30: 94, doi: 10.11604/pamj.2018.30.94.14672, indexed in Pubmed: 30344878.
7. Aidan P, Francois M, Prunel M, et al. Cellulites de la région orbitaire chez l'enfant. Arch Pédiatr. 1994; 1: 879–885.
8. Chandler JR, Langenbrunner DJ, Stevens ER. The pathogenesis of orbital complications in acute sinusitis. Laryngoscope. 1970; 80(9): 1414–1428, doi: 10.1288/00005537-197009000-00007, indexed in Pubmed: 5470225.
9. Seongmu L, Michael TY. Management of preseptal and orbital cellulitis. Saudi J Ophthalmol. 2011; 25: 21–29.
10. Kikkawa DO, Heinz GW, Martin RT, et al. Orbital cellulitis and abscess secondary to dacryocystitis. Arch Ophthalmol. 2002; 120(8): 1096–1099, indexed in Pubmed: 12149070.
11. Tzili N, Chefchaouni MC, El kh, et al. Cellulite rétroséptale de l'orbite chez l'enfant: à propos de 25 cas. Opht J Soc Maroc Ophtalmol. ; 2014(23).
12. Bouziane M, Saoud S, Benna N, et al. Apport de la TDM dans la cellulite orbitaire. JFR EPOS. ; 2014.
13. Ryan JT, Preciado DA, Bauman N, et al. Management of pediatric orbital cellulitis in patients with radiographic findings of subperiosteal abscess. Otolaryngol Head Neck Surg. 2009; 140(6): 907–911, doi: 10.1016/j.otohns.2009.02.014, indexed in Pubmed: 19467413.
14. Smelt GJ, Migdal CS. Acute blinding sinusitis. Br Med J (Clin Res Ed). 1983; 287(6398): 1051–1052, doi: 10.1136/bmj.287.6398.1051, indexed in Pubmed: 6412944.
15. Chaudhry IA, Shamsi FA, Elzaridi E, et al. Outcome of treated orbital cellulitis in a tertiary eye care center in the middle East. Ophthalmology. 2007; 114(2): 345–354, doi: 10.1016/j.ophtha.2006.07.059, indexed in Pubmed: 17270683.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0020

Clinico-demographic profile of young people presenting with refractive errors to a medical college hospital of Bihar, India

Prateek Nishant, Sony Sinha, Ranjeet Kumar Sinha, Shekhar Choudhary

Patna Medical College, Ashok Rajpath, Patna, Bihar, India

ABSTRACT

BACKGROUND: Refractive errors are the second most important cause of blindness and account for 18% of the burden. An estimated 123.7 million people suffer from visual impairment due to unaddressed refractive errors worldwide. International agencies recognize that globally, there is insufficient data on the prevalence and types of refractive errors in different populations and age groups. The present study evaluated the proportion of refractive errors with their clinico-demographic context among 10–24-year old patients, presenting to the Ophthalmology Outpatient Department (OPD) of a tertiary hospital of Bihar state of India.

MATERIAL AND METHODS: This prospective, descriptive study collected information about refractive errors in 2739 eyes of 1482 young people. The association between the refractive errors and clinico-demographic variables such as age group, gender, residential background and educational status was evaluated using the chi-square test (taking $p < 0.05$ as significant).

RESULTS: Hypermetropic errors were more common (51%) comprising of hypermetropia (32%) and hypermetropic astigmatism (19%). They marginally exceeded myopic errors (about 49%), comprising myopic astigmatism (26%) and myopia (22%) while mixed astigmatism was the least common (0.4%). Myopic errors were significantly more common in the 10–14 years age group (76%) while hypermetropic errors predominated in older age-groups (54%, $p < 0.001$). Myopia predominated in females (39%) and in rural young people (53%), myopic astigmatism in the illiterate (45%) but hypermetropia in males (37%, $p < 0.001$), urban (35%, $p < 0.001$) and literate young people (31%, $p < 0.001$).

CONCLUSIONS: This study revealed a broad picture of proportion and predominance of different refractive errors and their associations with clinico-demographic profile of the patients.

KEY WORDS: age distribution; sex distribution; residence characteristics; educational status; ametropia

Ophthalmol J 2020; Vol. 5, 93–100

INTRODUCTION

This study intended to explore the distribution of refractive errors with respect to clinico-demographic variables in young people (aged 10–24 years [1]) presenting to the Ophthalmology Outpatient Department (OPD) of a medical college hospital, a premier tertiary care hospital of Bihar.

Refractive errors are the second most important cause of blindness and account for 18% of the burden. Of the estimated 2.2 billion people

CORRESPONDING AUTHOR:
Dr Sony Sinha, Flat 201, Sharda Enclave, Plot 213A, Sahdeo Mahto Marg, Shrikrishnapuri, Patna 800001, Bihar, India, tel: (+91) 98350 95863, (+91) 99346 40080; e-mail: nishanteyecare@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

worldwide who have visual impairment or blindness, an estimated 123.7 million people suffer from visual impairment due to unaddressed refractive errors. They are the main cause of visual impairment in children aged 5–15 years [2, 3]. It has been estimated that over 40 million school-aged children have visual acuity of ≤ 6/12 from uncorrected or improperly corrected refractive errors and that the highest prevalence is in South-East Asia and China, particularly in urban areas [4]. The National Blindness and Visual Impairment Survey of India (2015–2019) revealed that refractive errors contribute to 29.6 per cent of visual impairment in 0–49 years age population [5].

The World Health Organization (WHO) and International Agency for the Prevention of Blindness (IAPB), recognize that globally, there is insufficient data on the prevalence and types of refractive errors in different populations and age groups [3]. The challenges in establishing an effective system to address the burden of uncorrected refractive errors in India include the development of optimally trained optometry workforce, the establishment of multi-tiered points of delivery of refractive care services and optical dispensing units, and seamless integration of these initiatives into existing or novel models of comprehensive eye care [6].

Given the aforesaid challenges, a large number of young people present to tertiary OPDs for refraction and prescription of glasses, the pattern and reasons for which have been enumerated in earlier publications [8, 9]. The overall incidence of refractive errors has been reported to be up to 55% in ophthalmology OPDs of vision centres as well as tertiary hospitals [9–11]. Various hospital-based studies have concluded that myopic errors (myopia [11–18] or myopic astigmatism [19]) are the most common refractive errors; myopia is, in general, more prevalent than astigmatism and hypermetropia, and myopic astigmatism is more common compared to hypermetropic or mixed astigmatism.

The mean age of presentation of refractive errors in adolescents has been estimated to be 14.3 years, but the prevalence has been reported to be maximum in the extremes of adolescence [9, 10, 18].

There is conflicting information on whether particular refractive errors are more prevalent in a particular gender. Some have found hypermetropic errors to be more common in females [20–22]. The Andhra Pradesh Eye Diseases Study (APEDS), which is the largest study regarding ocular morbidity in the South Indian population, found hypermetropic errors to be more common in urban females in the 16–29 years age group [20] compared to urban males, and myopic errors in rural females of 7–15 years age group [23] compared to rural males. The study from Kashmir [11] found no significant difference between males and females overall. To the knowledge of the investigators, only two similar community-based studies of schoolchildren have been conducted till date in Bihar — in one study, screening for refractive errors in 252 children aged 11–16 years revealed prevalence of refractive errors in 17.5% of males and 19.4% of females [24]. Another study, on the contrary, observed that among 131 children aged 10–14 years, screening revealed refractive errors in about 25.8 % of males and 17.7% of females [25]. These studies, however, did not analyse if particular refractive errors are more prevalent in a particular gender.

Reports from the WHO have stated that refractive errors are a growing problem among urban people in South-East Asia [4]. In Indian studies, myopia was prevalent amongst 4.1% rural [20] as compared to 7.4% amongst urban children [26]. Hypermetropia was found to be prevalent in 0.8% of rural [23] as compared to 7.7% urban children [26].

The APEDS [20] found that among rural persons aged 21–60 years, the more educated had more myopia and less hypermetropia compared to the less educated, while a study from Bangladesh [34] found the converse, that educational level is significantly associated with hypermetropia. These findings are not specific to young people.

Even with extensive literature review, the pattern of refractive errors that is prevalent among young people presenting to tertiary care institutions in Bihar state of India is yet unknown. We undertook the present epidemiological study with the objective to determine the clinico-demographic profile of young people presenting to our tertiary institution with refractive errors, as an initial step to enable hospital services to cater to them in a better manner, increasing their productivity for the development of the nation.

MATERIAL AND METHODS

A prospective observational study was conducted at the outpatient department (OPD) of the Upgraded Department of Ophthalmology of a medical college of Bihar, India, with its patients aged 10–24 years as the study population. Both objective

and subjective methods of refraction were used to assess refractive error in OPD patients with subnormal visual acuity improving with pinhole, and those with asthenopic symptoms. Patients with bilateral organic defects such as strabismus, corneal opacity, the opacity of the lens, and choroid and retinal disorders were excluded. Eyes with unilateral organic defects were also excluded from consideration [7, 23].

The objective method of autorefraction was employed first, using the Topcon RM-8800 autorefractor (Topcon Inc., USA) without cycloplegia-mydriasis. This was followed by subjective verification of refractive prescription using a standard trial frame and lenses and Snellen's Chart for 6 metres distance. Subsequently, upon the clinical decision in patients with asthenopia, autorefraction was repeated with cycloplegia-mydriasis using Cyclopentolate 1% alternating with tropicamide 0.8% + phenylephrine 5% eye drops [CTC technique (cyclopentolate–tropicamide–cyclopentolate)] followed by subjective verification.

Myopia was said to have been diagnosed in a particular eye when refractive correction prescribed amounted to ≥ 0.50 DSph(–) without any cylindrical correction. Similarly, hypermetropia was diagnosed when refractive correction prescribed amounted to ≥ 0.50 DSph(+) without any cylindrical correction. Myopic astigmatism was diagnosed when the power was ≥ 0.50 DCyl(–) with zero or negative spherical correction. Similarly, hypermetropic astigmatism was diagnosed when the power was ≥ 0.50 DCyl(+) with zero or positive spherical correction. Mixed astigmatism was diagnosed if the power contained both spherical and cylindrical corrections bearing opposite mathematical signs but with numerical values ≥ 0.50 D despite transposition.

The Indian Council of Medical Research (ICMR) and the Institutional Ethics Committee approved the study protocol. Accordingly, informed consent was obtained from the patients over 18 years of age and from the accompanying guardians of patients under 18 years of age. Using a pre-structured performa over a two-month period, clinico-demographic information with respect to their age, gender, residential background and literacy was collected along with recording for each eye, the refractive error diagnosed subsequently.

Raw data was entered in Microsoft Excel Spreadsheet 2013 (Microsoft Corporation, USA). Statistical Analyses were performed using the software SPSS 16.0 for Windows (Statistical Package for the Social Sciences, SPSS Inc., USA). Bivariate comparisons were made between the demographic variables and the types of refractive errors found. For qualitative analysis, the Chi-Square test was applied, taking $p < 0.05$ as significant.

RESULTS

During the study period, refractive correction was prescribed for a total of 1482 young people (2739 eyes). Among them, hypermetropic errors were more common [about 51%; comprising of hypermetropia (about 32%) and hypermetropic astigmatism (about 19%)]. This closely exceeded myopic errors [about 49%; myopic astigmatism (about 26%) and myopia (about 22%)]. The difference between the spherical and astigmatic errors was statistically significant ($\chi^2 = 2367.35$, df = 1, $p < 0.001$). Mixed astigmatism was the least common among all refractive errors (0.43%) (Tab. 1).

More young people from the 20–24 years age group (710 patients; 1347 eyes, about 50%) presented to the OPD compared to the 10–14 years (133 patients; 230 eyes, 8%) and 15–19 years (639 patients; 1162 eyes, 42%) age-groups. Myopic errors were more common in the 10-14 years age group (76%), while hypermetropic errors were more common and approximately equal in the 15–19 years (53%) and 20–24 years age group (54%). This difference was statistically significant ($\chi^2 = 107.554$, df = 4, $p < 0.001$). Mixed astigmatism remained low across all age-groups (Tab. 1, Fig. 1).

More males (81%) presented to the OPD than females (19%). Myopia was found to be the most prevalent refractive error in females (39%) while in males, this was the case with hypermetropia (37%, Tab. 1, Fig. 2). The distribution of refractive errors among the genders was statistically significant ($\chi^2 = 115.701$, df = 2, $p < 0.001$). Also, spherical errors were significantly more common in males, and astigmatism in females ($\chi^2 = 6.888$, df = 1, $p = 0.009$; OR = 1.29).

More urban (88%) than rural patients (12%) visited the OPD. Among rural patients, myopia was more common (53%), while among urban patients, this was the case with hypermetropia (35%, Tab. 1, Fig. 3). This difference was statistically significant ($\chi^2 = 104.873$, df = 2, $p < 0.001$). Also, spherical errors were significantly more common in rural, and astigmatism in urban patients ($\chi^2 = 14.172$, df = 1, $p < 0.001$; OR = 1.59).

Table 1. Classification and clinicodemographic distribution of refractive errors

	Grand Total (%)	Myopic errors			Hypermetropic errors			Mixed astigmatism (%)
		Total (%)	Myopia (%)	Myopic astigmatism (%)	Total (%)	Hypermetropia (%)	Hypermetropic astigmatism (%)	
Number of eyes	2739 (100.0)	1331 (48.6)	610 (22.3)	721 (26.3)	1396 (51.0)	879 (32.1)	517 (18.9)	12 (0.4)
Age group								
10–14 years	230 (100.0)	174 (75.7)	99 (43.0)	75 (32.6)	50 (21.7)	23 (10.0)	27 (11.7)	6 (2.6)
15–19 years	1162 (100.0)	539 (46.4)	151 (13.0)	388 (33.4)	619 (53.3)	442 (38.0)	177 (15.2)	4 (0.3)
20–24 years	1347 (100.0)	618 (45.9)	360 (26.7)	258 (19.2)	727 (54.0)	414 (30.7)	313 (23.2)	2 (0.1)
Gender								
Male	2213 (100.0)	968 (43.7)	403 (18.2)	565 (25.5)	1238 (55.9)	827 (37.4)	411 (18.6)	7 (0.3)
Female	526 (100.0)	363 (69.0)	207 (39.4)	156 (29.7)	158 (30.0)	52 (9.9)	106 (20.2)	5 (1.0)
Residence								
Rural	326 (100.0)	245 (75.2)	173 (53.1)	72 (22.1)	81 (24.8)	36 (11.0)	45 (13.8)	0 (0.0)
Urban	2413 (100.0)	1086 (45.0)	437 (18.1)	649 (26.9)	1315 (54.5)	843 (34.9)	472 (19.6)	12 (0.5)
Education								
Literate	2335 (100.0)	1098 (47)	559 (23.9)	539 (23.1)	1225 (52.5)	726 (31.1)	499 (21.4)	12 (0.5)
Illiterate	404 (100.0)	233 (57.7)	51 (12.6)	182 (45.6)	171 (42.3)	153 (37.1)	18 (4.5)	0 (0.0)

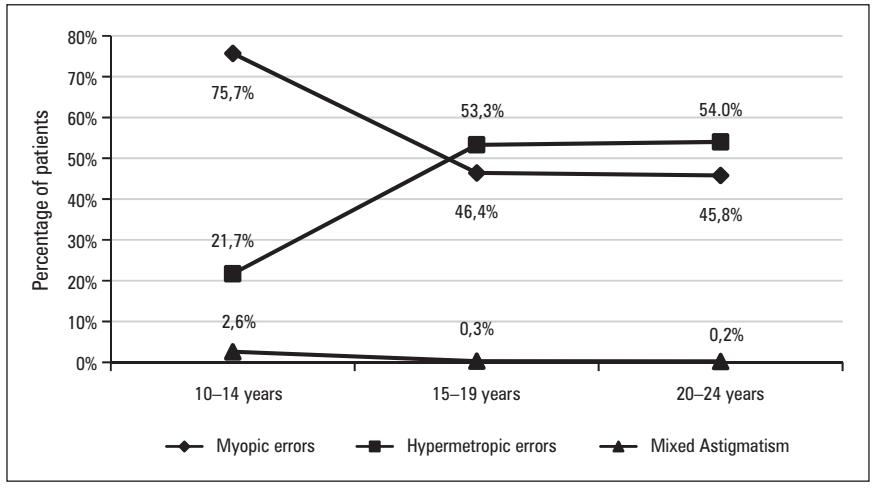

FIGURE 1. Comparison of refractive status with age-group (n = 2739)

More literate (85%) than illiterate patients (15%) visited the OPD. Among literate patients, hypermetropia was more common (31%), while among illiterate patients, this was the case with myopic astigmatism (45%, Tab. 1, Fig. 4). This difference was statistically significant (χ^2 = 17.057,

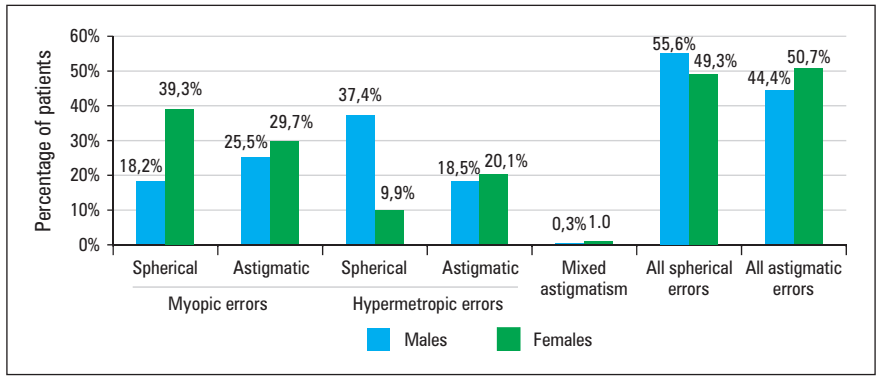

FIGURE 2. Comparison of refractive status with gender (n = 2739)

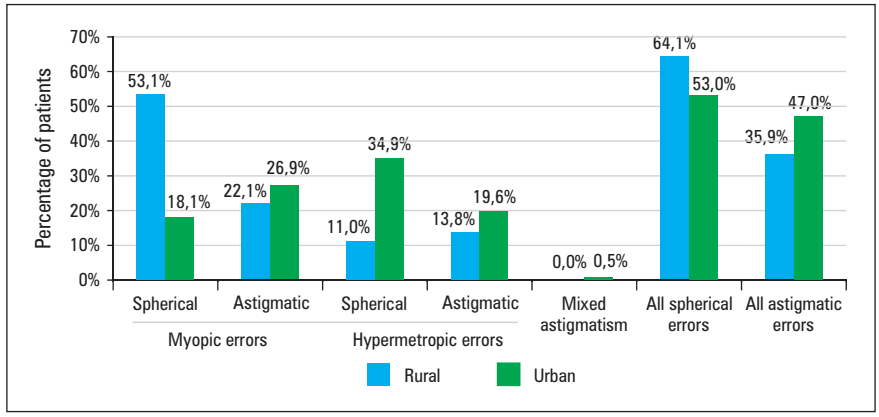

FIGURE 3. Comparison of refractive status with residential background (n = 2739)

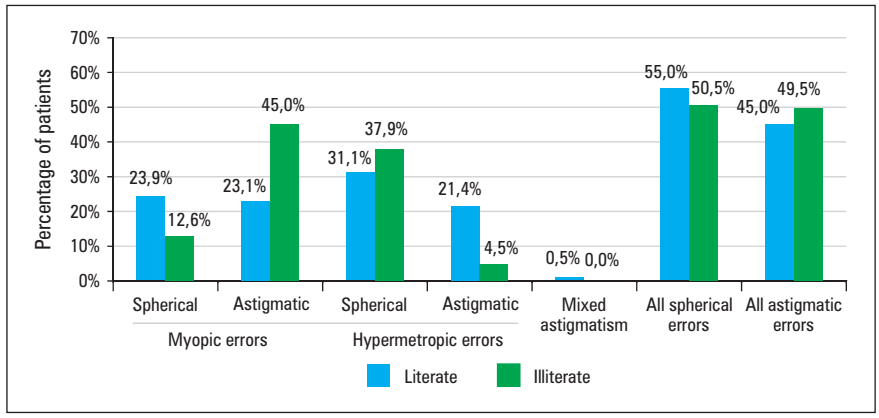

FIGURE 4. Comparison of refractive status with education (n = 2739)

df = 2, p < 0.001). Spherical errors were more common in the literate than astigmatism in the illiterate, but this was not significant (χ^2 = 2.858, df = 1, p = 0.091; OR = 1.20).

DISCUSSION

This study of 2739 eyes of 1482 young persons aged 10 to 24 years, an age-range that consists of extremely important formative and early produc-

tive years of citizens, was conducted to find out the distribution of refractive errors amongst them. It was conducted in a high-volume tertiary centre that meets the felt need of this section of the population, mostly students.

A large number of previous studies [9–27] have attempted to fill the gaps in knowledge regarding the distribution of refractive errors. In the present study, the frequencies of refractive errors, in descending order, were found as follows: hypermetropia (32%), myopic astigmatism (26%), myopia (22%), hypermetropic astigmatism (19%), and mixed astigmatism (0.4%; Fig. 1, Tab. 1). Overall, hypermetropic errors were more common (51%) than myopic errors (49%), but the difference was marginal. This presents an opposite picture when compared to various other studies which concluded that myopic errors (inclusive of myopia [11–18] and myopic astigmatism [19]) are the most common refractive errors in the population. The hospital data from the present study probably represent a compound picture wherein hypermetropia is more frequent in OPD patients because it is the refractive error causing the most asthenopic symptoms and thereby the need to visit the OPD; it is followed by myopic astigmatism and myopia that are the most common refractive errors in the population. This emphasizes that addressing the problem of hypermetropia may be more important in a hospital setting than previously thought.

In the present study, the young people who presented to the OPD belonged more to the 20–24 (50%) and 15–19 years age group (42%) compared to the 10–14 (8%) age group. This agrees with the studies in Kashmir [11], West Bengal [12] and Odisha [15], which found that refractive errors in adolescents peaked in the upper age-groups. It may be explained by the fact that asthenopia is increasingly manifested in students receiving higher education with the need for long periods of study. The present hospital-based study has found myopic errors to be more common in the 10–14 years age group (76%), and hypermetropic errors to be more common (and approximately equal in frequency) in the 15–19 years (53%) and 20–24 years age groups (54%, Tab. 1, Fig. 1). An increase in the presentation in the OPD of hypermetropic errors with age may be attributed to hypermetropia causing more asthenopic symptoms as discussed above.

As previously stated, available literature presents a conflicting picture regarding the gender distribution of refractive errors in India in general [9–18] and Bihar in particular [24, 25]. In the present study, about four times as many males presented to the OPD with refractive error as females, and myopic errors in general and myopia, in particular, were the most prevalent refractive error in females (39%, Tab. 1, Fig. 2). The difference could be probably because cultural constraints enable more males to step out of their homes for education than females. In addition, because myopia causes less asthenopia compared to hypermetropia, and, as above, although myopic errors are more common in females, a large proportion of females in the community would rather prefer not to wear glasses and not arrive for OPD consultation at all. However, the argument provided by the APEDS [20], that females have smaller eyes applies in India, does not seem to stand true. In addition, spherical errors were significantly more common in males, and astigmatic errors in females ($p = 0.009$; OR = 1.29). No comparable studies could be found in this regard.

Far more urban (88%) than rural young people (12%) visited the OPD. This is because the hospital is situated in an urban area, but may reflect that refractive errors are a growing problem in urban settings as identified by the WHO [4]. The reasons of reporting to a tertiary care hospital have been enumerated in a previous study [8]. Among rural patients, myopia was more common (53%), while among urban patients, this was the case with hypermetropia (35%, Tab. 1, Fig. 3). This difference was statistically significant ($p < 0.001$). This disagrees with the population-based Indian studies comparing similar age-groups [20, 26], wherein both myopia (7.4% *vs.* 4.1%) and hypermetropia (7.7% *vs.* 0.8%) were more common amongst urban children. In addition, spherical errors were significantly more common in rural, and astigmatisms in urban patients ($p < 0.001$, OR = 1.59). No comparable studies could be found in this regard.

More literate (85%) than illiterate patients (15%) visited the OPD. This is because the medical college is flanked with a number of educational institutions in the vicinity. Among literate patients, hypermetropia was most common (31%, Tab. 1, Fig. 4) which was similar to a study from Bangladesh [27] but contrary to APEDS [20]. These studies found myopia more prevalent in the educated, whereas in the present study, myopic astigmatism was found to be more common in rural patients (45%). This was a statistically

significant difference ($p < 0.001$), probably arising out of the particular age-range considered in the present study, as well as the protocol of performing cycloplegia in all patients who reported asthenopic symptoms. Spherical errors were more common in the literate than astigmatisms in the illiterate, but this was not significant ($p = 0.091$; OR = 1.20)

The present study provides a broad picture of refractive errors and the clinico-demographic profile of patients who present to the ophthalmology OPD. Further multi-centric studies could be done to compare medical college hospitals in rural areas with urban ones and to compare tertiary hospitals of different states at different stages of development, that would have a bearing on the prevalent conditions of care in rural areas in order to enact a uniform standard of basic minimum care for the country.

CONCLUSION

This study yielded several insights into the clinico-demographic profile of young people presenting with refractive errors to the Ophthalmology OPD of the medical college hospital. It achieved its objectives in providing a broad picture of an area of research that has stayed unattended in the state of Bihar, India.

It is concluded that in the outpatient setting of the tertiary hospital, there is a predominance of symptomatic myopic errors in the age group of 10–14 years, which changes to hypermetropic in the age group 15–19 and 20–24 years. There is a predominance of myopia in females and rural young people, of myopic astigmatism in the illiterate but hypermetropia in males, in urban young people and the literate. Addressing the problem of hypermetropia may be more important in a hospital setting than previously thought.

Conflict of interests

The authors report no competing interests.

Funding source

Indian Council of Medical Research (ICMR) vide STS award, reference number 2015-04003.

REFERENCES

1. Park K. Textbook of Preventive and Social Medicine, 22nd Ed. M/S Banarsidas , Bhanot 2013: 548.
2. Bourne R, Flaxman S, Braithwaite T, et al. Magnitude, temporal trends, and projections of the global prevalence of blindness and distance and near vision impairment: a systematic review and meta-analysis. Lancet Global Health. 2017; 5(9): e888–e897, doi: 10.1016/s2214-109x(17)30293-0.
3. World Health Organisation, Action Plan 2006–2011, VISION 2020 Global Initiative for the Elimination of Avoidable Blindness. https://www.iapb.org/wp-content/uploads/VISION-2020-Action-Plan-2006-2011.pdf.
4. Resnikoff S, Pascolini D, Mariotti SP, et al. Global magnitude of visual impairment caused by uncorrected refractive errors in 2004. Bull World Health Organ. 2008; 86(1): 63–70, doi: 10.2471/blt.07.041210, indexed in Pubmed: 18235892.
5. National blindness and visual impairment survey India 2015–2019: A summary report, Ministry of Health and Family Welfare, Government of India: 2.
6. Honavar SG. The burden of uncorrected refractive error. Indian J Ophthalmol. 2019; 67(5): 577–578, doi: 10.4103/ijo.IJO_762_19, indexed in Pubmed: 31007210.
7. Sinha S, Sinha RK, Nishant P. Prevalence of spectacle use and amblyopia among young people presenting to a tertiary care institution of Bihar. Trop J Ophthal Otolaryngol. 2019; 4(2): 151–156, doi: 10.17511/jooo.2019.i02.14.
8. Nishant P, Sinha S, Sinha RK. Refraction-seeking behaviour among young people presenting to a medical college hospital of Bihar. Ind J Clin Exp Ophthalmol. 2018; 4(2): 254–257, doi: 10.18231/2395-1451.2018.0056.
9. Sudhan A, Pandey KP, Khare M, et al. Vision Centre' as a strategy to provide eye care services to underserved populations: Results from Satna district of Madhya Pradesh, India. Community Eye Health J Indian Supplement. 2008; 21(68): 117–118.
10. Bhardwaj M, Singh L, Gupta A, et al. Pattern of refractive errors among the patients presenting to eye department of district hospital of Uttarakhand. Ind J Clin Exp Ophthalmol. 2016; 2(3): 248, doi: 10.5958/2395-1451.2016.00053.6.
11. Rohul J, Maqbool A, Hussain S, et al. Prevalence of Refractive Errors in Adolescents in Out-patient Attendees of the Preventive Ophthalmology Clinic of Community Medicine, SKIMS, Kashmir, India. J Health Allied Sci NU. 2013; 03(01): 17–20, doi: 10.1055/s-0040-1703627.
12. Saha M, Ranjan A, Islam MN, et al. Prevalence of Refractive Errors among the School going Children at a Tertiary Center of West Bengal. Int J Sci Stud. 2017; 5: 179–182.
13. Natung T, Taye T, Lyngdoh LA, et al. Refractive errors among patients attending the ophthalmology department of a medical college in North-East India. J Family Med Prim Care. 2017; 6(3): 543–548, doi: 10.4103/2249-4863.222023, indexed in Pubmed: 29417005.
14. Hazarika H, Bhuyan D, Hazarika S, et al. Refractive errors in age group seven to fifteen years: North-east India scenario. Int J Community Med Public Health. 2017; 4(6): 1928, doi: 10.18203/2394-6040.ijcmph20172151.
15. Rao GN, Sabnam S, Pal S, et al. Prevalence of ocular morbidity among children aged 17 years or younger in the eastern India. Clin Ophthalmol. 2018; 12: 1645–1652, doi: 10.2147/OPTH.S171822, indexed in Pubmed: 30233126.
16. Singh HV, Kumar D. Refractive error scenario in paediatric age group (7-15 years) in Assam: A hospital based study. IP Int J Ocul Oncol Oculoplasty. 2019; 4(4): 148–150, doi: 10.18231/2581-5016.2018.0038.
17. Mittal S, Maitreya A, Dhasmana R. Clinical profile of refractive errors in children in a tertiary care hospital of Northern India. Int J Community Med Public Health . 2016: 1189–1194, doi: 10.18203/2394-6040.ijcmph20161382.
18. Matta S, Matta P, Gupta V, et al. Refractive Errors among Adolescents attending Ophthalmology OPD. Ind J Comm Med. 2006; 31: 114–115.
19. Rizyal A, Ghising R, Shrestha RK, et al. Pattern of refractive errors among patients at a tertiary hospital in Kathmandu. Nepal Med Coll J . 2011; 13(3): 172–174, indexed in Pubmed: 22808808.
20. Dandona R, Dandona L, Naduvilath TJ, et al. Refractive Errors in an Urban Population in Southern India: The Andhra Pradesh Eye Disease Study. Invest Ophthalmol Vis Sci. 1999; 40: 2810–2818, indexed in Pubmed: 10549640.

21. Raju P, Ramesh SVe, Arvind H, et al. Prevalence of refractive errors in a rural South Indian population. Invest Ophthalmol Vis Sci. 2004; 45(12): 4268–4272, doi: 10.1167/iovs.04-0221, indexed in Pubmed: 15557431.
22. Kalikivayi V, Naduvilath TJ, Bansal AK, et al. Visual impairment in school children in Southern India. Indian J Ophthalmol. 1997; 45(2): 129–134, indexed in Pubmed: 9475034.
23. Dandona R, Dandona L, Srinivas M, et al. Refractive error in children in a rural population in India. Invest Ophthalmol Vis Sci. 2002; 43(3): 615–622, indexed in Pubmed: 11867575.
24. Bharati D. A cross-sectional study on pattern of ocular morbidity and the prevalence of refractive errors among school children of 11 to 16 years in the rural area of Maner, Patna Bihar, India. J Med Sci Clin Res. 2019; 7(2), doi: 10.18535/jmscr/v7i2.46.
25. Sinha RK. Ocular Morbidity Pattern in Schoolchildren in Muzaffarpur, Bihar. J Ophthalmol. 2006; 31: 66–67.
26. Murthy GV, Gupta SK, Ellwein LB, et al. Refractive error in children in an urban population in New Delhi. Invest Ophthalmol Vis Sci. 2002; 43(3): 623–631, indexed in Pubmed: 11867576.
27. Bourne RRA, Dineen BP, Huq DM, et al. Correction of refractive error in the adult population of Bangladesh: meeting the unmet need. Invest Ophthalmol Vis Sci. 2004; 45(2): 410–417, doi: 10.1167/iovs.03-0129, indexed in Pubmed: 14744879.

REVIEW PAPER
DOI: 10.5603/OJ.2020.0021

Diet and supplements as a supportive treatment for age-related macular degeneration

Jan Ostrowski[1], Karolina Kątska-Ostrowska[2], Wieslaw I. Gruszecki[3], Robert Rejdak[1]

[1]Department of General Ophthalmology, Medical University of Lublin, Lublin, Poland
[2]Department of Diagnostic and Microsurgery of Glaucoma, Medical University of Lublin, Lublin, Poland
[3]Department of Biophysics, Institute of Physics, Maria Curie-Sklodowska University, Lublin, Poland

ABSTRACT

Age-related macular degeneration (AMD) is one of the leading causes of blindness in developed countries. It is estimated that about 196 million people worldwide suffer from AMD. So far, despite many studies, no causative treatment that can be used large scale has been discovered. In order to slow down, the progression of the disease, a change of the modifiable risk factors such as diet and prophylaxis in the form of nutritional supplements are recommended. The purpose of this work is to present types of supplementation and draw attention to the proper diet containing products rich in substances such as lutein and zeaxanthin protecting the eye against the rapid progression of dry AMD.

KEY WORDS: AMD; dietary supplements; carotenoids; xanthophylls; lutein, zeaxanthin

Ophthalmol J 2020; Vol. 5, 101–106

INTRODUCTION

Age-related macular degeneration (AMD) is one of the leading causes of non-reversible visual impairment in humans over 50 years old and frequently increases in those after 65 years of age [1]. The prevalence of AMD is about 196 million people worldwide [2, 3]. The disease affects the central part of retina called *macula lutea* and results in loss of central and sharp vision which is required for daily living activities as reading, driving and watching television.

Age-related macular degeneration can be classified as non-exudative (dry) or exudative (wet). Whereas wet AMD can be treated using anty-VEGF injections with a good clinical result, for the dry form of the disease there is no causative treatment [2, 4, 5]. Thus, the question appears — is it possible to prevent AMD and/or slow down its progression?

The pathogenesis of the disease is multifactorial and not fully understood but many publications point out the significant role of oxidative stress (OS) [6, 7]. In the course of AMD, the loss of retinal pigment epithelium (RPE) cells and photoreceptors in the macula area is observed. The retinal examination reveals the presence of drusen — extracellular deposits, which are located between Bruch's membrane and RPE. RPE cells have a high metabolic rate and therefore have the ability to produce reactive oxygen species (ROS). What's more, they are exposed to ROS through iron ion accumulation, exposure to high light and smoking. The pigment epithelium consisting of two carotenoids, which are lutein and zeaxanthin [two stereoisomers: (3R,3'R)-zeaxanthin, and (3R,3'S)-zeaxanthin (*meso*-zeaxanthin)], is a natural protective barrier for the retina of the human eye from OS [7]. This discovery became the basis for the use of substances with antioxidant properties such as carotenoids (lutein, zeaxanthin), vitamin C and E and zinc in the prevention and treatment of this disease.

CORRESPONDING AUTHOR:
Jan Ostrowski, MD, Department of General Ophthalmology, Medical University of Lublin, Lublin, Poland; e-mail: jasion1@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

There are several modifiable and non-modifiable risk factors connected with the progression of AMD. The most important are sex, age, genetic, diet, smoking, sunlight exposure, obesity and hypertension [8, 9]. In this paper, we would like to emphasize the protective role of diet in the disease progression.

A review of the latest and most frequently cited literature was carried out. We searched for the articles which focus on the relationship between nutritional factors and AMD progression. They included works related to the diet in age-related macular degeneration and the latest information on AMD treatment methods.

Scientific research in the field of biochemistry was also cited, in which the level of dietary components in the supportive treatment of AMD was determined.

THE ROLE OF SUPPLEMENTATION IN AMD

One of the most significant multicentral clinical trials that evaluate the role of antioxidants supplementation on the rate of AMD progression were The Age-Related Eye Disease Study (AREDS) and The Age-Related Eye Disease Study 2 (AREDS2).

The Age-Related Eye Disease Study involved 4757 patients, aged 55 to 80 years, presenting of extensive small drusen, intermediate or large drusen, noncentral geographic atrophy, or pigment abnormalities in one or both eyes, or advanced AMD or vision loss due to AMD in one eye. Patients were randomly assigned to one of four groups depending on the type of oral supplementation (Tab. 1):

— antioxidants (vitamin C — 500 mg; vitamin E — 400 IU; and β-carotene — 15 mg);
— zinc — 80 mg (as zinc oxide) and copper — 2 mg (as cupric oxide);
— antioxidants plus zinc;
— placebo [10].

The study revealed that patients receiving zinc, antioxidants, or the combination of both showed a decrease in the rate of progression to advanced AMD. It was estimated that those receiving both zinc and antioxidants achieved a 25% reduction of progression to advanced AMD relative to placebo. The decreased percentage in visual acuity scores from 29% for those assigned to placebo to 23% for those assigned to antioxidants plus zinc. Moreover, the AREDS showed a statistically significant association between the incidence of AMD and risk factors such as smoking, BMI, race, education, and age [11].

Table 1. Commercially available formulas based on the Age-Related Eye Disease Study — AREDS/AREDS2

Nutrient	AREDS formula	AREDS2 formula
Vitamin C	400 mg	500 mg
Vitamin E	400 IU	400 IU
β-carotene	15 mg	–
Lutein	–	10 mg
Zeaxanthin	–	2 mg
Zinc	80 mg	80 mg
Copper	2 mg	2 mg

Due to the significant progress in the study of the effect of supplementation on AMD development, soon after the publication of the results of AREDS in 2001, it was necessary to start further research in this direction, that was AREDS2 [11]. Modification of supplementation was also caused by reports of an increased risk of lung cancer in smokers after using β-carotene as well as urogenital infections resulting from taking zinc [12, 13].

In addition, the natural occurrence of lutein and zeaxanthin in the pigment epithelium was the basis for using these substances in further studies on AMD supplementation. The aim of the AREDS2 was to show whether adding lutein + zeaxanthin, omega-3 long-chain polyunsaturated fatty acids [docosahexaenoic acid (DHA) + eicosapentaenoic acid (EPA)], or both to the AREDS formulation reduces the risk of developing advanced AMD. It is worth mentioning that DHA is an important structural component of the retina, and EPA may play the role of a precursor to signalling molecules that can affect retinal function, which was the basis for studying these nutrients. The second aim of the research was to evaluate the effect of eliminating β-carotene, lowering zinc doses, or both in the AREDS formulation [14]. The conclusion of the AREDS2 was that comparing to placebo, the addition of lutein/zeaxanthin and/or omega-3 fatty acids to the previous AREDS formulation had no significant effect on AMD progression of visual acuity loss. Moreover, the results showed no effect of β-carotene elimination or lower-dose zinc on progression to advanced AMD. However, because of potential increased incidence of lung cancer in former smokers, lutein + zeaxanthin could be an appropriate carotenoid substitute in the AREDS formulation. Addition of lutein and zeaxanthin may have some

effect on AMD progression in those populations in which the dietary intake of these nutrients is low.

Over the years, many studies have been conducted to assess the effect of antioxidants supplementation on AMD. Feng et al. based on a meta-analysis of nine randomized trials (a total of 920 eyes) have shown that lutein supplementation at a dose of 10 or 20 mg daily for more than 6 months can contribute to an increase in macular pigment optical density (MPOD), improvement of visual acuity and a better sense of contrast in patients with AMD [15]. Macular pigment levels, usually measured in terms of MPOD, may correspond with normal retinal function [15–20].

The role of omega-3 fatty acids supplementation in AMD is also worth mentioning. They have the ability to renew in RPE cells, their deficiency can lead to degradation of photoreceptors as well as the accumulation of lipid filled drusen in RPE and sub-RPE space [21]. A number of studies have been conducted to assess the effects of omega-3 supplementation on the development and progression of AMD. The Eye Disease Case-Control Study showed that the higher intake of n-3 fatty acids may be associated with the lower risk of AMD among patients with the lower linoleic acid (omega-6 fatty acid) consumption [22, 23]. The Nutritional AMD Treatment 2 (NAT2) study showed that higher EPA and DHA content in red blood cell membranes may have protective effects against AMD [24]. Some authors suggest that high doses of EPA (3.4 g) and DHA (1.6 g) daily for six months can result in improved visual acuity in patients with dry AMD [25]. On the other hand, a 2015 Cochrane meta-analysis report that there is no evidence confirming that supplementation with Omega-3 fatty acids prevents or slows the progression of AMD [26].

To sum up, although some scientific studies indicate a positive effect of omega-3 fatty acid supplementation in preventing the progression of AMD, it should be emphasized that most studies are observational and not supported by randomized controlled studies [21, 26]. Therefore, it seems appropriate to recommend that patients eat fatty fish or omega-3 fatty acid supplements as potentially beneficial in reducing the progression of AMD while informing patients that most of the data is based on observational studies [26].

Noteworthy is also another substance — resveratrol, which is a plant polyphenolic compound commonly found in peel and grape seeds as well as in red and white wine [27]. Resveratrol has antioxidant, anti-angiogenic and anti-inflammatory properties, which are used not only in the prevention of eye diseases but also in the prevention of cardiovascular, cancer and neurodegenerative diseases [28]. Based on the literature, it is known that resveratrol acts on various types of eye cells by increasing the level of natural enzymes and the ability to molecularly defend antioxidants. This substance, by limiting pro-inflammatory factors such as interleukins and prostaglandins, as well as reducing chemical attraction and recruitment of immune cells to the inflammatory site, has anti-inflammatory capabilities. In addition, resveratrol has been shown to have anti-VEGF activity and inhibits vascular endothelial cell proliferation and migration. Resveratrol has been shown to be successfully used in many ophthalmic diseases based on animal models and in vivo experiments [28].

One of the more interesting and recent studies on the effects of resveratrol on RPE cells is the study by Nashine et al. The study evaluated the effects of over-the-counter nutrient supplements containing resveratrol and HPLC-purified resveratrol, in human transmitochondrial age-related macular degeneration (AMD) retinal pigment epithelial (RPE) patient cell lines. These cell lines were obtained from dry and wet AMD patients. It turned out that resveratrol treatment with different resveratrol formulations improved cell viability and decreased reactive oxygen species generation in each AMD patient cell line. Although further studies are required to establish the cytoprotective potential of resveratrol under different physiological conditions, this novel study established the positive effects of resveratrol supplements in macular degeneration patient cell lines in vitro [27]. The study used a maximum concentration of 1000 μM resveratrol as this dose was confirmed to be effective in previous studies that evaluated a wide range of resveratrol doses in AMD RPE [27].

DIET IN AMD

When discussing the role of dietary supplements in the context of AMD, it should be emphasized that any supplementation can replace a proper, well-balanced diet. Therefore, it is important to determine which nutritional ingredients and in what proportions may have a beneficial effect in the prevention of AMD and patients with already diagnosed disease. Many studies have tried to determine the dietary patterns recommended in AMD

but it still seems difficult to develop general guidelines based on them [29–31]. Koning-Backus et al. investigated whether general dietary guidelines for healthy lifestyles are associated with a reduced risk of AMD. The study analyzed recommended minimum intake values for various food categories and standards, based on publicly available dietary recommendations from national food centers operating in many developed countries. In addition, they calculated the percentage of the population that followed these recommendations, characterized their profile, and examined the risk of AMD.

The study included four thousand two hundred and two participants in the Rotterdam study ≥ 55 years who were free from AMD at baseline and followed for 9.1 ± 5.8 years. Dietary data were collected using a verified 170 food frequency questionnaire, and food consumption was divided into nutritional patterns based on Health Council guidelines.

The results of the study were as follows — seven hundred and fifty-four people developed AMD. The consumption of the recommended amounts of vegetables (≥ 200 g/day), fruits (2 ×/day) and fish (2 ×/week) was 30.6%, 54.9% and 12.5% respectively. In particular, fish consumption (2 ×/week) reduced the risk of AMD. Consumption of the recommended amounts of all 3 food groups was only 3.7%, but following this pattern showed a further reduction in the risk of AMD.

To sum up, a diet of 200 g a day of vegetables, fruit twice a day and fish twice a week is associated with a significantly reduced risk of AMD [32].

A systematic literature review conducted by Chapman et al. identified eighteen high-quality studies evaluating the role of diet and food intake in AMD. This work showed that the diet has a multifactorial effect on the occurrence and progression of AMD. The authors of the review recommend adhering to the Mediterranean diet, which is based on a high intake of fruits, vegetables, legumes, whole grains and nuts; moderate consumption of fish, poultry and dairy products, the use of olive oil instead of fats, small amounts of red wine and limited consumption of red meat. As for other diets, the Oriental diet pattern with higher intake of vegetables, legumes, fruits, whole grains, tomatoes and seafood is considered more favorable compared to the Western diet pattern, which is characterized by higher consumption of red meat, processed meat, and high-fat products dairy fried potatoes, refined beans and eggs. In addition, it was noted that high consumption of vegetables rich in carotenoids and fatty fish containing omega-3 fatty acids were beneficial for those at risk of AMD. However, in order to reduce the risk of AMD progression, a minimum intake of vegetable oils and animal fats containing omega-6 fatty acids and red or processed meat is recommended. In addition, foods with a low glycemic index (IG) are preferred to foods with a high IG, and alcohol consumption should be limited.

CONCLUSION

The treatment of the dry form of age-related macular degeneration has been a big challenge for scientists for many years. To date, despite numerous scientific studies including clinical trials, no causative treatment of this disease is known. Among the modifiable factors affecting the incidence and progression of AMD, it has been shown that supplementation and, above all, a proper diet are very important. The currently recommended dietary supplementation in AMD patients has been developed based on the AREDS and AREDS2 studies (Tab. 2). This formula includes the intake of 500 mg vitamin C, 400 IU. vitamin E, 25 mg zinc, 2 mg copper, 10 mg lutein and 2 mg zeaxanthin per day. A special role is assigned to xanthophyll carotenoids-lutein and zeaxanthin, which are the main components of the macular pigment. They are thought to play an important role in maintaining the morphological and functional integrity of the retina. Concentrated in the macula, these substances have the ability to filter blue light and

Table 2. Recommended composition of dietary supplements for patients with age-related macular degeneration (AMD) and their sources in nutritional products

Nutrient	Food source
Carotenoids	Kale, spinach, watercress, basil, peas, lettuce, zucchini, broccoli, tomatoes, corn, Brussels sprouts, spring onions, egg yolk, pumpkin and leeks
Omega-3 fatty acids	Salmon, anchovy mackerel, tuna, sardines, and swordfish
Vitamin C	Fresh vegetables and fruits, especially brassicas, berries
Vitamin E	Olive oil, hazelnut oil, sunflower, almond, grape seed, almond, nuts, leafy vegetables, cereal grains
Zinc	Mussels, oysters, pork liver, almonds, beans, wholemeal flour

deactivate reactive oxygen species, thus protecting against light-induced oxidative damage that is involved in AMD pathogenesis. Studies have shown that consumption of lutein and zeaxanthin is associated with a lower risk of AMD progression, but remaining inconsistent about preventive effects of supplementation on AMD.

As mentioned earlier, diet has a vital role in AMD, so the provision of appropriate nutritional advice to those at risk of AMD is recommended. Current evidence suggests that improving diet quality, increasing the intake of foods containing the nutrients required by the retina, and avoiding foods that cause oxidative damage will play an important role in protecting against AMD. With the approaching increase in the number of AMD patients in the aging population, healthcare professionals should actively promote food choices that minimize AMD risk.

Acknowledgements

Foundation for Polish Science is acknowledged for financial support within the project "Xanthophylls in the Retina of the Eye (TEAM/2016-3/21).

REFERENCES

1. Bird AC, Bressler NM, Bressler SB, et al. An international classification and grading system for age-related maculopathy and age-related macular degeneration. Surv Ophthalmol. 1995; 39(5): 367–374, doi: 10.1016/s0039-6257(05)80092-x.
2. Wong WL, Su X, Li X, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. Lancet Glob Health. 2014; 2(2): e106–e116, doi: 10.1016/S2214-109X(13)70145-1, indexed in Pubmed: 25104651.
3. Nowak JZ. AMD — the retinal disease with an unprecised etiopathogenesis: in search of effective therapeutics. Acta Pol Pharm . 2014; 71(6): 900–916.
4. Pennington KL, DeAngelis MM. Epidemiology of age-related macular degeneration (AMD): associations with cardiovascular disease phenotypes and lipid factors. Eye Vis (Lond). 2016; 3: 34, doi: 10.1186/s40662-016-0063-5, indexed in Pubmed: 28032115.
5. Rinninella E, Mele MC, Merendino N, et al. The Role of Diet, Micronutrients and the Gut Microbiota in Age-Related Macular Degeneration: New Perspectives from the Gut Retina Axis. Nutrients. 2018; 10(11), doi: 10.3390/nu10111677, indexed in Pubmed: 30400586.
6. Datta S, Cano M, Ebrahimi K, et al. The impact of oxidative stress and inflammation on RPE degeneration in non-neovascular AMD. Prog Retin Eye Res. 2017; 60: 201–218, doi: 10.1016/j.preteyeres.2017.03.002, indexed in Pubmed: 28336424.
7. Domènech EB, Marfany G. The Relevance of Oxidative Stress in the Pathogenesis and Therapy of Retinal Dystrophies. Antioxidants (Basel). 2020; 9(4), doi: 10.3390/antiox9040347, indexed in Pubmed: 32340220.
8. Heesterbeek TJ, Lorés-Motta L, Hoyng CB, et al. Risk factors for progression of age-related macular degeneration. Ophthalmic Physiol Opt. 2020; 40(2): 140–170, doi: 10.1111/opo.12675, indexed in Pubmed: 32100327.
9. Shim SH, Kim SG, Bae JH, et al. Risk Factors for Progression of Early Age-Related Macular Degeneration in Koreans. Ophthalmic Epidemiol. 2016; 23(2): 80–87, doi: 10.3109/09286586.2015.1129425, indexed in Pubmed: 26950426.
10. Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. Arch Ophthalmol. 2001; 119(10): 1417–1436, doi: 10.1001/archopht.119.10.1417, indexed in Pubmed: 11594942.
11. Gorusupudi A, Nelson K, Bernstein PS. The Age-Related Eye Disease 2 Study: Micronutrients in the Treatment of Macular Degeneration. Adv Nutr. 2017; 8(1): 40–53, doi: 10.3945/an.116.013177, indexed in Pubmed: 28096126.
12. Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The Effect of Vitamin E and Beta Carotene on the Incidence of Lung Cancer and Other Cancers in Male Smokers. New Engl J Med. 1994; 330(15): 1029–1035, doi: 10.1056/nejm199404143301501, indexed in Pubmed: 8127329.
13. Johnson AR, Munoz A, Gottlieb JL, et al. High dose zinc increases hospital admissions due to genitourinary complications. J Urol. 2007; 177(2): 639–643, doi: 10.1016/j.juro.2006.09.047, indexed in Pubmed: 17222649.
14. Age-Related Eye Disease Study 2 Research Group. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. JAMA. 2013; 309(19): 2005–2015, doi: 10.1001/jama.2013.4997, indexed in Pubmed: 23644932.
15. Feng L, Nie K, Jiang H, et al. Effects of lutein supplementation in age-related macular degeneration. PLoS One. 2019; 14(12): e0227048, doi: 10.1371/journal.pone.0227048, indexed in Pubmed: 31887124.
16. Bernstein PS, Li B, Vachali PP, et al. Lutein, zeaxanthin, and meso-zeaxanthin: The basic and clinical science underlying carotenoid-based nutritional interventions against ocular disease. Prog Retin Eye Res. 2016; 50: 34–66, doi: 10.1016/j.preteyeres.2015.10.003, indexed in Pubmed: 26541886.
17. Ozawa Y, Shigeno Y, Nagai N, et al. Absolute and estimated values of macular pigment optical density in young and aged Asian participants with or without age-related macular degeneration. BMC Ophthalmol. 2017; 17(1): 161, doi: 10.1186/s12886-017-0557-5, indexed in Pubmed: 28851319.
18. Loane E, Kelliher C, Beatty S, et al. The rationale and evidence base for a protective role of macular pigment in age-related maculopathy. Br J Ophthalmol. 2008; 92(9): 1163–1168, doi: 10.1136/bjo.2007.135566, indexed in Pubmed: 18669545.
19. Sabour-Pickett S, Nolan JM, Loughman J, et al. A review of the evidence germane to the putative protective role of the macular carotenoids for age-related macular degeneration. Mol Nutr Food Res. 2012; 56(2): 270–286, doi: 10.1002/mnfr.201100219, indexed in Pubmed: 22121091.
20. Puell MC, Palomo-Alvarez C, Barrio AR, et al. Relationship between macular pigment and visual acuity in eyes with early age-related macular degeneration. Acta Ophthalmol. 2013; 91(4): e298–e303, doi: 10.1111/aos.12067, indexed in Pubmed: 23575039.
21. Mukhtar S, Ambati BK. The value of nutritional supplements in treating Age-Related Macular Degeneration: a review of the literature. Int Ophthalmol. 2019; 39(12): 2975–2983, doi: 10.1007/s10792-019-01140-6, indexed in Pubmed: 31313070.
22. Aoki A, Inoue M, Nguyen E, et al. Dietary n-3 Fatty Acid, -Tocopherol, Zinc, vitamin D, vitamin C, and β-carotene are Associated with Age-Related Macular Degeneration in Japan. Sci Rep. 2016; 6: 20723, doi: 10.1038/srep20723, indexed in Pubmed: 26846575.
23. Seddon JM, George S, Rosner B. Cigarette smoking, fish consumption, omega-3 fatty acid intake, and associations with age-related macular degeneration: the US Twin Study of Age-Related Macular Degeneration. Arch Ophthalmol. 2006; 124(7): 995–1001, doi: 10.1001/archopht.124.7.995, indexed in Pubmed: 16832023.
24. Borrelli E, Souied EH, Freund KB, et al. The role of omega-3 and micronutrients in age-related macular degeneration. Surv Ophthalmol. 2014; 59(5): 532–539, doi: 10.1016/j.survophthal.2014.01.001, indexed in Pubmed: 24657038.

25. Georgiou T, Neokleous A, Nicolaou D, et al. Pilot study for treating dry age-related macular degeneration (AMD) with high-dose omega-3 fatty acids. PharmaNutrition. 2014; 2(1): 8–11, doi: 10.1016/j.phanu.2013.10.001.
26. Lawrenson JG, Evans JR. Omega 3 fatty acids for preventing or slowing the progression of age-related macular degeneration. Cochrane Database Syst Rev. 2012; 11: CD010015, doi: 10.1002/14651858.CD010015.pub2, indexed in Pubmed: 23152282.
27. Nashine S, Nesburn AB, Kuppermann BD, et al. Role of Resveratrol in Transmitochondrial AMD RPE Cells. Nutrients. 2020; 12(1), doi: 10.3390/nu12010159, indexed in Pubmed: 31935891.
28. Lançon A, Frazzi R, Latruffe N. Anti-Oxidant, Anti-Inflammatory and Anti-Angiogenic Properties of Resveratrol in Ocular Diseases. Molecules. 2016; 21(3): 304, doi: 10.3390/molecules21030304, indexed in Pubmed: 26950104.
29. Amirul Islam FM, Chong EW, Hodge AM, et al. Dietary patterns and their associations with age-related macular degeneration: the Melbourne collaborative cohort study. Ophthalmology. 2014; 121(7): 1428–1434.e2, doi: 10.1016/j.ophtha.2014.01.002, indexed in Pubmed: 24560564.
30. Chiu CJ, Chang ML, Zhang FF, et al. The relationship of major American dietary patterns to age-related macular degeneration. Am J Ophthalmol. 2014; 158(1): 118–127.e1, doi: 10.1016/j.ajo.2014.04.016, indexed in Pubmed: 24792100.
31. Merle B, Silver B, Rosner JM. Adherence to a Mediterranean diet, genetic susceptibility, and progression to advanced macular degeneration: a prospective cohort study. Am J Clin Nutr. 2015; 102(5): 1196–1206, doi: 10.3945/ajcn.115.111047, indexed in Pubmed: 26490493.
32. de Koning-Backus APM, Buitendijk GHS, Kiefte-de Jong JC, et al. Intake of Vegetables, Fruit, and Fish is Beneficial for Age-Related Macular Degeneration. Am J Ophthalmol. 2019; 198: 70–79, doi: 10.1016/j.ajo.2018.09.036, indexed in Pubmed: 30312575.
33. Chapman NA, Jacobs RJ, Braakhuis AJ. Role of diet and food intake in age-related macular degeneration: a systematic review. Clin Exp Ophthalmol. 2019; 47(1): 106–127, doi: 10.1111/ceo.13343, indexed in Pubmed: 29927057.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0022

Induced glare testing — an underutilized test in evaluating visual disability in patients presenting with symptomatic cataracts

Satheesh Solomon T. Selvin[1], Abhriya Dey[2, 1], Chris Elsa Samson Jacob[3, 1], Thomas Kuriakose[1]

[1]Department of Ophthalmology, Christian Medical College, Vellore, India
[2]Mission of Mercy AG Hospital, Kolkata, West Bengal, India
[3]Sankara Nethralaya, Chennai, Tamil Nadu, India

ABSTRACT

BACKGROUND: Cataract increases intraocular light scatter which affects the retinal image contrast and sensitivity. Symptomatic patients with cataract complain of a drop in the quality of vision or glare affecting daily routine even with preserved visual acuity. This study was aimed to quantify the drop in the glare induced visual acuity (VA) and contrast sensitivity (CS) in different morphological types of cataracts.

MATERIAL AND METHODS: This was an observational study on a prospective cohort, conducted at a tertiary-care centre in South-India. Patients admitted for cataract surgeries between March and September 2017 with BCVA ≥ 6/60 (Snellen) and ≥ 40 years were enrolled. LogMAR VA and CS were measured pre and post-operatively, with and without glare induction using brightness acuity tester. Patients were sub-categorised based on morphology and the presence of glare as a symptom. Paired-t test for the pre- and post-operative values and analysis with Bonferroni's adjustment were the statistical methods used.

RESULTS: Data of 78 patients were sub-categorised and analysed. Glare induction with high glare was significant in all the studied groups. LogMAR VA was affected most in group 3 (0.20, 10 letters, $p < 0.05$) and the CS in group 2 (0.62, 4.1 step drop, $p < 0.05$). Patients who had glare as a symptom had an average greater drop in LogMAR VA (0.30, $p = 0.01$) and CS (–0.29, $p = 0.03$) when induced with a high glare.

CONCLUSIONS: All morphological types of cataracts affect VA and CS to a greater extent in conditions of bright lighting. Glare induced VA and CS testing is a sensitive and an adjunct tool to traditional high contrast VA testing, in evaluating the visual dysfunction of patients presenting with symptomatic cataracts.

KEY WORDS: brightness acuity tester; cataract; contrast sensitivity; glare, logMAR

Ophthalmol J 2020; Vol. 5, 107–113

INTRODUCTION

Visual acuity (VA) is a special sense and a decrease in which can result in difficulties of all functional domains of day-today activities. The visual experience of a human eye is not just isolated to the VA alone but involves the various attributes of vision [1–3]. The physiology of the visual system is a series of complex tasks, which includes the transmission of visual sensations forming representations, stereopsis, perception of movement, colour vision, contrast perception etc [1–6].

Ocular pathologies with media opacity lead to light scattering resulting in glare and affects the contrast of the visual scene for the individual. Contrast

CORRESPONDING AUTHOR:
Dr Satheesh Solomon T. Selvin, Assoc. Prof, Schell Eye Hospital; No 1, Arni Road, Vellore 632001, Tamil Nadu, India, tel: (+ 91) 416 228 1309, fax: (+91) 416 222 2115; e-mail: ssts@rediffmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

sensitivity (CS) is the ability to discern and detect an object against its background whereas glare is the contrast reducing effect secondary to stray light in the visual scene [7–9]. Individual variations are seen with CS and it physiologically declines with age whereas glare could become bothersome depending on its severity and the individual needs. Cataract is the most common condition which results in increased intraocular light scatter affecting the CS and thereby the quality of the visual perception and the image [10–14]. Visual acuity though is the traditional standard measure of visual function, is retained till advance stages of cataracts, even in the presence of other visual complaints [14, 15] The advice on surgery largely depends on the measured VA in most hospitals and has become the sole criteria to advice the patient.

A brightness acuity tester (BAT) with a standardized glare induction can measure the drop in glare-induced VA and CS [16, 17]. A measure of these parameters when compared to the post-operative recovery will provide information about the visual disability of the patients, which retrospectively will quantify as the extent of visual quality deterioration. In our study, we evaluated and quantified glare induced degradation of VA (LogMAR — logarithm of the minimum angle of resolution) and CS (Pelli-Robson chart) in patients who were admitted for cataract surgeries.

MATERIAL AND METHODS

This was an observational study on a prospective cohort of patients, conducted at a tertiary care centre in southern India between March and September 2017. The study was approved by the Institutional Review Board and the Ethics Committee and followed the Tenets of the Declaration of Helsinki.

SAMPLE SIZE CALCULATION

We needed to study 77 patients (eyes) to study a difference of 0.8 between the pre and post-operative (90% power at a 5% level of significance). The sample size was calculated based on the study by Wood et al [18]. We enrolled 90 patients with an assumption of about 15–20% as the drop-out rate during follow up.

ENROLLMENT

Patients admitted for cataract surgeries during the study period were enrolled after informed consent. Demographic data and symptomatology pertaining to cataract affecting their daily routine were collected. Patients with best corrected visual acuity (BCVA) of Snellen equivalent of 6/60 or better, and above 40 years with the ability to read English alphabets were identified and included in the study. Patients with corneal degenerations, dystrophies or scars in the visual axis, synechiae and abnormalities of pupil, retinal and optic nerve pathologies were excluded. Other exclusion criteria included were the usage of dilating drops in the preceding 48 hours and dilated or non-reacting pupil as these could exaggerate the glare perception.

METHODOLOGY

All patients who were enrolled underwent BCVA measurement with LogMAR chart (Weber contrast 97%, Appasamy I Chart Lite, 100 cd/m^2) by the primary investigator. Patients had their CS measurement with the Pelli-Robson chart (3 m, 80 cd/m^2) following which the LogMAR vision and CS were measured again in low-glare (10 foot-lamberts) and high-glare (100 foot-lamberts) respectively using a BAT (Marco, BAT-2000, Jacksonville, Florida) by the co-investigator. The horizontal pupillary diameter was then measured (NIDEK Optical Biometry, Nidek CO., Ltd., Japan Model 2000) under normal room lighting conditions (LUX 32 cd/m^2) by the primary investigator. The luminance was measured with the Secure Life Illumination meter (Class B per DIN 5032-7, Gossen Mavolux Ltd.). Patients were examined for the type and the morphology of the cataract by a single ophthalmologist (Slit-lamp, HAAG Streit, International 10) using LOCS III (Lens Opacities Classification System III). To avoid observation bias, the measurements were done independently and all three investigators were blinded from each other's readings. Patients underwent their planned surgeries and all the readings were repeated with the same protocol at the scheduled follow up visit between 6 ± 1 weeks following their cataract surgeries. Further, at follow up, the resolution of the symptoms were recorded in a Likert Scale of 0 to 10 with 10 being the complete resolution of the same.

STATISTICAL ANALYSIS

Data was entered into Microsoft Excel and analysed using STATA/IC 13.1. Data was summarised using mean (standard deviation) for continuous variables and frequency (%) for categorical variables. Continuous variables were analysed using ANOVA, categorical variables using paired-t-test for pre and post-operative differences and statistical significance kept at 5% level ($p < 0.05$). Bonferroni

correction adjustment was applied for the analysis of the measured values between groups.

RESULTS

Ninety patients were enrolled in the study of which 12 patients did not follow up as per the study protocol as defined in the study; data of 78 patients were analysed. The mean age of the participants was 61.68 years (range 41–80 years). Primary complaints were either decreased vision or glare with 47 patients in our study population had both the symptoms. Almost 70% of our study population (54 patients) experienced glare from the headlamps of the oncoming vehicles or on exposure to bright sunlight. Of the patients who had glare, 20 patients drove vehicles on a regular basis, and all of them experienced troubling glare from headlights of the oncoming vehicles. Forty-six of the 54 patients who had symptoms of glare had a component of posterior sub-capsular cataract. All except three patients had a complete reduction of glare postoperatively, and the three patients had reported a score of 5 on a Likert Scale of 0 to 10 for reduction of glare post-operatively. The evaluation revealed two patients having minimal residual central striate keratopathy involving the pupillary axis and one with an IOL dislocation with a fixed mid-dilated pupil of 4.1 mm, as the possible reasons for the residual complaints of glare.

Patients were grouped based on the morphological type of cataracts — nuclear sclerosis (NS) — Group 1 (20 patients, 25.64%), posterior capsule cataract (PSC) — Group 2 (11 patients, 14.10%) and a combination of nuclear sclerosis with posterior capsule cataract (NS + PSC, Group 3, 47 patients, 60.26%). Presence of cortical opacities in the central 3 mm zone (visual axis) was also noted. The mean pre-operative horizontal pupillary diameter as measured with Optical Biometer, was 2.87 mm (SD ± 0.08) and post-operatively was 3.17 mm (SD ± 0.08) and the mean difference of 0.3 mm between the subgroups was clinically negligible and not statistically significant.

Table 1 gives an overview of the raw data of the mean values of the LogMAR and the CS val-

Table 1. Raw data of the mean values of the LogMAR and contrast sensitivity (CS) induced with low and high-glare with the brightness acuity tester in the various study groups

	LogMAR Vision	LogMAR vision in low glare	LogMAR vision in high glare	Contrast sensitivity	Contrast sensitivity in low glare	Contrast sensitivity in high glare
Preoperative measurements Mean values (± SD)						
Group 1 (n = 20)	0.35 (0.15)	0.36 (0.13)	0.51 (0.26)	1.11 (0.32)	1.10 (0.33)	0.61 (0.41)
Group 2 (n = 11)	0.37 (0.24)	0.38 (0.24)	0.51 (0.44)	1.03 (0.39)	1.02 (0.39)	0.41 (0.51)
Group 3 (n = 47)	0.52 (0.22)	0.53 (0.21)	0.72 (0.35)	0.80 (0.38)	0.79 (0.40)	0.26 (0.33)
Total (n = 78)	0.46 (0.22)	0.46 (0.22)	0.64 (0.36)	0.91 (0.40)	0.91 (0.41)	0.37 (0.41)
Post-operative measurements Mean values (± SD)						
Group 1 (n = 20)	0.08 (0.11)	0.08 (0.11)	0.11 (0.13)	1.52 (0.25)	1.52 (0.25)	1.29 (0.26)
Group 2 (n = 11)	0.09 (0.16)	0.08 (0.15)	0.10 (0.16)	1.60 (0.16)	1.56 (0.12)	1.47 (0.22)
Group 3 (n = 47)	0.10 (0.11)	0.10 (0.11)	0.10 (0.13)	1.43 (0.24)	1.44 (0.24)	1.27 (0.23)
Total (n = 78)	0.10 (0.12)	0.10 (0.12)	0.11 (0.14)	1.48 (0.24)	1.49 (0.24)	1.31 (0.25)

SD — standard deviation

Table 2. Mean pre-operative LogMAR and contrast sensitivity (CS) values pre subcategorised with a glare as a symptom at presentation

Pre-operative values	Glare as a symptom at presentation		
	Present (n = 53) Mean (± SD)	Absent (n = 25) Mean (± SD)	Difference (p value)
LogMAR vision	0.51 (0.21)	0.35 (0.20)	0.16 (0.04)
LogMAR vision in low glare	0.51 (0.21)	0.37 (0.19)	0.14 (0.05)
LogMAR vision in high glare	0.70 (0.35)	0.40 (0.18)	0.30 (0.01)
Contrast sensitivity	0.85 (0.39)	1.04 (0.42)	–0.19 (0.04)
Contrast sensitivity in low glare	0.84 (0.38)	1.03 (0.43)	–0.19 (0.04)
Contrast sensitivity in high glare	0.30 (0.37)	0.59 (0.45)	–0.29 (0.03)

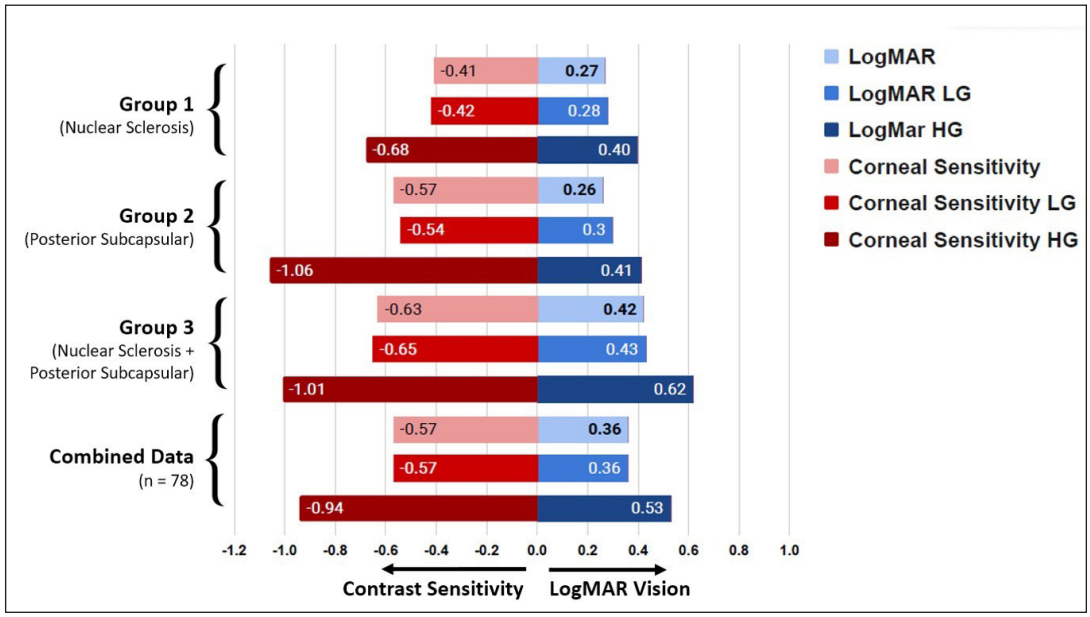

FIGURE 1. Difference between the pre and post-operative values of the LogMAR vision and the contrast sensitivity with and without induction of low glare (LG) and high glare (HG)

Table 3. Odds ratio of the presence of glare as a symptom to the various morphological types of cataracts in the study population

	Glare *vs.* cortical riders	Glare *vs.* NS (Group 1)	Glare *vs.* PSC alone (Group 2)	Glare *vs.* NS + PSC (Group 3)	Glare *vs.* presence of PSC
Odds ratio	1.2209	0.1926	1.3037	3.4688	5.1923
Confidence interval (95%)	0.342–4.354	0.065–0.570	0.134–5.401	1.282–9.351	1.75–15.39

NS — nuclear sclerosis; PSC — posterior subcapsular cataract

ues among the three morphological groups pre and post-surgery, with and without the induction of glare with BAT. Similarly, Table 2 shows the mean values of the patients pre and post-surgery categorised with the presence or absence of glare. All values of LogMAR or CS in different situations of induction with BAT not only were statistically significant but were also clinically significant. Figure 1 shows the mean improvement in the LogMAR and CS following surgery as compared to the pre-operative values, with and without induction with low and high glare respectively. Table 3 shows the Odd's

ratio of glare to the presence of the morphological characteristics of the cataract to assess the risk of having glare as a symptom associated with the presence of it. The presence of either cortical riders or PSC is shown to have the associated risk of glare with the presence of PSC alone, showing a 5 fold risk association.

DISCUSSION

Discomforting or the disabling glare in the visual scene results in sub-optimal visual performance. Disability glare due to light scatter or discomforting glare resulting in an instinctive desire to look away from the light source, both of which can be distracting and blinding in extreme situations. Light scattering is a normal consequence of the aging process, which leads to a patient having a decreased retinal contrast and glare disability [12–15]. Presence of cataractous changes in the lens, increases the intraocular light scatter and thereby reduces retinal image contrast and degradation of visual quality [15–17]. There is no defined cut-off of BCVA to define cataract, although symptomatic patients can complain of glare even without any drop in the measured vision [15]. Patients with significant cataractous change often deal with glare on a daily basis which can be unpleasant depending on the visual needs and demands of the individual.

Cataracts of all types theoretically can drop VA and CS in situations that induce glare [19–23]. The difference between the mean LogMAR vision and CS-induced with a high glare in our study population, showed a statistically significant difference between the pre and post-operative values irrespective of the sub-groups and the morphological types (Tab. 1, Fig. 1). However, this difference was not significant between the pre and post-operative values on induction with low glare. Though glare disability could act as an adjunct tool to VA measurement to advice on cataract surgery, the visual need of the varies with individuals [20, 23]. The tropical sunny climate of South India and with most patients in our study from an agricultural background is likely the reason for nearly 70% of our study patients complaining of glare as a symptom. In real-life situations, working in fields under a sunny climate of a tropical region or being on a sunny beach can be considered equivalent to high glare induction [16, 17]. Though CS and LogMAR vision assessment with and without glare induction provide useful information on the visual disability in day-today activities, neither is quantified in different types of morphological cataracts to advise patients on the requirement of surgery.

All morphological forms of cataract are reported to cause glare disability to varied extents. From clinical experience, one would anticipate patients with PSC to have the maximum effect on the vision when induced with glare [12, 21, 22]. This is evident in our study as well where the glare induced VA and CS in Group 2 and 3 had the highest drop. However, when the patients with glare were compared with the ones who did not complain of glare, the VA and CS showed a statistically significant difference in the measure values (Tab. 2). This difference was greater when induced with high glare and was statistically and clinically more significant. Moreover, the recovery of the VA and CS following surgery in simulated testing (induced glare) conditions, are indirect measures of the glare disability in day today activities. Studies have reported a significant drop of CS in patients even with the presence of milder forms of PSC [19, 21, 22] again a consistent finding as seen in our study with Group 2 (PSC alone). Brightness acuity tester in conjunction with CS has been reported to be more sensitive than VA alone especially with VA ≥ 20/80 [8, 18, 21]. The odds of having glare as a symptom in our study was the highest in patients with PSC, and is again the highest in our study, as seen to be three to five times in these patients (Tab. 3). The strong influence of the PSC to the visual symptoms resulting in decreased VA and impairment of CS can be attributed to the proximity of the location of PSC to the nodal point.

In real-life situations, one would expect a combination of NS with PSC to affect the CS more than either of the morphology alone. In our study population, the LogMAR vision seems most affected in group 3, whereas it is less affected with a similar pattern in the other two morphological groups (Fig. 1). Similarly, CS is affected most in Group 2 (presence of PSC only) and group 3 (PSC in association with NS), as compared by NS alone (Group 1) (Fig. 1). Majority of patients (47 patients, 60.3%) in our study had a combination of NS with PSC, which is a true representation of the distribution of patients seeking surgery in routine practice [22, 24, 25]. When induced with high glare, Group 1 had a drop in the LogMAR (0.16) and CS (0.50), Group 2 with LogMAR (0.14) and CS (0.62) and Group 3 had a drop in LogMAR (0.20) and CS (0.54) respectively (Tab. 1). With each letter valued to be 0.02 units in LogMAR assessment, an average drop of about

9 letters ($p < 0.05$) is evident in our study population (Tab. 1). This is equivalent to a 2 lines drop in LogMAR VA assessment, which is clinically significant in any testing conditions. Similarly, an average of 0.54 drop in the CS, translates to around 3.6 ($p < 0.05$) step drop with the Pelli-Robson chart in our study population. This deterioration on induced glare testing is clinically significant and could be extremely bothersome to the patients in the day-today activities. Though the change in the values in the three groups are linear with the induction of high glare, the visual degradation of LogMAR VA and the CS are not similar and may not be to the same extent. In a clinical setup and in the evaluation of the patients towards cataract surgeries, both glare induced VA and CS have its advantages to quantify the change and one cannot be ignored over the information obtained from the other.

Symptomatic patients with a significant drop in the CS but not with LogMAR are the group of patients seem to present late in the course of the disease. With slow progress in cataractous changes, the individual may fail to notice the change in the quality of the image. This probably is because such patients are getting neuro-acclimatised over time and the sensory image may be regarded as "acceptably clear" due to gradual habituation and tolerance of the individual. The glare induced VA and CS drop, simulate the real-life scenarios of patients with symptomatic cataracts, and would better correlate to the symptoms to advise patients with visual disability. The patients with reasonably good pre-operative VA and have opted for surgery had the greatest drop in their CS ascertains the fact stronger. Since our sample only included patients who presented for surgery, it may be interpreted vice versa. This retrospectively suggests that the additional contribution of cataract to the glare and why the patients are symptomatic despite a good measured VA.

To quantify the quality of vision by a single parameter is often difficult and this statistically significant effect of cataract in the vision parameters supports the clinical relevance of measuring the same with glare induction [15, 17, 21]. It would be prudent to test glare induced VA and CS degradation along with the routine vision assessment, which will help us to understand the symptomatology better in patients presenting with symptoms of cataract. Testing VA and CS with BAT in patients who request surgery at good levels of vision can give us a better insight into why these patients want surgery and to understand the visual change characteristics. A drop in vision on induced glare testing among such patients can then justify advising surgery. However, it is not true otherwise, to use BAT testing to justify cataract surgery in patients who have do not have symptoms. VA and CS degradation with glare induction will act as more sensitive methods of testing visual function than the routine measurements of the high contrast based VA measurements alone. Done routinely, glare testing will predict real-life visual disability better in patients who have cataracts with symptoms.

Limitation of our study includes evaluating with our working conditions, which were possibly different the other studies (as all the studies have not reported the ambient intensity), which could have altered the absolute value of BAT. Our study included only patients admitted for cataract surgeries and hence extrapolation of these observations to a general population should be done with caution as this may not represent the true distribution of an epidemiological cataract population.

CONCLUSIONS

Cataracts affect vision and contrast to a greater extent in conditions of high glare and bright lighting. The presence of PSC either alone or in combination with NS has a significant effect on the glare induced CS as well as the VA of an individual. Performing a glare induced VA and CS testing in patients presenting with cataracts for advice, are sensitive ancillary measurements that will simulate real-life situations and will provide a comprehensive assessment of vision disability affecting the daily routine.

Conflict of interests

The authors have not conflicts of interests to disclose.

REFERENCES

1. Frisén L, Frisén M. How good is normal visual acuity?. A study of letter acuity thresholds as a function of age. Albrecht Von Graefes Arch Klin Exp Ophthalmol. 1981; 215(3): 149–157, doi: 10.1007/BF00413146, indexed in Pubmed: 6908464.
2. Bailey IL, Jackson AJ. Changes in the clinical measurement of visual acuity. J Phys: Conference Series. 2016; 772: 012046, doi: 10.1088/1742-6596/772/1/012046.
3. Colenbrander A. The Historical Evolution of Visual Acuity Measurement. Vis Impair Res. 2009; 10(2-3): 57–66, doi: 10.1080/13882350802632401.
4. Brown B, Yap MK. Differences in visual acuity between the eyes: determination of normal limits in a clinical population. Ophthalmic Physiol Opt. 1995; 15(3): 163–169, doi: 10.1046/j.1475-1313.1995.9590568m.x, indexed in Pubmed: 7659416.
5. Pointer JS. Evaluating the visual experience: visual acuity and the visual analogue scale. Ophthalmic Physiol Opt. 2003; 23(6): 547–552, doi: 10.1046/j.1475-1313.2003.00152.x, indexed in Pubmed: 14622359.

6. Cvintal V, Delvadia R, Sun Y, et al. Contrast Sensitivity in Patients with Cataract: Comparing Pelli-Robson with SPARCS Testing Methods. Invest Ophthalmol Vis Sci. 2014; 55: 758.
7. Abrahamsson M, Sjöstrand J. Impairment of contrast sensitivity function (CSF) as a measure of disability glare. Invest Ophthalmol Vis Sci. 1986; 27(7): 1131–1136, indexed in Pubmed: 3721791.
8. Bal T, Coeckelbergh T, Van Looveren J, et al. Influence of cataract morphology on straylight and contrast sensitivity and its relevance to fitness to drive. Ophthalmologica. 2011; 225(2): 105–111, doi: 10.1159/000317076, indexed in Pubmed: 20881445.
9. Elliott DB, Bullimore MA. Assessing the reliability, discriminative ability, and validity of disability glare tests. Invest Ophthalmol Vis Sci. 1993; 34(1): 108–119, indexed in Pubmed: 8425818.
10. Stifter E, Sacu S, Thaler A, et al. Contrast acuity in cataracts of different morphology and association to self-reported visual function. Invest Ophthalmol Vis Sci. 2006; 47(12): 5412–5422, doi: 10.1167/iovs.05-1564, indexed in Pubmed: 17122131.
11. Williamson TH, Strong NP, Sparrow J, et al. Contrast sensitivity and glare in cataract using the Pelli-Robson chart. Br J Ophthalmol. 1992; 76(12): 719–722, doi: 10.1136/bjo.76.12.719, indexed in Pubmed: 1486072.
12. Shandiz JH, Derakhshan A, Daneshyar A, et al. Effect of cataract type and severity on visual acuity and contrast sensitivity. J Ophthalmic Vis Res. 2011; 6(1): 26–31, indexed in Pubmed: 22454703.
13. Elliott DB, Hurst MA. Simple clinical techniques to evaluate visual function in patients with early cataract. Optom Vis Sci. 1990; 67(11): 822–825, doi: 10.1097/00006324-199011000-00006, indexed in Pubmed: 2250890.
14. Adamsons IA, Vitale S, Stark WJ, et al. The association of postoperative subjective visual function with acuity, glare, and contrast sensitivity in patients with early cataract. Arch Ophthalmol. 1996; 114(5): 529–536, doi: 10.1001/archopht.1996.01100130521004, indexed in Pubmed: 8619761.
15. Aslam TM, Haider D, Murray IJ. Principles of disability glare measurement: an ophthalmological perspective. Acta Ophthalmol Scand. 2007; 85(4): 354–360, doi: 10.1111/j.1600-0420.2006.00860.x, indexed in Pubmed: 17313443.
16. Bailey IL, Bullimore MA. A new test for the evaluation of disability glare. Optom Vis Sci. 1991; 68(12): 911–917, doi: 10.1097/00006324-199112000-00001, indexed in Pubmed: 1787947.
17. Prager TC, Urso RG, Holladay JT, et al. Brightness acuity test and outdoor visual acuity in cataract patients. J Cataract Refract Surg. 1987; 13(1): 67–69, doi: 10.1016/s0886-3350(87)80016-0, indexed in Pubmed: 3559957.
18. Wood JM, Carberry TP. Bilateral cataract surgery and driving performance. Br J Ophthalmol. 2006; 90(10): 1277–1280, doi: 10.1136/bjo.2006.096057, indexed in Pubmed: 16825273.
19. Elliott DB, Gilchrist J, Whitaker D. Contrast sensitivity and glare sensitivity changes with three types of cataract morphology: are these techniques necessary in a clinical evaluation of cataract? Ophthalmic Physiol Opt. 1989; 9(1): 25–30, doi: 10.1111/j.1475-1313.1989.tb00800.x, indexed in Pubmed: 2594373.
20. Jaffe NS. Glare and contrast: indications for cataract surgery. J Cataract Refract Surg. 1986; 12(4): 372–375, doi: 10.1016/s0886-3350(86)80098-0, indexed in Pubmed: 3735114.
21. Stifter E, Sacu S, Weghaupt H. Functional vision with cataracts of different morphologies: comparative study. J Cataract Refract Surg. 2004; 30(9): 1883–1891, doi: 10.1016/j.jcrs.2004.01.038, indexed in Pubmed: 15342050.
22. Chua BE, Mitchell P, Cumming RG. Effects of cataract type and location on visual function: the Blue Mountains Eye Study. Eye (Lond). 2004; 18(8): 765–772, doi: 10.1038/sj.eye.6701366, indexed in Pubmed: 15044934.
23. Fujikado T, Kuroda T, Maeda N, et al. Light scattering and optical aberrations as objective parameters to predict visual deterioration in eyes with cataracts. J Cataract Refract Surg. 2004; 30(6): 1198–1208, doi: 10.1016/j.jcrs.2003.12.023, indexed in Pubmed: 15177593.
24. Rubin GS, Adamsons IA, Stark WJ. Comparison of acuity, contrast sensitivity, and disability glare before and after cataract surgery. Arch Ophthalmol. 1993; 111(1): 56–61, doi: 10.1001/archopht.1993.01090010060027, indexed in Pubmed: 8424725.
25. Fu J, Wang J, Wang NI, et al. [Early clinical evaluation of visual function in patients with age-related cataract]. Zhonghua Yan Ke Za Zhi. 2006; 42(3): 236–240, indexed in Pubmed: 16643756.

CASE REPORT
DOI: 10.5603/OJ.2020.0024

Progressive bilateral ocular ischemic syndrome despite previously performed carotid endarterectomy

Marta Świerczyńska[1, 2], Lech Sedlak[1, 2], Mariola Dorecka[1, 2]

[1]Department of Ophthalmology, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland
[2]Department of Ophthalmology, Kornel Gibiński University Clinical Center, Medical University of Silesia, Katowice, Poland

ABSTRACT

The ocular ischemic syndrome (OIS) is a rare condition with vision-threatening potentials. It is characterized by chronic ischemia of the anterior and/or posterior segment of the eye primarily caused by severe carotid artery occlusive diseases. In this article, we present a case of a 67-year-old male patient presented with the gradual diminution of vision in the right eye for 6 months. The patient had undergone a right internal carotid artery (ICA) endarterectomy (CEA) twice before. On the day of admission, intraocular pressure (IOP) was 34 mm Hg in the right eye (RE) and 20 mm Hg in the left eye (LE). On anterior segment examination, neovascularization of iris in the right eye was noted. On fundoscopy dilated retinal veins, attenuated retinal arteries, blot hemorrhages, cotton wool spots and microaneurysms were present. The patient underwent the appropriate investigations including computed tomography angiography (CTA) of carotid arteries, fundus fluorescence angiography (FFA) and Doppler ultrasound (DUS) of ophthalmic and central retinal arteries, which were all consistent with a diagnosis of bilateral OIS. Intraocular pressure was pharmacologically reduced and stabilized. Subsequently, panretinal photocoagulation (PRP) of peripheral capillary nonperfusion areas was performed in both eyes.

KEY WORDS: bilateral ocular ischemic syndrome; IOS; carotid artery occlusion; neovascular glaucoma

Ophthalmol J 2020; Vol. 5, 114–119

INTRODUCTION

The ocular ischemic syndrome (OIS) is caused by arterial hypoperfusion of the eye due to severe stenosis or occlusion of the ipsilateral common or internal carotid artery (ICA) [1, 2]. The reported incidence is 7.5 cases per million persons every year [3]. The average age of patients with OIS is 65 and it is rarely diagnosed among people before the age of 50 [2]. This condition is twice as common in men due to the higher incidence of cardiovascular and atherosclerotic diseases compared to women [3, 4]. Other risk factors include hypertension, hyperlipidemia, uncontrolled diabetes mellitus, smoking addiction and vasculitis [4]. Loss of vision is usually unilateral and progresses slowly. However, there are cases of sudden blindness [1]. In about 20% of cases, bilateral IOS occurs [3], which more often affects patients with the aortic arch syndrome, hyperhomocysteinemia and Takayasu arteritis [2, 5].

Visual loss of varying degree is the most common symptom [4]. Changes of the anterior segment include conjunctival and episcleral injection, rubeosis iridis, secondary neovascular glaucoma, iridocyclitis, iris atrophy, anterior and posterior synechiae, sluggish pupillary reaction to light, corneal edema with Descemet's folds, asymmetric cataract. More

CORRESPONDING AUTHOR:
Marta Świerczyńska, MD, Department of Ophthalmology, Kornel Gibiński University Clinical Center, Medical University of Silesia, Katowice, Poland, 35 Ceglana Street, 40–514 Katowice, Poland, tel: +48 697314696; e-mail: m.swierczynska93@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

characteristic are changes related to the posterior segment, such as narrowed retinal arteries, dilated but not tortuous retinal veins, neovascularization of the optic disc and the retina, perifoveal telangiectasias, retinal hemorrhages, microaneurysms, cotton wool spots, areas of chorioretinal atrophy, macular edema or vitreous hemorrhage. These symptoms may co-occur with the orbital infarction syndrome, which includes ophthalmoplegia, orbital pain, hypotony and ptosis [1, 2, 4, 6].

The aim of this study was to present a case of a progressive bilateral ocular ischemic syndrome despite previously performed carotid endarterectomy.

CASE REPORT

A 67-year-old male presented to the emergency room complaining of recurrent unilateral eye pain and gradual decrease and blurring of the vision in his right eye for the past 6 months. His medical history included hypertension, coronary artery disease, hypercholesterolemia, type 2 diabetes mellitus and diabetic nephropathy.

He underwent artery bypass surgery nine years ago, percutaneous coronary intervention three years ago. He had twice undergone an ICA endarterectomy (in 2017 and 2018). There was no history of ocular or head trauma.

At the time of presentation, the best-corrected visual acuity (BCVA) was 5/50 in the RE and 5/8 in the LE. Anterior segment examination showed conjunctival injection and anterior synechiae in both eyes. The pupil in the RE was semi-dilated and non-reactive. Moreover, in the RE, there was advanced iris neovascularization and the presence of new vessels in the iridocorneal angle on gonioscopy. Fundus examination in both eyes showed attenuated retinal arteries, dilated retinal veins, cotton-wool spots, microaneurysms and blot hemorrhages at the retinal mid-periphery (Fig. 1). Intraocular pressure was 34 mm Hg in the RE and 20 mm Hg in the LE on applanation tonometry. The patient was admitted to the Department of Ophthalmology to reduce IOP and for further work-up.

Computed tomography angiography (CTA) of carotid arteries revealed critical narrowing (over 90%) of the proximal segment of the right internal and external carotid arteries, confirming that the patient had developed carotid artery restenosis after his previous carotid endarterectomies (CEAs). Moreover, the CTA showed narrowing 60% of the proximal segment of the left ICA and occlusion of the right vertebral artery. There were no changes inside the orbital cavities that could lead to pressure on the blood vessels and ischemia of the eyeballs for reasons other than atherosclerosis.

Fundus fluorescence angiography (FFA) of the RE revealed prolonged arm-to-choroid and arm-to-retina circulation time, arteriovenous transit time delay, extensive non-perfusion areas within the peripheral retina, staining of the retinal vessels at the late phase and hyperfluorescence of the optic disc (Fig. 2). In the LE, non-perfusion zones in the temporal quadrants and macular edema were seen. Microaneurysms were also noted in both eyes (Fig. 3). This picture suggested diabetic retinopathy of both eyes. However, significant asymmetry of ischemic changes more strongly marked in the RE indicated OIS.

Doppler ultrasound (DUS) examination showed high retrograde flows in both ocular arteries (OA) (Fig. 4). Whereas in the central retinal arteries, the

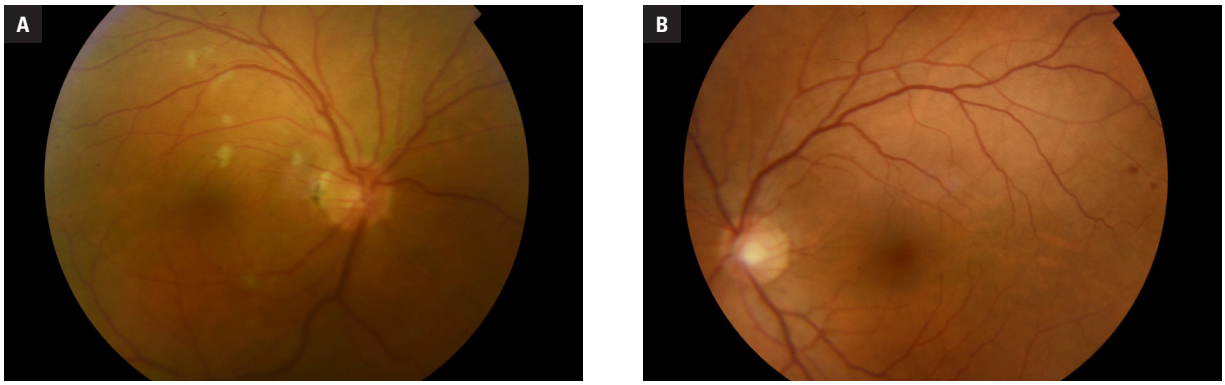

FIGURE 1AB. Fundus photographs of the right and left eye: dilated but not tortuous retinal veins, narrowed retinal arteries, cotton wool spots, microaneurysms and retinal hemorrhages at the mid-periphery

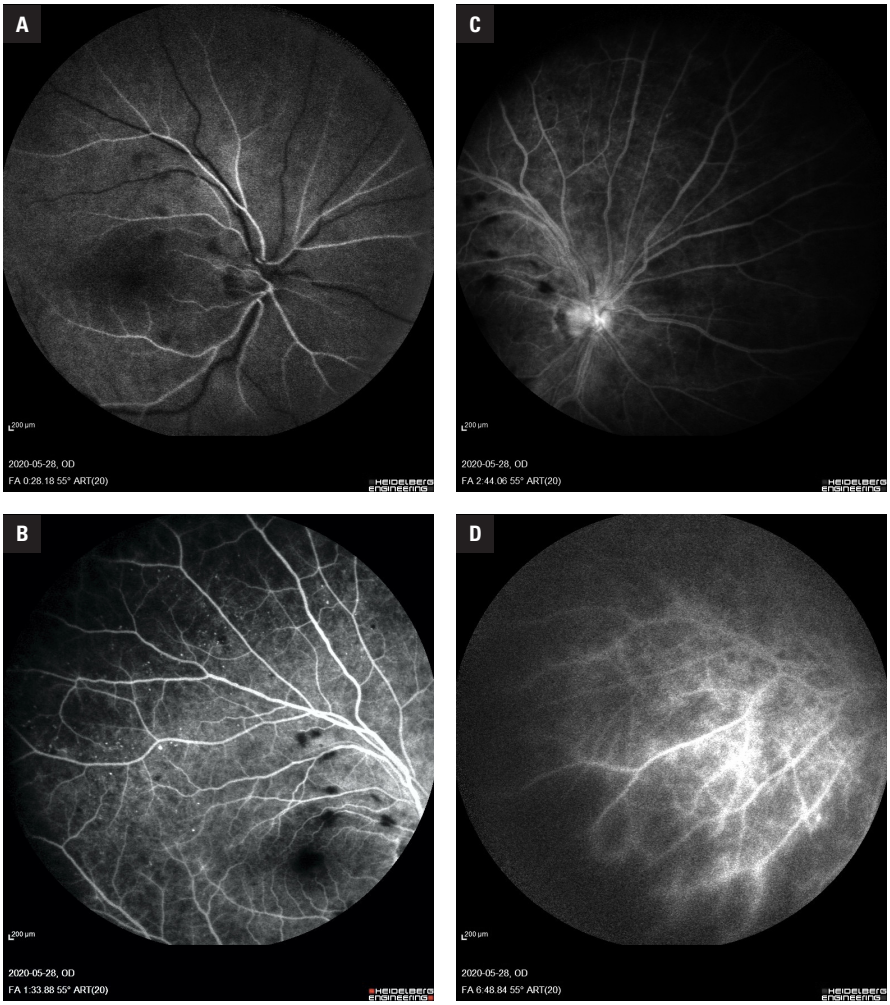

FIGURE 2A-D. AFF of the right fundus: delayed arterial phase (0:28), foci of blocked fluorescence from cotton-wool spots, hyperfluorescence of the microaneurysms, extensive non-perfusion zones at the periphery (1:33), hyperfluorescence of the optic disc, non-perfusion zones at the periphery (2:44), and staining of the retinal vessels at the late phase (6:48)

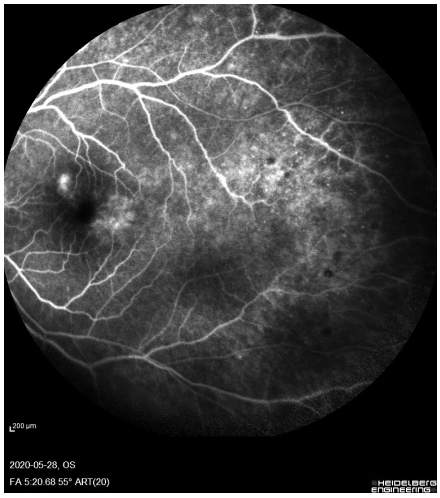

FIGURE 3. AFF of the left fundus: macular edema, microaneurysms, and peripheral non-perfusion zones (5:20)

flows were disturbed, and the resistances increased (Tab. 1).

Due to the poor view of the fundus, optical coherence tomography (OCT) could not be performed. Complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), coagulogram, and lipid profile were within normal limits. In contrast, fasting blood sugar (FBS) was 193 mg/dL (normal: 70–99 mg/dL), and glycated hemoglobin (HBA_{1c}) level was 6.8% (the norm in properly managed diabetes is up to 7%).

Based on the above findings, the patient was diagnosed with bilateral OIS. Treatment with topical β-adrenergic blocker and α2-agonists along with carbonic anhydrase inhibitors was included, resulting in reduction and stabilization of IOP. Then, he was planned for panretinal photocoagulation (PRP)

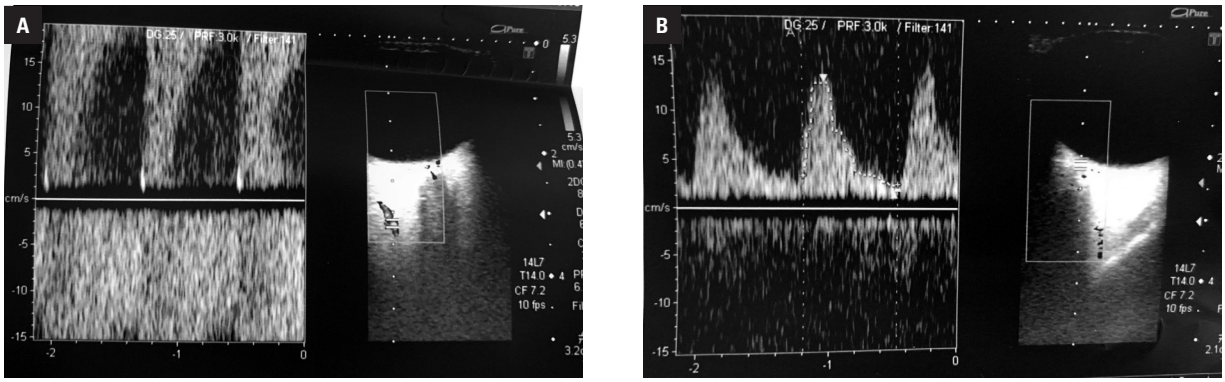

FIGURE 4. Color-coded duplex ultrasonography (Toshiba Xario, Model SSA-660A, Tokyo, Japan): **A.** Doppler signal of an inverted right ophthalmic artery flow due to right ICA stenosis (over 90%) showing negative velocities; B. Doppler ultrasound (DUS) of right central retinal artery

Table 1. Doppler ultrasound (DUS) of central retinal arteries in both eyes

	RE	LE
Vmax	1.2 cm/s	12.9 cm/s
Vmin	2.5 cm/s	2.8 cm/s
PI	1.63	1.57
RI	0.8	0.77

RE — right eye; LE — left eye; Vmax — maximal velocity; Vmin — minimal velocity; PI — pulsatility index; RI — resistance index

of peripheral capillary nonperfusion areas in both eyes. The procedure was performed in a typical way, without complications. The man was discharged from the hospital and informed about the need for further treatment of vascular changes as a matter of urgency by the vascular surgeon, cardiologist, neurologist due to the threat of vision in both eyes, as well as the diabetologist in order to stabilize blood glucose level. At the 3-month clinical follow-up, BCVA was still 5/50 in the RE and 5/8 in the LE.

DISCUSSION

In patients with OIS, a narrowing of the internal or common carotid arteries 90% or more is usually present on the same side as the symptoms. In half of the cases, complete occlusion is detected. Less often, the symptoms are caused by the occlusion of OA. There is a greater chance of developing OIS if the patient has poorly developed collateral circulation between the internal and external carotid arteries or between the two ICAs. In such circumstances, even a 50% stenosis can cause OIS [1, 6, 7].

Atherosclerosis, progressing with age and/or due to dyslipidemia, is a major factor in sclerosis and stenosis of the carotid arteries resulting in ocular hypoperfusion [1, 2]. Other causes include dissecting aneurysm of the carotid artery, aortic arch syndrome, giant cell arteritis, Takayasu arteritis, Behcet's disease, fibrovascular dysplasia, trauma or inflammation causing stenosis of the carotid arteries as well as complications after intravitreal anti vascular endothelial growth factor (anti-VEGF) injections or after radiotherapy for nasopharyngeal carcinoma [1, 3, 8–10].

Often, asymptomatic onset (pain occurs in about 40% of cases) [1], as well as a wide and complex spectrum of ophthalmic symptoms causes that many patients with OIS remain undiagnosed or misdiagnosed, which may later contribute to irreversible loss of vision, as well as increased mortality [2, 3, 6]. Imaging studies of the carotid arteries play a key role in diagnosing OIS. Among them, the most common and non-invasive method is DUS of carotid arteries. CTA or, less often, magnetic resonance angiography are also used. Moreover, a useful test is DUS of retrobulbar vessels, in which decreased or reversed blood flow in the OA can be seen. Reversed blood flow in the OA arises when, as a result of the coexistence of severe ICA stenosis and incomplete blood circulation in the circle of Wills, the blood flow in the OA reverses to supply the ipsilateral brain. It is otherwise referred to as "steal-phenomenon" and leads to reduced retrobulbar blood flow, hypoperfusion and ischemia of ocular tissues. It is a highly specific indicator of ipsilateral stenosis or occlusion of ICA [1, 6].

Another test used in the diagnosis of OIS is FFA, where delayed arm-to-choroid and arm-to-retina circulation time is a common symptom. In almost 60% of cases, patchy or delayed choroidal

filling time occurs, which is the most specific angiographic sign of OIS. However, the most sensitive angiographic sign of OIS (present in up to 95% of patients) is prolonged retinal arteriovenous time [1, 3]. Another common angiographic sign (observed in 85% of cases) is staining of the retinal vessels (primarily arteries) due to their increased permeability induced by endothelial cell damage because of chronic ischemia. In addition, hyperfluorescence of the optic disc is caused by leaks from disc capillaries. Moreover, cotton wool spots, edema of the nerve fiber layer of the optic disc and choroidal atrophy can also appear due to choroidal vascular compromise [1]. FFA can show the presence of microaneurysms around the macula or at the mid-periphery [11], as well as retinal capillary non-perfusion found mostly at the mid-periphery [3]. Indocyanine green angiography (ICG) is also helpful in assessing choroidal vascular abnormalities in eyes with OIS [1, 2]. Furthermore, enhanced depth imaging optical coherence tomography (EDI-OCT) shows choroidal thinning and smaller luminal and stromal area in people with OIS or with significant stenosis of the carotid arteries [6, 12].

Differential diagnosis of IOS should primarily include moderately advanced central retinal vein occlusion (CRVO) and diabetic retinopathy (DR), then the hyperviscosity syndromes or autoimmune uveitis. Absence of tortuous retinal vein and sometimes retinal artery pulsations present in OIS help to distinguish it from CRVO. Cotton wool spots can be found in both OIS and DR. However, more intraretinal hemorrhages and the presence of hard exudates suggest diabetic etiology, while it should be borne in mind that DR and OIS may co-occur. Therefore, patients with asymmetric retinopathy should be examined for possible carotid artery stenosis. During FFA, the lack of retinal arterial stasis and choroidal filling defects in CRVO and DR allows them to be differentiated from OIS [2, 3].

The most dangerous effect of chronic retinal and choroidal ischemia is the increased production of VEGF, which causes neovascularization in the anterior (iris, iridocorneal angle) as well as posterior segment (retina, optic disc). Changes in the anterior segment may lead to the development of neovascular secondary glaucoma. At the early stages of glaucoma, topical β-adrenergic blockers or $\alpha 2$-agonists along with carbonic anhydrase inhibitors are mainly used to reduce IOP. Prostaglandin analogues, however, due to their potential pro-inflammatory effects, should not be used when neovascularization is accompanied by inflammation. Pilocarpine is also not recommended, as it may lead to posterior synechiae and increase occlusion of the iridocorneal angle. Moreover, it is also recommended to use mydriatics. [1, 2]. Trabeculectomy should be considered for patients not responding to drug treatment, with limited angle neovascularization and preserved VA. If this procedure is ineffective or significant angle neovascularization is present, it is recommended to implant aqueous shunt implants [2, 13]. In the posterior segment, new vessels are more often formed at the optic disc than in the retina. They can cause bleeding, result in hemorrhages into the vitreous body and fibrovascular proliferation. To inhibit the formation of new vessels, PRP is performed. However, it should be noted that the effectiveness of this procedure is only 36% (because choroidal ischemia alone, without accompanying retinal ischemia, can induce neovascularization) and it does not show any promising effect in the visual outcome [1, 2]. Moreover, there are studies on the use of anti-VEGF injections to treat neovascular glaucoma and macular edema associated with OIS [14].

Surgical treatments for carotid artery stenosis include CEA, which is 70–90% effective for symptomatic and 60% for asymptomatic patients [15]. An alternative treatment method is carotid artery stenting (CAS). However, with total occlusion, arterial by-pass surgery remains the only treatment option [1, 16]. Restoration of normal blood flow, especially before the onset of iris neovascularization and secondary glaucoma, allows stabilization of existing VA. Performing the surgery at an early stage of the development of neovascularization may in turn contribute to the regression of changes that have already developed at the angle. However, it should be borne in mind that after revascularization surgery, as a result of increased oxygen distribution and re-production of aqueous humor by the ciliary body, IOP may increase [2, 3, 16]. The case described by us shows that despite proven high effectiveness, CEA is not always able to protect the patient from restenosis and OIS, which other authors have also encountered [17, 18].

In 29% of patients, symptomatic carotid stenosis co-occurs with changes in the retinal arteries, often without any symptoms, and 1.5% per year progress to symptomatic OIS. On the other hand, it is assumed that OIS may occur as the first symptom of ICA occlusion in 69% of patients [19]. According to Hayreh et al. [20], the incidence of myocardial ischemia before or after the onset of

OIS was 22%, whereas the incidence of transient ischemic attack (TIA)/stroke was 17%. Furthermore, given that the 5-year survival rate in patients with OIS is only 60% [4, 21], it is extremely important for patients with OIS to have a neurological, cardiological and vascular surgical consultation as soon as possible to minimize the risk of morbidity and mortality.

CONCLUSION

OIS is a rare condition associated with systemic diseases and can result in irreversible vision loss as well as increased mortality rate. In the case where OIS is the first symptom of significant stenosis of the carotid arteries, the role of an ophthalmologist is extremely important and consists not only in making the right and early diagnosis and initiating appropriate treatment but also in cooperation with other specialists to prevent cerebrovascular and cardiovascular complications.

Acknowledgements

None.

Statement of competing interests

The authors declare that they have no conflict of interest.

Ethics approval and consent to participate

Ethics approval and consent to participate are not applicable in this case report.

REFERENCES

1. Mendrinos E, Machinis TG, Pournaras CJ. Ocular ischemic syndrome. Surv Ophthalmol. 2010; 55(1): 2–34, doi: 10.1016/j.survophthal.2009.02.024, indexed in Pubmed: 19833366.
2. Terelak-Borys B, Skonieczna K, Grabska-Liberek I. Ocular ischemic syndrome - a systematic review. Med Sci Monit. 2012; 18(8): RA138–RA144, doi: 10.12659/msm.883260, indexed in Pubmed: 22847215.
3. Sharma S, Brown GC. Ocular Ischemic Syndrome. In: Ryan SJ, Hinton DR, Schachat AP. ed. Retina. Elsevier, New York 2006: 1491–1502.
4. Luo J, Yan Z, Jia Yu, et al. Clinical Analysis of 42 Cases of Ocular Ischemic Syndrome. J Ophthalmol. 2018; 2018: 2606147, doi: 10.1155/2018/2606147, indexed in Pubmed: 29713523.
5. Hong IH, Ahn JK, Chang S, et al. Diagnostic efficacy of total homocysteine and C-reactive protein for ocular ischemic syndrome. Eye (Lond). 2011; 25(12): 1650–1654, doi: 10.1038/eye.2011.232, indexed in Pubmed: 21921951.
6. Wang H, Wang Y, Li H. Multimodality Imaging Assessment of Ocular Ischemic Syndrome. J Ophthalmol. 2017; 2017: 4169135, doi: 10.1155/2017/4169135, indexed in Pubmed: 29375911.
7. Mizener J, Podhajsky P, Hayreh S. Ocular Ischemic Syndrome. Ophthalmology. 1997; 104(5): 859–864, doi: 10.1016/s0161-6420(97)30221-8.
8. Peter J, David S, Danda D, et al. Ocular manifestations of Takayasu arteritis: a cross-sectional study. Retina. 2011; 31(6): 1170–1178, doi: 10.1097/IAE.0b013e3181fe540b, indexed in Pubmed: 21317836.
9. Tang Y, Luo D, Peng W, et al. Ocular ischemic syndrome secondary to carotid artery occlusion as a late complication of radiotherapy of nasopharyngeal carcinoma. J Neuroophthalmol. 2010; 30(4): 315–320, doi: 10.1097/WNO.0b013e3181dee914, indexed in Pubmed: 20736842.
10. Huang ZL, Lin KH, Lee YC, et al. Acute vision loss after intravitreal injection of bevacizumab (avastin) associated with ocular ischemic syndrome. Ophthalmologica. 2010; 224(2): 86–89, doi: 10.1159/000235726, indexed in Pubmed: 19707032.
11. Chen CS, Miller NR. Ocular ischemic syndrome: review of clinical presentations, etiology, investigation, and management. Compr Ophthalmol Update. 2007; 8(1): 17–28, indexed in Pubmed: 17394756.
12. Kang HM, Choi JH, Koh HJ, et al. Significant changes of the choroid in patients with ocular ischemic syndrome and symptomatic carotid artery stenosis. PLoS One. 2019; 14(10): e0224210, doi: 10.1371/journal.pone.0224210, indexed in Pubmed: 31639146.
13. Wierzbowska J, Robaszkiewicz J, Figurska M, et al. Future possibilities in glaucoma therapy. Med Sci Monit. 2010; 16(11): RA252–RA259, indexed in Pubmed: 20980972.
14. Choi EY, Lee SC, Kim M. Optical Coherence Tomography Angiography Before and After Bevacizumab Injection in Ocular Ischemic Syndrome. Retina. 2018; 38(3): e23–e25, doi: 10.1097/IAE.0000000000001981, indexed in Pubmed: 29206756.
15. Dzierwa K, Pieniazek P, Musialek P, et al. Treatment strategies in severe symptomatic carotid and coronary artery disease. Med Sci Monit. 2011; 17(8): RA191–RA197, doi: 10.12659/msm.881896, indexed in Pubmed: 21804476.
16. Kawaguchi S, Iida JI, Uchiyama Y. Ocular Circulation and Chronic Ocular Ischemic Syndrome before and after Carotid Artery Revascularization Surgery. J Ophthalmol. 2012; 2012: 350475, doi: 10.1155/2012/350475, indexed in Pubmed: 23316337.
17. Tripathy K, Mazumdar S. Recurrent retinal and choroidal ischemia in a case of ocular ischemic syndrome. Ther Adv Ophthalmol. 2019; 11: 2515841419848926, doi: 10.1177/2515841419848926, indexed in Pubmed: 31321381.
18. Fintelmann RE, Rosenwasser RH, Jabbour P, et al. An old problem, a new solution. Surv Ophthalmol. 2010; 55(1): 85–88, doi: 10.1016/j.survophthal.2009.03.005, indexed in Pubmed: 19726066.
19. Klijn CJM, Kappelle LJ, van Schooneveld MJ, et al. Venous stasis retinopathy in symptomatic carotid artery occlusion: prevalence, cause, and outcome. Stroke. 2002; 33(3): 695–701, doi: 10.1161/hs0302.104619, indexed in Pubmed: 11872890.
20. Hayreh SS, Zimmerman MB. Ocular arterial occlusive disorders and carotid artery disease. Ophthalmol Retina. 2017; 1(1): 12–18, doi: 10.1016/j.oret.2016.08.003, indexed in Pubmed: 28547004.
21. Mills RP. Anterior segment ischemia secondary to carotid occlusive disease. J Clin Neuroophthalmol . 1989; 9(3): 200–204, indexed in Pubmed: 2529282.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0023

Ocular penetrating injuries in children

Imane Chabbar, Amina Berraho

Ophthalmology B Department, Ibn Sina University Hospital, Rabat, Morocco

ABSTRACT

BACKGROUND: Ocular penetrating injuries in children are common and potentially serious. They take on a special character because of the major risk of amblyopia that they generate in children. The objective of this work is to analyze the epidemiological and clinical aspects of these serious traumas and to study the functional prognosis in Moroccan children.

MATERIAL AND METHODS: We conducted a retrospective study of 83 children between January 2016 and December 2019. The average age of children is 6.5 years, with 64 boys and 19 girls.

RESULTS: The circumstances of penetrating eye injuries are accidental dominated by street games. Corneal wounds represented 67.5% associated with iris prolapse in 39 cases and hyphema in 34 cases. In 30.1% of cases, a post-traumatic cataract is associated, and a foreign body is detected in 6% of cases. Final visual acuity ≥ 5/10 is objectified in 30% of cases.

CONCLUSIONS: This study highlights the importance of preventing these serious childhood traumas by implementing education and awareness-raising measures.

KEY WORDS: penetrating eye injury; children; management; prognosis

Ophthalmol J 2020; Vol. 5, 120–124

INTRODUCTION

Penetrating eye injuries represent a major threat to vision, whether at work, at home, during sport [1] but also at school. They are responsible not only for unilateral blindness [2, 3] but also for a profound emotional trauma for patients and their families [2]. Treatment is long and expensive, but despite this, the prognosis is often severe. These perforating traumas take on a special character in children because of the major risk of amblyopia that they generate. Their socio-economic repercussions are very important because they involve the educational and professional future of these child victims. The causes of these traumas are multiple and are directly linked to the socio-economic level of each country [4]. Several studies conducted in developed [5, 6] and underdeveloped countries [7–9] have analyzed the epidemiological parameters and risk factors associated with the occurrence of penetrating ocular injuries.

The objective of this study is to determine the epidemiological and clinical characteristics of penetrating eye injuries in Moroccan children, the main causes adapted to the Moroccan socio-economic context and the impact on the visual prognosis of these child victims.

MATERIAL AND METHODS

We conducted a retrospective study of children aged from 0 to 14 years presenting penetrating eye injuries, hospitalized in Ophthalmology B Department at Ibn-Sina University Hospital in Rabat-Morocco. The period covered was between January 2016 and December 2019.

Penetrating eye injury in this study was defined as an open globe injury with or without a retained intraocular foreign body.

CORRESPONDING AUTHOR:
Imane Chabbar, Ophthalmology B Department, Ibn Sina University Hospital, Rabat, Morocco; e-mail: imana1chab@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

Three age groups were studied: pre-schoolers 0–5 years, school-aged 6–10 years, and adolescents 12–14 years.

We collected for each case demographic parameters (age, sex, origin), the admission delay, the circumstances, place and agent of the trauma. The slit-lamp examination specified the anatomical location of the lesions, uveal prolapse and ocular structures damage in order to assess the severity of the trauma. We noted the surgical treatment and the final visual outcome of each patient.

RESULTS

AGE, SEX

A total of 83 children presenting penetrating eye injuries were identified with male predominance (64 boys and 19 girls).

The average age of children was 6.5 years with extremes between 18 months and 14 years. 74.7% of children came from urban areas (62 cases). Penetrating eye injuries were more common in the 6–14 age group (Fig. 1).

DELAY OF THE ADMISSION

Thirty four cases (38.5 %) were taken to hospital the same day, 29 cases (35 %) were taken the day after the trauma. Sixteen cases (19.3%) were taken between 48 h and one week after the trauma. The maximum consultation delay was 10 days in 4 children from rural areas.

CIRCUMSTANCES OF THE TRAUMA

Circumstances of the trauma are presented in Figure 2. The street was the predominant place of these ocular trauma accidentally occurring during children's games. The second place was domestic accidents at home. Two cases of eye injuries have occurred in school. One case of a 14-year-old child, injured at the workplace, has been noted: He was a blacksmith, injured by a foreign object when he hammered a metal bar.

AGENT OF THE TRAUMA

The nature of the traumatic agent was identified in the majority of cases (Fig. 3).

The agent of trauma was metallic in 37% of cases (wire, knife), then tree branches especially in rural areas, stone throws was the third cause during children brawls.

ANATOMICAL LOCATION

Penetrating eye injuries were unilateral in all cases, involving the right eye in 38 cases and the left eye in 45 cases (Fig. 4, 5).

Corneal wounds represented 67.5% of cases, scleral wounds 7.2% and corneoscleral wounds 25.3% of cases.

SLIT LAMP EXAMINATION

The slit lamp examination objectified an iris prolapse in 39 cases, a hyphema in 34 cases, a posttraumatic cataract in 25 cases and an involvement of the

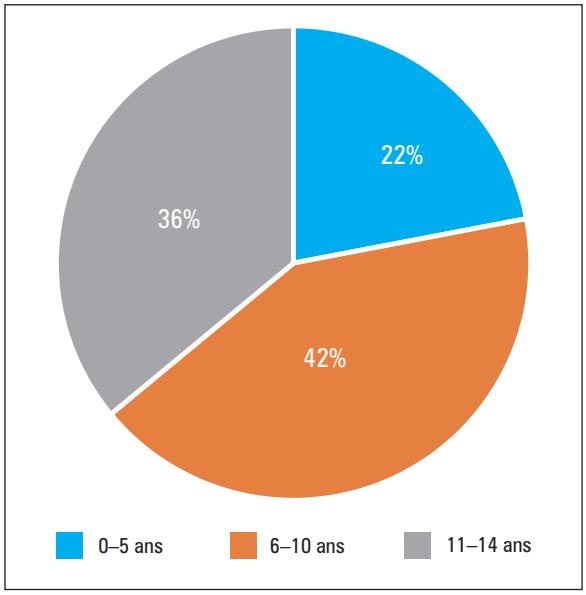

FIGURE 1. Distribution of penetrating eye injuries by age group

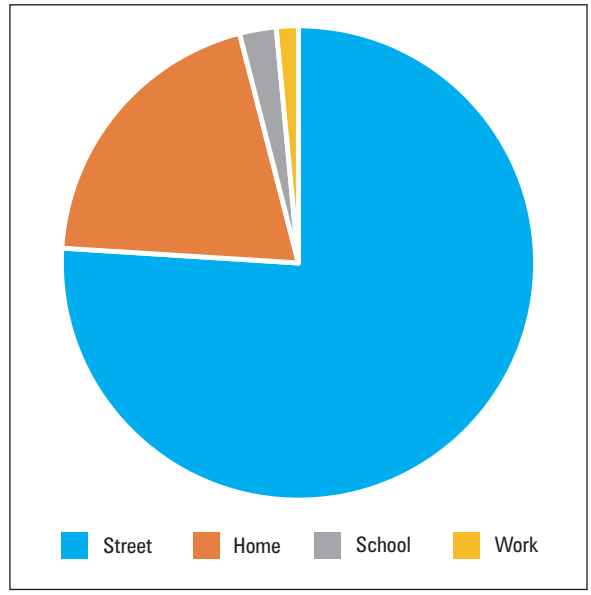

FIGURE 2. Circumstances of trauma

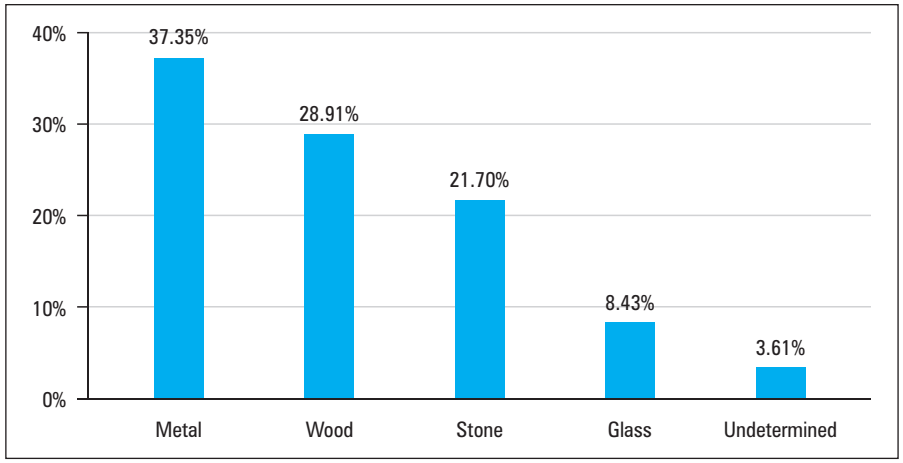

FIGURE 3. Agent of trauma

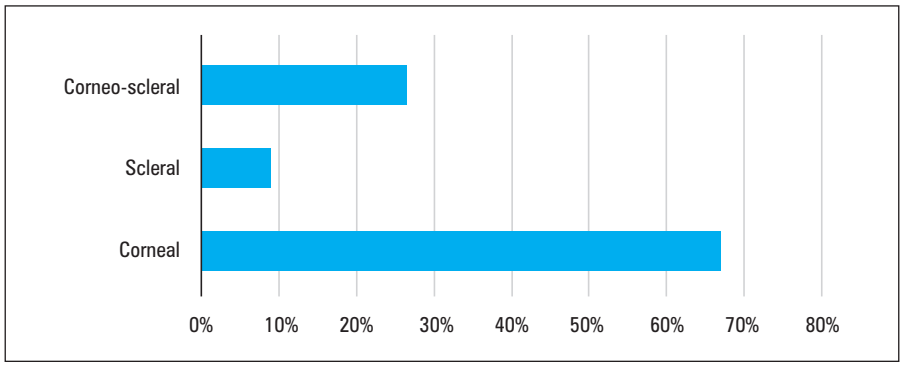

FIGURE 4. Anatomical location of ocular penetrating injuries

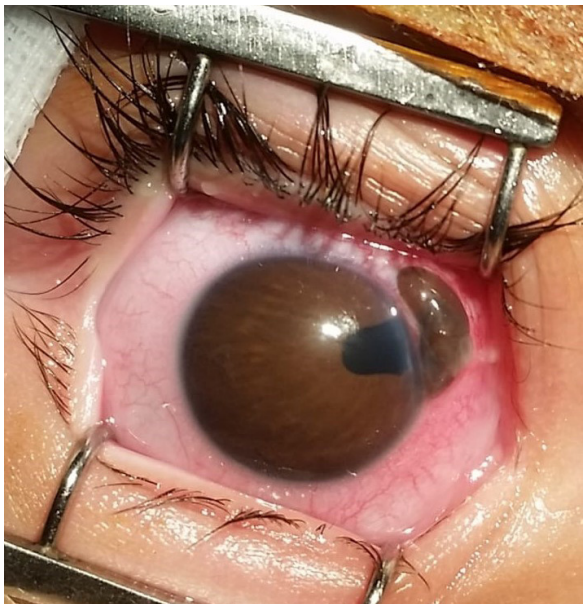

FIGURE 5. Paralimbic scleral wound with iris prolapse and flat anterior chamber in an 18-month-old infant

posterior segment in 13 cases. In 6% of cases, a retained foreign body was detected clinically or radiologically: of corneal location in two cases, in the anterior chamber in two cases and in the vitreous in one case.

SURGICAL MANAGEMENT

Surgical management under general anesthesia was performed in all cases. It consisted of a surgical exploration with eye damage assessment followed by suturing of wounds after possible reintegration of the prolapsed uvea (Fig. 6). No evisceration was carried out.

OVERALL VISUAL OUTCOME

The initial visual acuity before surgical treatment was noted in cooperating children. It varied between 5/10 and 7/10 in 13 patients (15,6%), between 5/10 and 3/10 in 21 children (25,3%), ≤ 1/10 in 26 children (31.3%) and was not measurable in 23 children (27.7%).

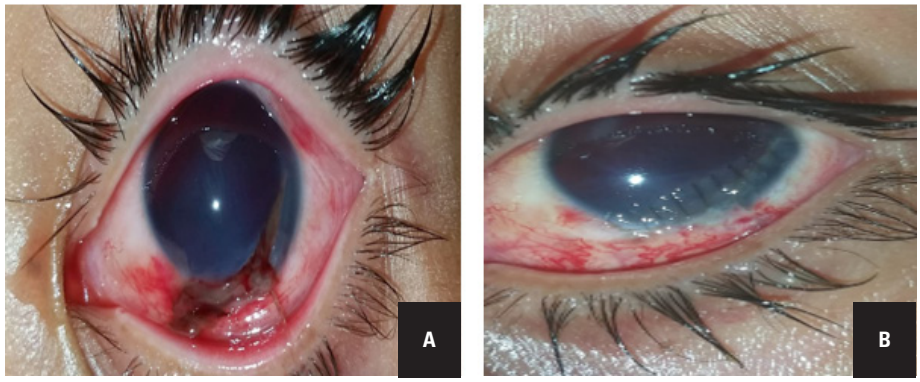

FIGURE 6. **A**. Corneal wound extended from 3 to 8 o'clock with total hyphema. **B**. Postoperative appearance after anterior chamber washout and corneal suturing

After surgical management and during the follow-up, a final visual acuity ≥ 5/10 was objectified in 25 cases (30%) of which 15 (18%) returned to normal vision. While 5 cases (6%) had a negative light perception progressing towards the phthisis bulbi. The poor visual outcome was especially objectified in children presenting severe penetrating injuries with involvement of the posterior segment.

DISCUSSION

Ocular penetrating injuries are a major and preventable cause of childhood blindness. The World Health Organization (WHO) records some 55 million eye injuries per year, responsible for 19 million cases of monocular blindness, 32 to 75% of which occur in children [2, 4]. The male predominance in our study agrees with the literature [10, 11]. This high incidence of eye injuries in the 6–10 and 11–14 age groups is explained by the fact that school-aged children spend more time away from home and parental authority. Most of our patients were of urban origin. This is explained, on the one hand, by the scarcity and the remoteness of medical centers in rural areas and on the other hand by the lack of financial means; from where the interest of the creation of primary health centers for first aid and referral of patients to specialized centers. Most of our patients consulted 24 to 48 hours after the trauma. The long consultation delay of our 4 children was due either to an underestimation of the initial lesion or to the lack of financial means for the trip from the landlocked rural area. The place of predilection for these accidents was the street where children are engaged in games away from adult supervision. These findings do not join those of other studies [12] where the home is the main place of these accidents. This difference is probably due to cultural or climatic factors specific to each country. Despite the clear legislation prohibiting the work of minor children, we have identified one case of eye injury occurring at the workplace, which must encourage public authorities to rigorously apply and monitor the laws in force. Metallic agents (knives, scissors and metallic wires), vegetable thorns and stone-throwing represent the main traumatic agents. The severity of ocular lesions is directly linked to the sharp nature of traumatic agents, to which is added the septic risk linked to the plant or telluric nature of traumatic agents. Post-traumatic cataract has been associated in 30.1% of cases, it essentially poses the problem of aphakia correction [13] particularly in children who could not be implanted because of traumatic capsular rupture or zonular disinsertion [14]. The associated damage of posterior segment conditions the visual prognosis [15] since it can cause functional loss of the eye despite early and adequate treatment.

Visual outcome was poor in our series, however, it is difficult to compare our results with other studies because of the inconsistency of the parameters studied [4]. The prevention of these serious accidents remains a public health problem. It is based on the health and social education of the population, the creation of play areas suitable for children far from the violence of streets and the improvement of access to health care services [16].

CONCLUSION

Ocular penetrating injuries in children remain poor prognosis. Street games accidents away from

adult's supervision are the most frequent causes. The school-aged boys are the most exposed. The violence of the trauma and the functional results threaten the eyes of these children. Only prevention with an action strategy adapted to each society allows the fight against this major and preventable cause of blindness.

Conflict of interest

The authors do not declare any conflict of interest.

REFERENCES

1. McCormack P. Penetrating injury of the eye. Br J Ophthalmol. 1999; 83(10): 1101–1102, doi: 10.1136/bjo.83.10.1101, indexed in Pubmed: 10502565.
2. Négrel AD, Thylefors B. The global impact of eye injuries. Ophthalmic Epidemiol. 1998; 5(3): 143–169, doi: 10.1076/opep.5.3.143.8364, indexed in Pubmed: 9805347.
3. Thylefors B. Epidemiological patterns of ocular trauma. Aust N Z J Ophthalmol. 1992; 20(2): 95–98, doi: 10.1111/j.1442-9071.1992.tb00718.x, indexed in Pubmed: 1389141.
4. Rostomian K, Thach A, Isfahani A, et al. Open globe injuries in children. J AAPOS. 1998; 2(4): 234–238, doi: 10.1016/s1091-8531(98)90058-1, indexed in Pubmed: 10532742.
5. Fong LP. Eye injuries in Victoria, Australia. Med J Aust. 1995; 162(2): 64–68, indexed in Pubmed: 7838028.
6. Blomdahl S, Norell S. Perforating eye injury in the Stockholm population. An epidemiological study. Acta Ophthalmol (Copenh). 1984; 62(3): 378–390, doi: 10.1111/j.1755-3768.1984.tb08418.x, indexed in Pubmed: 6464687.
7. Gothwal VK, Adolph S, Jalali S, et al. Demography and prognostic factors of ocular injuries in South India. Aust N Z J Ophthalmol. 1999; 27(5): 318–325, doi: 10.1046/j.1440-1606.1999.00225.x, indexed in Pubmed: 10571392.
8. Umeh RE, Umeh OC. Causes and visual outcome of childhood eye injuries in Nigeria. Eye (Lond). 1997; 11 (Pt 4): 489–495, doi: 10.1038/eye.1997.132, indexed in Pubmed: 9425413.
9. Oluyemi F. Epidemiology of penetrating eye injury in ibadan: a 10-year hospital-based review. Middle East Afr J Ophthalmol. 2011; 18(2): 159–163, doi: 10.4103/0974-9233.80706, indexed in Pubmed: 21731328.
10. Farr AK, Hairston RJ, Humayun MU, et al. Open globe injuries in children: a retrospective analysis. J Pediatr Ophthalmol Strabismus. 2001; 38(2): 72–77, indexed in Pubmed: 11310710.
11. Beby F, Kodjikian L, Roche O, et al. Traumatismes oculaires perforants de l'enfant. J Fran Ophtalmol. 2006; 29(1): 20–23, doi: 10.1016/s0181-5512(06)73742-1.
12. Thompson CG, Kumar N, Billson FA, et al. The aetiology of perforating ocular injuries in children. Br J Ophthalmol. 2002; 86(8): 920–922, doi: 10.1136/bjo.86.8.920, indexed in Pubmed: 12140216.
13. Khokhar S, Gupta S, Yogi R, et al. Epidemiology and intermediate-term outcomes of open- and closed-globe injuries in traumatic childhood cataract. Eur J Ophthalmol. 2014; 24(1): 124–130, doi: 10.5301/ejo.5000342, indexed in Pubmed: 23918072.
14. Krishnamachary M, Rathi V, Gupta S. Management of traumatic cataract in children. J Cataract Refract Surg. 1997; 23 Suppl 1: 681–687, doi: 10.1016/s0886-3350(97)80054-5, indexed in Pubmed: 9278825.
15. Knyazer B, Levy J, Rosen S, et al. Prognostic factors in posterior open globe injuries (zone-III injuries). Clin Exp Ophthalmol. 2008; 36(9): 836–841, doi: 10.1111/j.1442-9071.2009.01922.x, indexed in Pubmed: 19278478.
16. World Health Organization. Preventing blindness in children. Report of a WHO/IAPB scientific meeting. Hyderabad, India 1999.

CASE REPORT
DOI: 10.5603/OJ.2020.0025

Traumatic endophthalmitis with intraocular metallic foreign body

Imane Chabbar, Amina Berraho

Ophthalmology B Department, Ibn Sina University Hospital, Rabat, Morocco

ABSTRACT

BACKGROUND: Post-traumatic endophthalmitis with retained intraocular foreign body is a severe complication of open globe injuries. It is generally associated with poor visual outcome and requires prompt and adapted management.

CASE REPORT: A 39-year-old male patient presented with open globe injury of the right eye due to a metallic foreign body projection. He was a victim of a neglected work accident 10 days ago when hammering a metallic bar. Visual acuity on admission was LP (+) in the right eye. The Slit-lamp examination revealed perikeratic injection, edematous cornea and severe inflammation of the anterior chamber with hypopyon. Ocular ultrasound showed a heterogeneous vitreous organization compatible with a vitreous abscess. Orbito-cerebral CT scan revealed a retained intraocular metallic foreign body located in the posterior segment, within the vitreous humor. The patient received local and general antibiotherapy associated with intravitreal injections of vancomycin and ceftazidime followed by a vitrectomy to remove the intraocular foreign body. The visual outcome was poor with an evolution towards phtysis bulbi. The aim of this case report is to study the risk factors of post-traumatic endophthalmitis with retained intraocular foreign body and to examine treatment principles and visual outcome of this severe complication.

KEY WORDS: traumatic endophthalmitis; intraocular foreign body; posterior segment; risk factor; intravitreal antibiotic, vitrectomy

Ophthalmol J 2020; Vol. 5, 125–129

INTRODUCTION

Post-traumatic endophthalmitis is a rare but serious complication of penetrating eye injuries. Despite therapeutic advances, it represents a major turning point for the patient's visual outcome [1].

The incidence of post-traumatic endophthalmitis varies between 3 and 17% of open globe injuries [2, 3]. The presence of intraocular foreign body is a major risk factor increasing this incidence to 48% [4, 5]. This increase in incidence is mainly related to the nature of the intraocular foreign body, the ocular damage and the contamination that it causes [6].

The management of this severe situation is not fully codified and several aspects remain controversial, including the timing of removal of the intraocular foreign body, systemic or intravitreal antibiotherapy, the timing and the route of administration of corticosteroid therapy The prevention of such a complication therefore remains an important issue in the management of patients with open globe injuries. Prompt management with suturing of the wound is the only clearly established recommendation.

The aim of this case report is to study the risk factors of post-traumatic endophthalmitis with retained intraocular foreign body and to examine treatment principles and visual outcome of this severe complication.

CORRESPONDING AUTHOR:
Imane Chabbar, Ophthalmology B Department, Ibn Sina University Hospital, Rabat, Morocco; e-mail: imana1chab@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

CASE REPORT

We report a case of a 39-year-old male patient, working as an industrial blacksmith, without any pathological history, presented with open globe trauma of the right eye caused by a metallic foreign body projection. Indeed, he was a victim of a neglected work accident 10 days ago, when hammering a metal bar. On admission, the visual acuity was LP + in OD and 10/10 in OS. The right eye examination (Fig. 1) revealed eyelids swelling, conjunctival and perikeratic congestion, edematous cornea without fluorescein staining and severe inflammation of the anterior chamber with hypopyon. The examination doesn't found any obvious wounds. The intraocular pressure was about 16 mm Hg. The examination of the lens and the eye fundus was difficult, hampered by corneal edema and anterior chamber inflammation.

Ocular ultrasound (Fig. 2) showed an intact lens in natural disposition, a heterogeneous vitreous organization in favor of a vitreous abscess with membrane formation, a choroidal thickening and an intact retina. An urgent orbito-cerebral CT scan (Fig. 3) revealed a millimeter foreign body located in the posterior segment, within the vitreous humor, of metallic nature, respecting the eyeball sphericity.

An urgent hospitalization was indicated and vitreous samples for cultures were sent for microbiological analysis. The patient was treated by systemic broadspectrum antibiotherapy based on intravenous

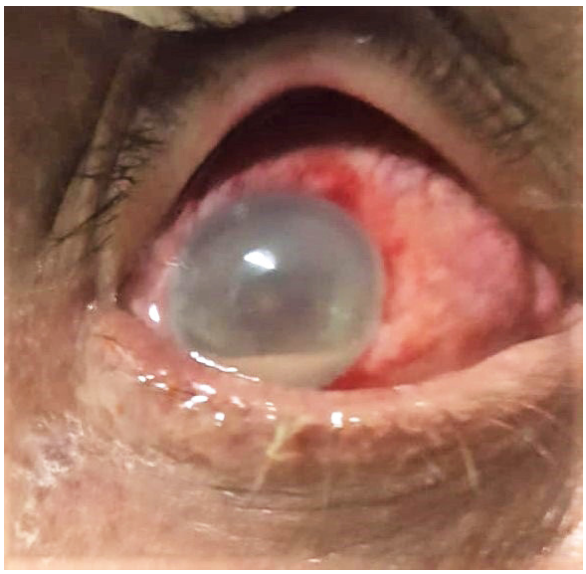

FIGURE 1. Severe inflammation of the anterior segment of the right eye: conjunctival and perikeratic congestion, corneal edema, aqueous flare and hypopyon

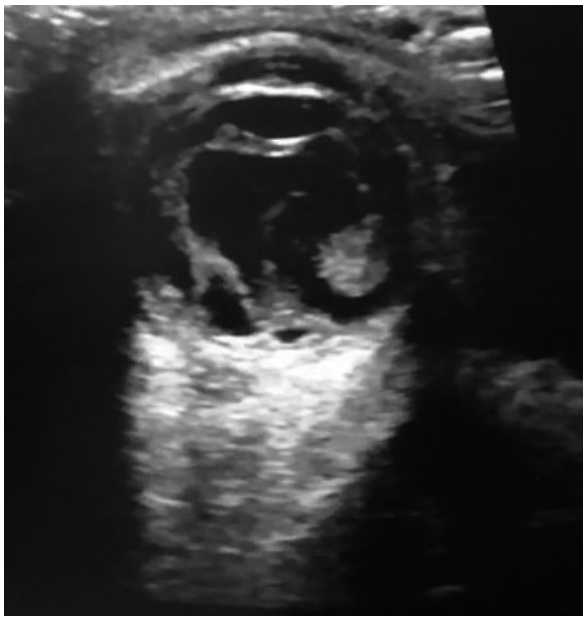

FIGURE 2. Ocular ultrasound of the right eye, showing a vitreous abscess with membrane formation, a choroidal thickening and an intact retina

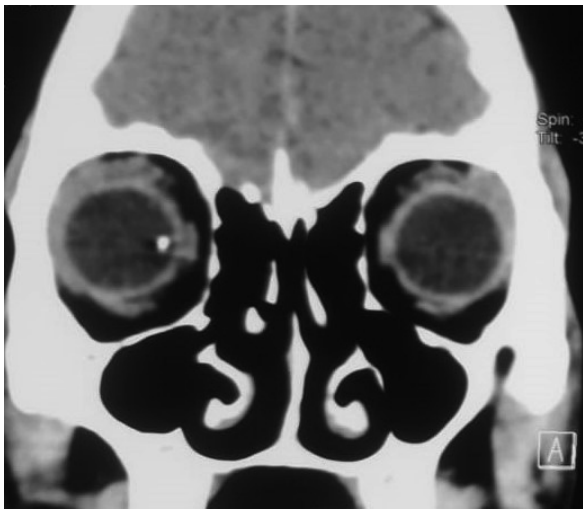

FIGURE 3. Orbito-cerebral CT scan showing in the right eye: posterior segment intraocular foreign of metallic nature, respecting the eyeball sphericity

injection of Ceftriaxone 2 g/24 hours and Fluoroquinolone per os 750 mg/12 hours, then adapted to the microbiological results that revealed *Staphylococcus Epidermidis*. Local treatment with fortified antibiotic eye drops was also associated. Moreover, the patient received 2 intravitreal injections of vancomycin 1 mg/0.1 mL and ceftazidime 2 mg/0.1 mL 48 hours apart followed by a vitrectomy in order to reduce the infectious mass, to improve antibiotics

diffusion and to remove the foreign body after enlargement of the sclerotomy. Indeed, given the poor visibility due to the corneal edema, the vitrectomy was limited and central with conservative vitreous shaving to avoid possible retinal tears on a retina weakened by the infection and the trauma. Silicone oil tamponade was not performed. The evolution was unfavorable and visual outcome was poor with the evolution towards phthisis bulbi.

DISCUSSION

Post-traumatic endophthalmitis is a rare but severe complication of penetrating eye injuries. The presence of an intraocular foreign body (IOFB) is a major risk factor increasing the incidence of this complication. A prospective randomized study, evaluating the interest of preventive treatment of open globe trauma, observes a significant association between post-traumatic endophthalmitis and the presence of retained IOFBs [7, 8].

The initially marked inflammation and deep eye pain may hamper the initial clinical examination and thus delay diagnosis and treatment, further worsening the visual prognosis. Yang and al. demonstrated in a retrospective study over a 20-year-period that 87% of open globe injuries patients with IOFB presented clinical signs of endophthalmitis at initial examination [9]. An increased risk of endophthalmitis was significantly related to delay in treatment exceeding 24 h after injury. Indeed, in our case, the long consultation delay, around 10 days, resulted in a poor visual outcome.

A retained IOFB represents a risk factor promoting microbial proliferation. The nature of IOFB is a determining parameter [6]. Indeed, organic IOFBs are very septic and significantly increase the risk of endophthalmitis [10]. However, IOFB retained during war trauma are associated with a low risk of infection. They are able to self-sterilize due to the nature of high velocity or high-temperature projectiles that are involved.

The anatomic location of the IOFB is another factor influencing significantly the visual outcome. IOFBs retained in the posterior segment of the eye compromise the visual prognosis and cause severe eye damage more than those retained in the anterior segment [11, 12]. Woodcock and al. demonstrated a significant relationship between poor visual acuity less than 20/200 and posterior location of IOFB [13].

The timing of surgical management of IOFB is still discussed. In the literature, several studies recommended the urgent removal of IOFB in order to reduce the risk of endophthalmitis and prevent proliferative vitreoretinopathy (PVR) and tractional complications [14]. In addition, Jonas et al. noted a satisfactory rate of anatomical success associated with early removal [15]. They found a lower PVR rate when IOFB was removed early within the first 24 hours after the trauma. Colyer et al. also showed a high risk of PVR when removal of IOFB was delayed, however, they found that functional success mainly depended on the extent and severity of intraocular damage and not on the vitrectomy delay [16].

In contrast, Ferrari and coworkers reported, in a retrospective study of 273 patients, that endophthalmitis was noted only in 2.3% of cases when the IOFB removal was before 24 hours after injury versus 15.7% when it was delayed beyond 24 hours [17].

Several authors have studied the influence of lens capsule rupture on the risk of post-traumatic endophthalmitis [18, 19]. These studies have demonstrated an increased risk of endophthalmitis associated with traumatic lens rupture. Indeed, the opening of the lens capsule facilitates the intravitreal penetration of microorganisms. In addition, this rupture hampers the normal circulation of aqueous humor, thus decreasing the elimination of microorganisms that proliferate and feed on the ruptured lens [17, 20].

The involvement of the posterior segment of the eye, particularly the retina, considerably influences the visual outcome. The association of retinal tears or even retinal detachment with endophthalmitis is an aggravating factor associated with a very poor visual prognosis and progression to the eyeball phtysis [21]. Older age could be also a risk factor due to the decrease in the immune response with age [22].

According to the literature, open globe injuries with the externalization of the intraocular tissues massively expose the globe to microorganisms' penetration and are associated with a high risk of endophthalmitis [23]. This exposure is greater if the wounds are very posterior and difficult to repair, thus promoting microbial invasion of posterior segment of the eye. However, Zhang et al. [24] noted, through a large retrospective study, that the risk of post-traumatic endophthalmitis is not increased by the presence of posterior wounds and that, on the contrary, the presence of uveal prolapse through the wound was a protective factor that may plug the wound and protect the eye against the development

of endophthalmitis. Further studies are needed to determine the real implication of uveal prolapse in the occurrence of post-traumatic endophthalmitis.

Thanks to the identification of these risk factors, the ophthalmologist can select the open globe injuries with IOFB having a high risk of endophthalmitis and then adapt their management according to this risk. Systemic antibioprophylaxis, after open globe injuries, is recommended to prevent traumatic endophthalmitis by the majority of authors, based on broad-spectrum antibiotics with good eye penetration [25].

Medical treatment of post-traumatic endophthalmitis is based on intravitreal injections of antibiotics. This route of administration is more efficient since it allows antibiotics to penetrate directly inside the globe and to reach very high concentrations [26]. Antibiotics must act against Gram-positive (particularly Staphylococcus epidermidis) and Gram-negative bacteria. For initial therapy, the combination of intravitreal injection of vancomycin and ceftazidime is recommended [25, 27, 28]. While awaiting culture results, intravenous antibiotic therapy is usually associated, covering both Gram-positive and Gram-negative organisms with several available options [29]. In order to increase the concentration of antibiotics in the eye, topical antibiotics or better fortified topical antibiotics are often combined with intravitreal injections of antibiotics, but they penetrate weakly inside the vitreous [30]. Subconjunctival injections achieve therapeutic levels of antibiotics in the anterior segment [31]. They are especially indicated in patients where multi-daily instillation of drops cannot be performed.

All administration modalities of corticosteroids in the management of traumatic endophthalmitis are still under discussion: the timing, the route of administration and the effective dose.

Theoretically, Corticosteroids provide a powerful anti-inflammatory action to quickly control the infection, shorten the endophthalmitis evolution and thus improve the visual outcome in anatomical and functional terms [32].

In addition to medical treatment, some authors recommend early vitrectomy [33] in patients with post-traumatic endophthalmitis. The basic principle of vitrectomy in the management of endophthalmitis is comparable to the principle of surgical drainage of collected abscesses. Moreover, the infected vitreous becomes very condensed with the formation of vitreous membranes increasing the risk of retinal traction. The techniques of vitrectomy are diverse; some authors recommend a large vitrectomy with posterior cortex removal [34]. However, given the poor visibility in the posterior segment, other authors recommend more limited initial vitrectomy without posterior hyaloid removal because that can be complicated by retinal tears or even retinal detachment. Some studies noted that the use of silicone oil tamponade after vitrectomy is recommended in the presence of retinal detachment or if there is a high risk of occult retinal tears [35–37]. In addition, thanks to its antimicrobial properties, the presence of silicone oil may protect against the vitreous cavity reinfection.

Our patient was a real challenge. The management of traumatic endophthalmitis was particularly difficult with the poor visual outcome, due to the following reasons: the neglected open globe injury with delayed consultation beyond 10 days, the poor initial visual acuity (LP +), the presence of posterior segment IOFB and the conservative surgical management because of the important corneal edema and the severe eye inflammation.

CONCLUSION

Despite medical and surgical advances, the visual prognosis of post-traumatic endophthalmitis with retained IOFB remains very poor. However, appropriate management based on rapid wound repair, IOFB extraction, early vitrectomy, and intravitreal injections of antibiotics may treat traumatic endophthalmitis and improve the visual outcome in some patients.

REFERENCES

1. Williams DF, Mieler WF, Abrams GW, et al. Results and prognostic factors in penetrating ocular injuries with retained intraocular foreign bodies. Ophthalmology. 1988; 95(7): 911–916, doi: 10.1016/s0161-6420(88)33069-1, indexed in Pubmed: 3262852.
2. Azad R, Ravi K, Talwar D, et al. Pars plana vitrectomy with or without silicone oil endotamponade in post-traumatic endophthalmitis. Graefes Arch Clin Exp Ophthalmol. 2003; 241(6): 478–483, doi: 10.1007/s00417-003-0670-4, indexed in Pubmed: 12756578.
3. Kong GYX, Henderson RH, Sandhu SS, et al. Wound-related complications and clinical outcomes following open globe injury repair. Clin Exp Ophthalmol. 2015; 43(6): 508–513, doi: 10.1111/ceo.12511, indexed in Pubmed: 25688653.
4. Kuhn F, Morris R, Witherspoon CD, et al. The Birmingham Eye Trauma Terminology system (BETT). J Fr Ophtalmol. 2004; 27(2): 206–210, doi: 10.1016/s0181-5512(04)96122-0.
5. Boldt H, Pulido J, Blodi C, et al. Rural Endophthalmitis. Ophthalmology. 1989; 96(12): 1722–1726, doi: 10.1016/s0161-6420(89)32658-3.
6. ESSEX R, YI Q, CHARLES P, et al. Post-traumatic endophthalmitis. Ophthalmology. 2004; 111(11): 2015–2022, doi: 10.1016/j.ophtha.2003.09.041.
7. Soheilian M, Rafati N, Mohebbi MR, et al. Prophylaxis of acute post-traumatic bacterial endophthalmitis: a multicenter, randomized clinical

trial of intraocular antibiotic injection, report 2. Arch Ophthalmol. 2007; 125(4): 460–465, doi: 10.1001/archopht.125.4.460, indexed in Pubmed: 17420365.
8. Dehghani AR, Rezaei L, Salam H, et al. Post traumatic endophthalmitis: incidence and risk factors. Glob J Health Sci. 2014; 6(6): 68–72, doi: 10.5539/gjhs.v6n6p68, indexed in Pubmed: 25363107.
9. Yang CS, Lu CK, Lee FL, et al. Treatment and outcome of traumatic endophthalmitis in open globe injury with retained intraocular foreign body. Ophthalmologica. 2010; 224(2): 79–85, doi: 10.1159/000235725, indexed in Pubmed: 19707031.
10. Jonas JB, Knorr HL, Budde WM. Prognostic factors in ocular injuries caused by intraocular or retrobulbar foreign bodies. Ophthalmology. 2000; 107(5): 823–828, doi: 10.1016/s0161-6420(00)00079-8, indexed in Pubmed: 10811069.
11. Woodcock MGL, Scott RAH, Huntbach J, et al. Mass and shape as factors in intraocular foreign body injuries. Ophthalmology. 2006; 113(12): 2262–2269, doi: 10.1016/j.ophtha.2006.06.002, indexed in Pubmed: 17157134.
12. Cebulla CM, Flynn HW. Endophthalmitis after open globe injuries. Am J Ophthalmol. 2009; 147(4): 567–568, doi: 10.1016/j.ajo.2008.12.016, indexed in Pubmed: 19327442.
13. Woodcock MGL, Scott RAH, Huntbach J, et al. Mass and shape as factors in intraocular foreign body injuries. Ophthalmology. 2006; 113(12): 2262–2269, doi: 10.1016/j.ophtha.2006.06.002, indexed in Pubmed: 17157134.
14. Chaudhry IA, Shamsi FA, Al-Harthi E, et al. Incidence and visual outcome of endophthalmitis associated with intraocular foreign bodies. Graefes Arch Clin Exp Ophthalmol. 2008; 246(2): 181–186, doi: 10.1007/s00417-007-0586-5, indexed in Pubmed: 17468878.
15. Jonas JB, Budde WM. Early versus late removal of retained intraocular foreign bodies. Retina. 1999; 19(3): 193–197, doi: 10.1097/00006982-199905000-00003, indexed in Pubmed: 10380023.
16. Colyer MH, Weber ED, Weichel ED, et al. and al. Delayed intraocular foreign body removal without endophthalmitis during Operations Iraqi Freedom and Enduring Freedom. Ophthalmology. 2007; 114(8): 1439–1447, doi: 10.1016/j.ophtha.2006.10.052, indexed in Pubmed: 17331579.
17. Ferrari TM, Cardascia N, Di Gesù I, et al. Early versus late removal of retained intraocular foreign bodies. Retina. 2001; 21(1): 92–93, doi: 10.1097/00006982-200102000-00026, indexed in Pubmed: 11217947.
18. Narang S, Gupta V, Simalandhi P, et al. Paediatric open globe injuries. Visual outcome and risk factors for endophthalmitis. Indian J Ophthalmol. 2004; 52(1): 29–34, indexed in Pubmed: 15132376.
19. Sabaci G, Bayer A, Mutlu FM, et al. Endophthalmitis after deadly-weapon-related open-globe injuries: risk factors, value of prophylactic antibiotics, and visual outcomes. Am J Ophthalmol. 2002; 133(1): 62–69, doi: 10.1016/s0002-9394(01)01320-4, indexed in Pubmed: 11755840.
20. Bhagat N, Nagori S, Zarbin M. Post-traumatic Infectious Endophthalmitis. Surv Ophthalmol. 2011; 56(3): 214–251, doi: 10.1016/j.survophthal.2010.09.002, indexed in Pubmed: 21397289.
21. Gokce G, Sobaci G, Ozgonul C. Post-Traumatic Endophthalmitis: A Mini-Review. Semin Ophthalmol. 2015; 30(5-6): 470–474, doi: 10.3109/08820538.2013.877939, indexed in Pubmed: 24571685.
22. Thompson WS, Rubsamen PE, Flynn HW, et al. Endophthalmitis after penetrating trauma. Risk factors and visual acuity outcomes. Ophthalmology. 1995; 102(11): 1696–1701, doi: 10.1016/s0161-6420(95)30807-x, indexed in Pubmed: 9098264.
23. Duch-Samper AM, Menezo JL, Hurtado-Sarrió M. Endophthalmitis following penetrating eye injuries. Acta Ophthalmol Scand. 1997; 75(1): 104–106, doi: 10.1111/j.1600-0420.1997.tb00263.x, indexed in Pubmed: 9088415.
24. Zhang Y, Zhang MN, Jiang CH, et al. Endophthalmitis following open globe injury. Br J Ophthalmol. 2010; 94(1): 111–114, doi: 10.1136/bjo.2009.164913, indexed in Pubmed: 19692359.
25. El Chehab H, Renard JP, Dot C. [Post-traumatic endophthalmitis]. J Fr Ophtalmol. 2016; 39(1): 98–106, doi: 10.1016/j.jfo.2015.08.005, indexed in Pubmed: 26563842.
26. Baum J, Peyman GA, Barza M. Intravitreal administration of antibiotic in the treatment of bacterial endophthalmitis. III. Consensus. Surv Ophthalmol. 1982; 26(4): 204–206, doi: 10.1016/0039-6257(82)90080-7, indexed in Pubmed: 6978542.
27. Chhabra S, Kunimoto DY, Kazi L, et al. Endophthalmitis after open globe injury: microbiologic spectrum and susceptibilities of isolates. Am J Ophthalmol. 2006; 142(5): 852–854, doi: 10.1016/j.ajo.2006.05.024, indexed in Pubmed: 17056367.
28. Narang S, Gupta V, Gupta A, et al. Role of prophylactic intravitreal antibiotics in open globe injuries. Indian J Ophthalmol. 2003; 51(1): 39–44, indexed in Pubmed: 12701861.
29. Kresloff MS, Castellarin AA, Zarbin MA. Endophthalmitis. Surv Ophthalmol. 1998; 43(3): 193–224, doi: 10.1016/s0039-6257(98)00036-8, indexed in Pubmed: 9862309.
30. Peyman GA, May DR, Homer PI, et al. Penetration of gentamicin into the aphakic eye. Ann Ophthalmol. 1977; 9(7): 871–880, indexed in Pubmed: 302661.
31. Theodore FH. Bacterial Endophthalmitis after Cataract Surgery. Int Ophthalmol Clin. 1964; 4: 839–859, doi: 10.1097/00004397-196412000-00005, indexed in Pubmed: 14231940.
32. Park SS, Samiy N, Ruoff K, et al. Effect of intravitreal dexamethasone in treatment of pneumococcal endophthalmitis in rabbits. Arch Ophthalmol. 1995; 113(10): 1324–1329, doi: 10.1001/archopht.1995.01100100112040, indexed in Pubmed: 7575268.
33. Mittra RA, Mieler WF. Controversies in the management of open-globe injuries involving the posterior segment. Surv Ophthalmol. 1999; 44(3): 215–225, doi: 10.1016/s0039-6257(99)00104-6, indexed in Pubmed: 10588440.
34. Abu el-Asrar AM, Tabbara KF. Clostridium perfringens endophthalmitis. Doc Ophthalmol. 1994; 87(2): 177–182, doi: 10.1007/BF01204795, indexed in Pubmed: 7835187.
35. Azad R, Ravi K, Talwar D, et al. Pars plana vitrectomy with or without silicone oil endotamponade in post-traumatic endophthalmitis. Graefes Arch Clin Exp Ophthalmol. 2003; 241(6): 478–483, doi: 10.1007/s00417-003-0670-4, indexed in Pubmed: 12756578.
36. Bali E, Huyghe Ph, Caspers L, et al. Vitrectomy and silicone oil in the treatment of acute endophthalmitis. Preliminary results. Bull Soc Belge Ophtalmol. 2003(288): 9–14, indexed in Pubmed: 12879720.
37. Siqueira RC, Gil AD, Canamary F, et al. Pars plana vitrectomy and silicone oil tamponade for acute endophthalmitis treatment. Arq Bras Oftalmol. 2009; 72(1): 28–32, doi: 10.1590/s0004-27492009000100006, indexed in Pubmed: 19347118.

CASE REPORT
DOI: 10.5603/OJ.2020.0026

Atypical presentation of optic neuritis with unilateral inferior altitudinal visual field defect in multiple sclerosis

Cheau Wei Chin, Mohammad Fathi Ismail

Department of Ophthalmology, Hospital Sultanah Aminah, Johor Bahru, Malaysia

ABSTRACT

BACKGROUND: The purpose of this paper was to report a case of retrobulbar optic neuritis as the first manifestation of multiple sclerosis, with atypical presentations which include a sudden painless reduction in vision, without optic disc swelling and presence of unilateral inferior altitudinal visual field defect.

CASE REPORT: A 17-year-old girl presented to our clinic with right eye sudden painless drop in visual acuity to counting finger associated with headache. Her right eye optic nerve function tests were positive, but her optic disc was not swollen. Bjerrum's visual field chart noted right eye unilateral inferior altitudinal visual field defect with foveal involvement. Her blood investigations were normal, and magnetic resonance imaging (MRI) of brain and orbit was suggestive of multiple sclerosis. She was commenced on three days of high dose intravenous steroi, and was referred to neuromedical team for further management. At 3-month follow up, her right eye visual acuity improved to 6/6 with the restoration of normal colour vision.

CONCLUSIONS: In presence of atypical presentation of optic neuritis, multiple sclerosis must be thought of especially in young patients. Hence early co-management with neuromedical discipline is important to reduce the frequency and severity of attacks in the future.

KEY WORDS: retrobulbar optic neuritis; inferior altitudinal defect; multiple sclerosis; visual field

Ophthalmol J 2020; Vol. 5, 130–135

INTRODUCTION

Optic neuritis (ON) refers to an inflammatory demyelinating disorder of the optic nerve, characterized by monocular, painful and subacute vision drop over a period of one to two weeks [1–3], commonly affecting young healthy females at mean age of 36 [4]. Rarely, ON may have atypical presentations such as the onset of fewes than 20 years old, painless and sudden onset of reduction in visual acuity [1, 2].

In addition, ON can present with any type of nerve-fibre-bundle-related visual field (VF) defect. Keltner et al summarized that diffuse and central VF defect predominated in the affected eye at the first visit, then mainly partial arcuate, paracentral, and arcuate VF defects during follow-up [5]. Although the pattern of VF defect is not diagnostic of ON, altitudinal VF defect remains uncommon and should be further investigated for other aetiologies [2].

Demyelinating ON can occur in isolation or be associated with multiple sclerosis (MS) or neuromyelitis optica (NMO) [3]. Multiple sclerosis is an inflammatory demyelinating disease of the central nervous system characterized by multicentric in-

CORRESPONDING AUTHOR:
Cheau Wei Chin, Department of Ophthalmology, Hospital Sultanah Aminah, Johor Bahru, Malaysia; e-mail: cheauwei.1808@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

flammation and myelin destruction. On the other hand, NMO is an antibody-mediated disorder of the central nervous system usually attacking the optic nerves and spinal cord, involving both gray and white matters [1].

In this article, we will discuss on the atypical presentations of ON and the uncommon visual field defects that may be present in ON. We also suggest that MS should be suspected in the case of young healthy female and refer to neuromedical team early for co-management to further reduce the risk of recurrence.

CASE REPORT

A 17-year-old Malay girl who has no known medical illness, noticed a sudden painless drop in visual acuity of her right eye right after she woke up from her nap. It was accompanied by on and off dull frontal headache. She denies of ocular pain upon eye movement. Furthermore, she volunteered the history of recent viral flu one week ago, which lasted for four days, and has resolved at the time of presentation. There were no preceding flash or floaters, and patient denies of any trauma or insect bites. She also denies of body weakness, raised intracranial pressure symptoms, fever or any constitutional symptoms. She has no past ocular history and her family history was unremarkable.

On examination, her visual acuity was hand movement in the right eye and that was 6/6 in the left eye. The relative afferent pupillary defect (RAPD) was grade I positive on the right eye, with a light brightness of 70% and red desaturation of 30%. Ishihara colour vision test was unable to be performed over the right eye due to the poor vision. Her anterior segment and intraocular pressure were normal. Her optic discs were not swollen nor hyperemic and no retinitis patch nor vitritis seen in posterior pole. Her extraocular muscle movements were intact and painless, and no other cranial nerves affected. The rest of her neurological examination was unremarkable.

B-scan ultrasonography showed thickened right eye retroorbital optic nerve measuring 6.3 mm while that of the left eye measured 4.0 mm. We proceeded with Bjerrum's screen chart as our patient had poor visual acuity and was unable to fixate on the stimulus target. Her Bjerrum's screen chart revealed right eye unilateral inferior altitudinal defect with foveal involvement, and the fellow eye showed supero-nasal arcuate defect (Fig. 1).

Her full blood count, renal function, erythrocyte sedimentation rate, C-reactive protein, folate and B12 level taken were within normal ranges. In addition, her serum anti-aquaporin-4 antibody returned negative. Her autoimmune screening and infective screening for venereal disease, human immunodeficiency virus (HIV), hepatitis B and C were non-reactive as well.

Magnetic resonance imaging (MRI) of brain and orbit reported multiple hyperintense lesions in pe-

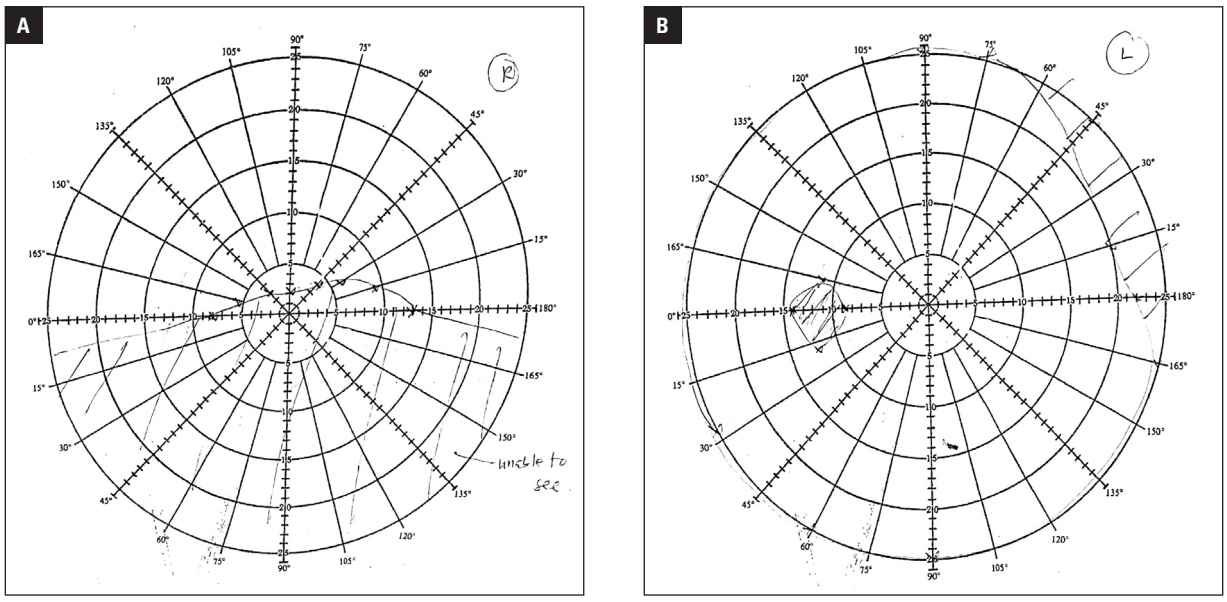

FIGURE 1. Bjerrum's Screen Chart of the (**A**) right and (**B**) left eye at initial visit

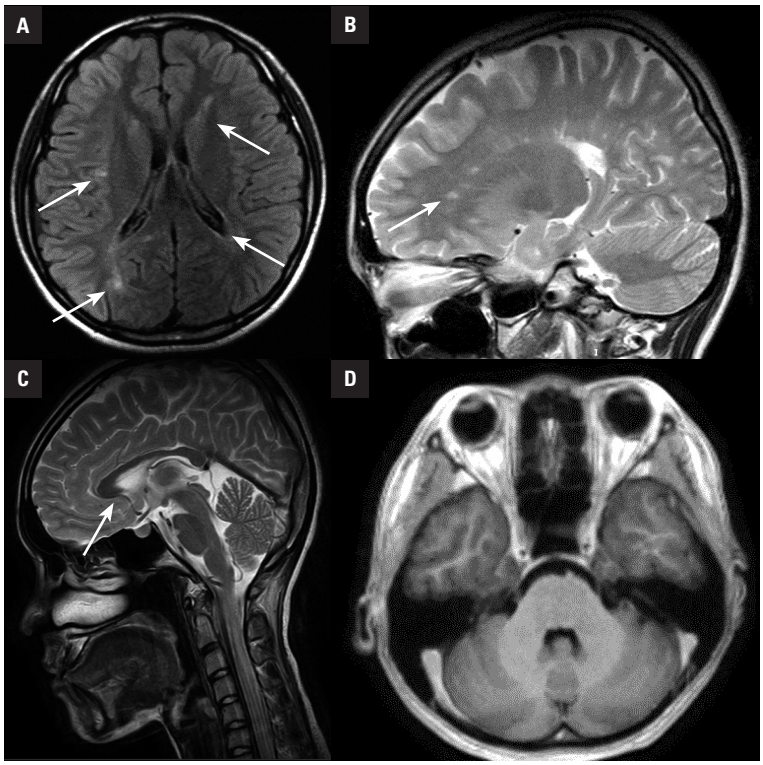

FIGURE 2. High intensity lesions at (**A**) periventricular, (**B**) juxtacortical and (**C**) pericallosal region

riventricular, juxtacortical and pericallosal region consistent with multiple sclerosis with dissemination in space, and no abnormal enhancement of optic nerve was seen (Fig. 2).

Furthermore, lumbar puncture was performed. The opening pressure was normal, and the cerebrospinal fluid (CSF) sample was clear, no signs of infection. Her CSF for anti-aquaporin-4 antibody was negative. On the other hand, her CSF electrophoresis revealed oligoclonal band with raised IgG index, which is consistent with multiple sclerosis.

Our patient was initially diagnosed with retrobulbar optic neuritis was secondary to viral flu in view of the history of recent flu prior to her presentation. However, the presence of bilateral visual field (VF) defect prompted us to proceed with contrast enhanced computerized tomography CECT brain and orbit to rule out the presence of space-occupying lesion. As there was no significant abnormality seen, we then proceeded with MRI brain and orbit, which suggested the diagnosis of multiple sclerosis. This is consistent with her CSF electrophoresis that revealed oligoclonal band with raised IgG index. This fulfils the Mcdonald criteria for the diagnosis of multiple sclerosis (MS) whereby she has one episode of attack, dissemination of space revealed by MRI and oligoclonal band present in CSF electrophoresis.

Other than MS, neuromyelitis optica spectrum disorder (NMOSD) is also commonly associated with ON in young healthy females. However, this was ruled out by the absence of anti-aquaporin-4 antibody in both serum and CSF. Although painless monocular vision loss and unilateral inferior altitudinal defect also paints a picture of non-arteritic anterior ischemic optic neuropathy (NAION), this does not fit her age group and there is lack of ischemic risk factors such as diabetes, hypertension or any history of major surgery to justify the diagnosis.

She was referred to neuromedical team, and was started on methylprednisolone 250 mg *i.v.* 6-hourly for 3 days, subsequently discharged home with oral Prednisolone 1mg/kg/day and slowly tapered over a period of 6 weeks as per neuromedical plan. Her right eye visual acuity has improved to 3/60 after completing 3 days of methylprednisolone treatment.

At 3-month follow up, her vision has improved to 6/6 both eyes, with normal colour vision. There was no more relative afferent pupillary defect (RAPD) present. Her anterior segment, intraocular pressure and posterior segment were normal, no

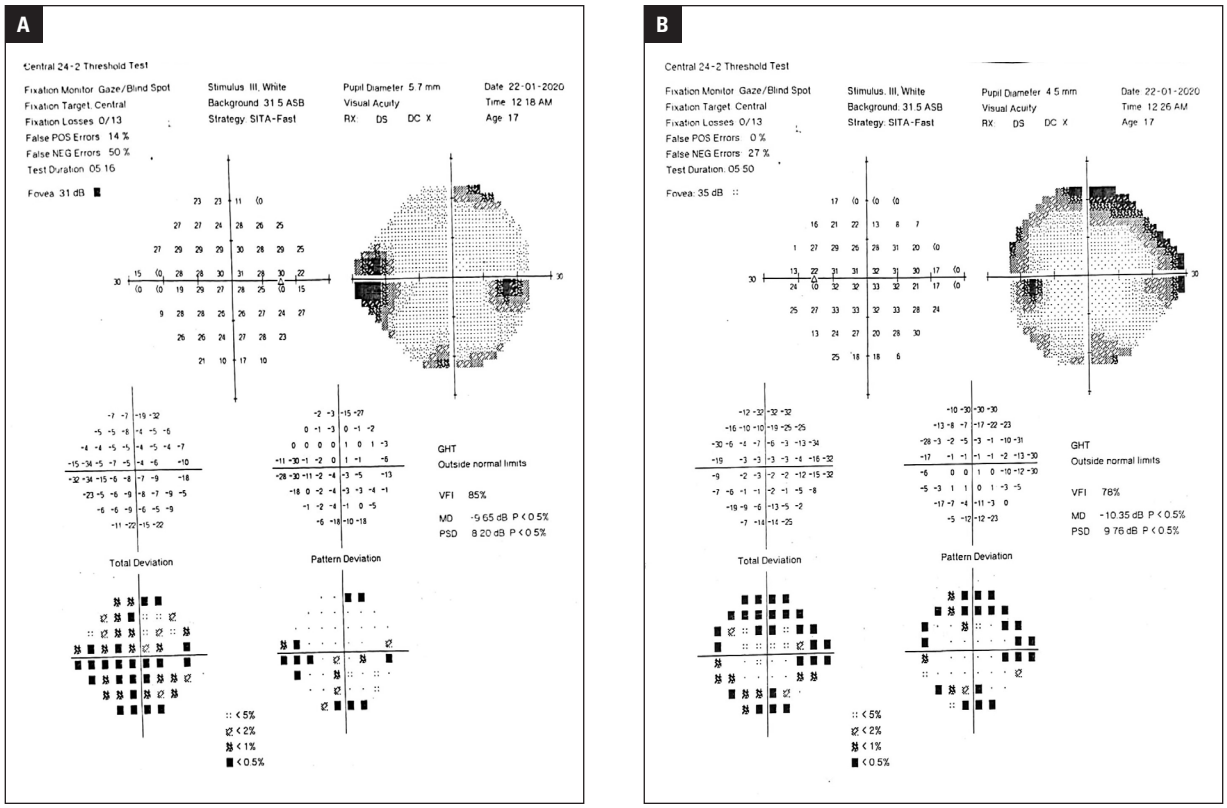

FIGURE 3. Humphrey visual field 24-2 of (**A**) right eye and (**B**) left eye at 3-month follow-up

disc pallor nor swelling noted. This time around we monitored her VF defect with Humphrey's visual field. Her right eye VF has cleared up leaving nasal step defect with some patchy loss, and left eye revealed superior arcuate defect (Fig. 3).

DISCUSSION

Wilhelm and Schabet [4] described a typical presentation of demyelinating ON as occurrence between age 18 to 50, unilateral, peribulbar pain, and improvement of vision after treatment. The mean age of onset is 36, and demyelinating ON is rare in patients below 18 years old. According to Kale [2], only 8% of patients with ON presented with painless vision loss, which is similar to our patient's presentation. This could be explained by the inflammation lying in the intracranial portion of optic nerve [4]. Gaier et al [1] and Hoorbakht et al [7] suggested that painless visual loss should raise suspicion for other causes such as non-arteritic anterior ischemic optic neuropathy (NAION) or Leber's hereditary optic neuropathy (LHON). However, both diagnoses did not fit our patient's age, gender, and risk factors.

Optic neuritis can be divided into:

— 1 — retrobulbar ON with normal disc appearance;

— 2 — papillitis involving the anterior aspect of the optic nerve with optic disc swelling;

— 3 — perineuritis with the involvement of the optic nerve sheath;

— 4 — neuroretinitis, with optic disc swelling and macular star [3]. Among these subtypes, retrobulbar and papillitis ON are more commonly associated with MS. ON that present in isolation accounts for 20% of the initial presentation of MS [2].

From the Optic Neuritis Treatment Trial (ONTT) [8], we learnt that the patients presented with various types of VF defect, predominantly diffuse (66%) and central field loss (27%) on the affected eye during their first presentation. Our patient presented with unilateral inferior altitudinal field defect on the affected eye during initial presentatio, and then transformed into a nasal step-defect during follow up. This is uncommon as Keltner et al [5] concluded that only 8% of the participants from the ONTT presented with altitudinal field defect initially, and no more than 2% developed nasal step defect during their follow up.

Furthermore, Keltner et al [5] revealed that 75% of the patients developed VF defect on the fellow eye during follow up, predominantly partial arcuate, paracentral, and arcuate defects. In this case, our patient developed superior arcuate defect over her fellow eye, suggesting the involvement of the optic nerve fibre bundle. Despite the limited use of VF in aiding diagnosis, Kale et al [2] suggested that the presence of altitudinal defect warrant consideration of other differential diagnosis. In this case, we have proceeded with urgent brain imaging and managed to rule out space occupying lesions and life-threatening intracranial pathologies.

In 1970, Hayreh [9] suggested that altitudinal VF defect without retinal lesion is caused by disruption in the posterior ciliary artery circulation. Despite the pathophysiology of ON remains unclear, it is postulated to result from inflammation and demyelination of the optic nerve [3]. Cytokines and other inflammatory mediators are released when activated peripheral T-cells cross the blood brain barrier, causing destruction of myelin, neural cell death and axonal degeneration [3, 7]. Here we suspect that either the inflammation of the optic nerve itself or the secondary perfusion defect caused by the inflammation of the optic nerve has resulted in an altitudinal VF defect in our patient.

Brain MRI is helpful diagnostically and prognostically to determine the risk of developing MS for patients with ON based on the number of demyelinating white matter lesions [3]. ONTT concluded that the risk of patients with ON developing MS by 15 years was 25% if their MRI brain was normal at time of diagnosis, and the risk triples to 78% if their MRI brain has more than three lesions [8]. In our patient's circumstance, she has lesions at periventricular, juxtacortical and pericallosal regions, and CSF electrophoresis has confirmed her diagnosis of MS.

However, no enhancement of optic nerve was seen in our patient's MRI. According to Kupersmith et al [10], enhancement of the optic nerve has a sensitivity of 94% in acute optic neuritis, and only 5% of patients with ON did not have enhancement of the affected optic nerve. Nonetheless, there wae no significant difference in terms of visual acuity and colour vision between those with and without optic nerve enhancement [10].

Intravenous methylprednisolone (IVMP) is recommended when there is monocular involvement, significant bilateral visual loss, or when fast recovery to normal visual acuity is required [3, 7]. Once systemic infection is ruled out, IVMP in a dose of 250 mg 6-hourly should be commenced over a 3-day course, followed by 11 days of daily oral prednisone (1 mg/kg/day) as per recommended by ONTT [8]. The main aim of treatment is to reduce the frequency and severity of attacks, and prevention of axonal loss in both ON and MS [7].

At 1-year follow-up, 94% of the patients who received IVMP in ONTT regained vision of 6/12 or better but subtle symptoms such as blurred vision may persist even with VA of > 6/6 [7]. Our patient has already achieved visual acuity of 6/6 with normal colour vision at 3-month follow-up.

CONCLUSION

Optic neuritis is a disease with many faces. Atypical presentations such as painless acute vision loss prompt other differential diagnoses but this does not rule out ON. It may also present with inferior altitudinal VF defect, which warrants further imaging to exclude other intracranial pathologies as this is an uncommon presentation. Brain MRI is important diagnostically and prognostically in monitoring disease progression. Last but not least, multiple sclerosis should be suspected in the case of young healthy female as early diagnosis and early co-management with neuromedical team reduces the frequency and severity of recurrence.

Consent for publication

The case patient had consented for publication of this case report, including the usage of her fundus photograph, OCT scans and recorded video of the surgery.

Conflicg of interests

The authors declare that there is no conflict of interest.

Funding acknowledgement

The authors received no financial support for the research, authorship, and/or publication of this article.

REFERENCES

1. Gaier ED, Boudreault K, Rizzo JF, et al. Atypical Optic Neuritis. Curr Neurol Neurosci Rep. 2015; 15(12): 76, doi: 10.1007/s11910-015-0598-1, indexed in Pubmed: 26467052.
2. Kale N. Optic neuritis as an early sign of multiple sclerosis. Eye Brain. 2016; 8: 195–202, doi: 10.2147/EB.S54131, indexed in Pubmed: 28539814.

3. Pau D, Al Zubidi Nu, Yalamanchili S, et al. Optic neuritis. Eye. 2011; 25(7): 833–842, doi: 10.1038/eye.2011.81, indexed in Pubmed: 21527960.
4. Wilhelm H, Schabet M. The Diagnosis and Treatment of Optic Neuritis. Dtsch Arztebl Int. 2015; 112(37): 616–25; quiz 626, doi: 10.3238/arztebl.2015.0616, indexed in Pubmed: 26396053.
5. Keltner JL, Johnson CA, Cello KE, et al. Optic Neuritis Study Group. Visual field profile of optic neuritis: a final follow-up report from the optic neuritis treatment trial from baseline through 15 years. Arch Ophthalmol. 2010; 128(3): 330–337, doi: 10.1001/archophthalmol.2010.16, indexed in Pubmed: 20212204.
6. Trapp BD, Peterson J, Ransohoff RM, et al. Axonal transection in the lesions of multiple sclerosis. N Engl J Med. 1998; 338(5): 278–285, doi: 10.1056/NEJM199801293380502, indexed in Pubmed: 9445407.
7. Hoorbakht H, Bagherkashi F. Optic neuritis, its differential diagnosis and management. Open Ophthalmol J. 2012; 6: 65–72, doi: 10.2174/1874364101206010065, indexed in Pubmed: 22888383.
8. Optic Neuritis Study Group. Multiple sclerosis risk after optic neuritis: final optic neuritis treatment trial follow-up. Arch Neurol. 2008; 65(6): 727–732, doi: 10.1001/archneur.65.6.727, indexed in Pubmed: 18541792.
9. Hayreh SS. Pathogenesis of visual field defects. Role of the ciliary circulation. Br J Ophthalmol. 1970; 54(5): 289–311, doi: 10.1136/bjo.54.5.289, indexed in Pubmed: 4987892.
10. Kupersmith MJ, Alban T, Zeiffer B, et al. Contrast-enhanced MRI in acute optic neuritis: relationship to visual performance. Brain. 2002; 125(Pt 4): 812–822, doi: 10.1093/brain/awf087, indexed in Pubmed: 11912114.

ORIGINAL PAPER
DOI: 10.5603/OJ.2020.0027

Knowledge and practice on solar ultraviolet radiation and its impact on vision: a case study among Kenyan optometrists

Shadrack Muma

Department of Public Health, Maseno University, Maseno, Kenya

ABSTRACT

BACKGROUND: The purpose of the study was to investigate optometrist's knowledge and practice on solar ultraviolet radiation and its implication on vision.

MATERIAL AND METHOD: A survey was conducted using purposive sampling. The study was conducted from January 2020 to February 2020 using emailed questionnaires. Basic socio-demographic characteristics, participants' knowledge and practice on solar ultraviolet radiation were assessed. The key variables under consideration were knowledge and practice on solar ultraviolet radiation. Odds ratios were calculated and chi-square test conducted.

RESULTS: A total of 270 optometrists received the survey with a response rate of 81% and mean age of 26.4 ± 4.3 years. Only 36% had good knowledge of the effects produced by solar radiation. On attenuation knowledge only 1% recommended contrast filters, 13% polarizing lenses and 4% polycarbonate. There solar ultraviolet radiation and cortical cataract (p = 0.012) was significantly different. Men had good knowledge about cataract (OR = 1.63, 95% CI = 1.56–1.76), keratopathy (OR = 1.72, 95% CI = 1.35–1.56), and pterygium (OR = 1.36, 95% CI = 1.32–1.43). Most respondents 66% could only dispense Photochromatic lenses because they are readily available.

CONCLUSION: The study denotes that solar ultraviolet radiation is an issue of global public health concern. Awareness is still a challenge and optometrists are well placed to create awareness. Public health act should initiate a policy on the attenuation of solar ultraviolet radiation.

KEY WORDS: solar; ultraviolet; radiation; optometrists; knowledge; practice

Ophthalmol J 2020; Vol. 5, 136–142

INTRODUCTION

Exposure to solar ultraviolet radiation has been shown to have significant public health implication. Overexposure is associated with various pathologies to the human eye. According to the World Health Organization, 20% of the global blindness is attributed to solar ultraviolet radiation [1]. Globally, overexposure to solar ultraviolet radiation has caused approximately 1.5 million disability adjusted life year and premature deaths totaling to 60,000 [2]. In the United Kingdom, it is estimated that over 14.5 million workers are exposed to solar ultraviolet radiation [1]. In sub-Saharan Africa, data on solar ultraviolet radiation is limited. However, cataract being one of the greatest burdens resulting from overexposure to solar ultraviolet radiation is at 14% of the global disease burden [3]. In Kenya, data on solar ultraviolet radiation does not exist, however, cataract is the leading cause of blindness. It contributes to 43% of the Kenyan blindness [4]. Therefore; knowledge of optometrists on solar ultraviolet radiation is sig-

CORRESPONDING AUTHOR:
Shadrack Muma, Department of Public Health, Maseno University, Po Box Private Bag, Maseno, Kenya; e-mail: mumashadrack275@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

nificant as they are well placed to create awareness to the public.

The total burden of disease caused by cataract globally is estimated at 25% and it is due to cortical cataract [2]. The ultraviolet radiation does not penetrate, however, it highly affects the human eye since the eye is sensitive to wavelength of 555 nanometer [5]. Absorbing the solar ultraviolet radiation produces photo luminescent and photo chemical effects to the crystalline lens. Based on occupation, at some point in time, one will have to be exposed to solar ultraviolet radiation. The magnitude of solar ultraviolet radiation to the eye depends on the time of exposure and the concentration. The effects produced by solar ultraviolet radiation to the eye include; pinguecula, pterygium, cortical cataract, keratopathy, photokeratitis and age related macular degeneration [3]. These are key ocular conditions which can only be understood by optometrists and ophthalmologists. In the African context, the chief complaint reported by patients is photophobia. A study in South Africa, among optometrists on the major complains raised by patient, 97% mentioned photophobia [6]. A similar high proportion was recorded in Nigeria where 89% complained of photophobia. While on functional low vision due to pterygium, 5000 per million were affected [7]. In Tanzania, a survey showed that there was a link between cortical cataract and solar ultraviolet radiation 33% [8]. This suggests that most exposed individuals seek advice from optometrists and other eye care providers. In Kenya, in as much as data on solar ultraviolet is not available, knowledge of optometrists on the same has not been assessed.

In as much as solar ultraviolet radiation is significant to public health, it is a great risk factor to other ocular conditions. Globally, the majority of citizens do outdoor jobs with only a few involved in indoor jobs. This is a clear indication that the general population is exposed to solar ultraviolet radiation. A study in South Africa showed that 78% of the working population does outdoor jobs with only 29% involved in indoor jobs [9]. Attenuation of solar ultraviolet radiation can only be achieved by using reflective lenses such as tinted lenses. A study conducted in the United States showed that 64% of the patients who had cortical cataract were involved in outdoor activities for a long period of time.[7] In sub Saharan Africa, studies on optometrists involvement in attenuation of solar ultraviolet radiation has not been well articulated [10]. However other countries such as South Africa and Nigeria have started developing strategies to curb solar ultraviolet radiation. In Kenya, attenuation on solar ultraviolet radiation is not known and optometrists are well placed to look at the issue. However, knowledge of Kenyan optometrists on the attenuation of solar ultraviolet radiation is not known.

Wearing gears for protection against solar ultraviolet radiation is very vital. To maximize awareness, optometrists practice is deemed necessary to the general public. A study in Australia reported that 67% of the interviewed optometrists were advising patients the management of solar ultraviolet radiation [3]. However, in Nigeria, only 2% of the optometrists could advise the patients on the effects of solar ultraviolet radiation [11]. This shows that developed countries are becoming more aware of solar ultraviolet radiation effects and the optometrists are playing a crucial role. The general population constitutes the literate and the illiterate, therefore public awareness on solar ultraviolet radiation is significant. In Kenya, little is known on solar ultraviolet radiation and no evidence of practice among optometrists exists. Therefore this study assessed the knowledge and practice on solar ultraviolet radiation.

MATERIAL AND METHODS

The questionnaires were given to optometrists practising all over Kenya. A quantitative approach was adopted in which questions were administered through their emails. The population of Kenya is estimated at 47 million with 47 counties. Primary eye care providers are distributed all over the counties with the majority based in Nairobi County. Only respondents who returned the consent were included in the study. The respondents were able to withdraw at anytime. An ethical approval was sought from Maseno University ethics review committee.

Recruitment was done from January 2020 to February 2020. A response rate of 81% was attained. The study adopted a purposive sampling (Fig. 1). The questionnaire had been pre-tested during a pilot to assess for Cronbach's' reliability (assessed at the level of 0.974 and 0.926 for knowledge and practice questionnaire respectively) and validity (assessed by performing a Pearson correlation coefficient and obtained $0.000 < 0.05$, $n = 30$). Participants who participated in the pilot study were excluded. Statistical Package for Social Sciences version 17 software was used to analyze the data. Values of $p < 0.05$ were considered statistically significant.

Sociodemographic characteristics

Age .....

Gender .....

Duration of practice .....

County of practice .....

Qualification .....

Knowledge on solar ultraviolet radiation

Do you know that solar ultraviolet radiation impacts negatively on vision?

☐ Yes

☐ No

If yes to 2 above, which of the following do believe is induced by solar ultraviolet radiation?

☐ Pinguecula

☐ Pterygium

☐ Keratopathy

☐ Photokeratitis

☐ Cataract

☐ Age related macular degeneration

Practice on solar ultraviolet radiation

Do you advise your patients on the impacts of solar ultraviolet radiation to the eye?

☐ Yes

☐ No

If yes to 4 above, which method of attenuation do you advice your patients on?

☐ Photochromatic lenses

☐ Contract filters

☐ Polarizing lenses

☐ Polycarbonate

☐ Yellow absorbing filters

FIGURE 1. The survey questionnaire

RESULTS

KNOWLEDGE OF SOLAR ULTRAVIOLET RADIATION

Most respondents 64% were not aware of the effects of solar ultraviolet radiation. However, less than half of the respondents (36%) knew the effects produced by solar ultraviolet radiation. Only 7% of the respondents could identify photochemical effects. A slightly higher proportion (72%) could identify the time of exposure as a factor responsible for solar ultraviolet radiation magnitude to the eye. Majority of the respondents (78%) had a good knowledge on cataract. However, knowledge of pterygium 24%, keratopathy 16%, pinguecula 21%, photokeratitis 12% and age-related macular degeneration 10% were significantly low. There was a statistically significant difference on solar ultraviolet radiation and cortical cataract ($p = 0.012$). Compared with women, men had good knowledge about cataract (OR = 1.63, 95% CI = 1.56–1.76), keratopathy (OR = 1.72, 95% CI = 1.35–1.56), and pterygium (OR = 1.36, 95% CI = 1.32–1.43) as conditions arising from exposure to solar radiation (Tab. 1).

KNOWLEDGE ON THE ATTENUATION OF SOLAR ULTRAVIOLET RADIATION

Majority of the respondents 63% agreed that sunlight is useful to the human body. Over three quarter of the respondents 87% were dispensing Photochromatic lenses. Other attenuation methods dispensation was significantly low. For example only 1% recommended contrast filters, 6% yellow absorbing filters, 13% polarizing lenses and 4% polycarbonate. Majority of the respondents 3% who recommended polycarbonate were based in Nairobi. Polycarbonate were 2.5 (95% CI = 2.1–3.5) times more likely to protect the eye from solar ultraviolet radiation than Photochromatic lenses. Compared with younger respondents

Table 1.Knowledge on solar ultraviolet radiation	
Variable	**Number (%)**
Do you know the effects produced by solar radiation?	
Yes	36
No	64
Which solar radiation induced eye effect do you know?	
Pinguecula	21
Pterygium	24
Keratopathy	16
Cortical cataract	78
Photokeratitis	12
Age-related macular degeneration	10

Table 2. Practice on solar ultraviolet radiation	
Variable	**Number (%)**
Do you advice your patients on solar radiation?	
Yes	48
No	52
Which methods of attenuation do you practice?	
Photochromatic lenses	78
Contrast filters	1
Polarizing lenses	13
Polycarbonate	3
Yellow absorbing filters	6

(25–30 years old), elderly individuals had less knowledge on contrast filters (35–40 years old: OR = 0.40, 95% CI = 0.39–0.67; ≥ 40 years old: OR = 0.61, 95% CI = 0.13–0.48), yellow absorbing (35–40 years old: OR = 0.57, 95% CI = 0.37-0.59; ≥ 40 years old: OR = 0.53, 95% CI = 0.25-0.41), and polarizing lenses (35–40 years old: OR = 0.89, 95% CI = 0.64–0.76; ≥ 40 years old, OR = 0.41, 95% CI = 0.41–0.60) as attenuation means for solar ultraviolet radiation.

PRACTICE ON SOLAR ULTRAVIOLET RADIATION

A relatively low proportion of the respondents 48% were advising patients on solar ultraviolet radiation. Majority of the respondents 78% were not concerned about solar ultraviolet radiation but refractive error correction. Most respondents 66% could only dispense Photochromatic lenses because they are readily available. The age-specific analysis found that middle-aged individuals (30–35 years old) were significantly less likely to identify the contribution of solar ultraviolet radiation (OR = 0.31, 95% CI = 0.13–0.45) to ocular pathologies (Tab. 2).

ASSOCIATION BETWEEN DEMOGRAPHIC CHARACTERISTICS AND KNOWLEDGE ON SOLAR RADIATION

Association between demographic characteristics and knowledge on solar radiation has been presented on Table 3.

DISCUSSION

The present study investigated optometrist knowledge and practice on solar ultraviolet radiation in Kenya. Solar ultraviolet radiation has been shown to produce side effect such as photochemical and photoluminscent effects. In this study the knowledge of optometrists was low. However, this could be attributed to the lack of policy guidelines on solar radiation by the ministry of health. A study

Table 3. Associations between demographic and knowledge on solar radiation				
Variable	**Knowledge**		**OR (95% CI)**	**p value**
	Good	**Poor**		
Age group(n = 219)				
25–30	24 (56%)	4 (24%)	12.0 (3.0–13.6)	< 0.155
35–40	7 (30%)	14 (70%)	1.0	
Duration of practice				
< 5	19 (6.0%	6 (25.0%)	1.0	
6–9	3 (1.0%)	5 (20.8%)	0.2 (0.0–0.3)	0.033
> 10	3 (2.0%)	13 (54.2%)	0.1 (0.0–0.3)	< 0.001
Qualification				
BSc Optometry	25 (14%)	7 (50%)	2.5 (0.5–9.2)	0.145
Dip Optometry	10 (8.6%)	7 (80%)	1.0	

conducted in the United States to investigate effects produced by solar radiation showed that 78% of the general population ware aware of the side effects [14]. This is relatively a greater proportion attributed to well establish policy to handle solar ultraviolet radiation. At the same time, awareness could have been established by the optometrists. However, there is no data on the knowledge of optometrists on solar radiation in the United States. In the African context, South Africa reported 60% of the general population being aware of solar radiation [15]. Being that South Africa comprises, both whites and blacks, the knowledge on radiation could have been improved as whites are at greater risk. In the Kenyan context, policy guidelines regulating solar ultraviolet radiation do not exist. Therefore, optometrists are well placed to create awareness. However their knowledge on solar ultraviolet radiation is significantly low. Being that policy does not exist, the optometrists ought to have taken the initiative to create public awareness on solar radiation effects to the eye.

Globally, everyone is exposed to solar ultraviolet radiation. However, with its adverse effects on the human eye, preventive measures should be adopted and applied. In Kenya, less than 50% are engaged in indoor jobs [16]. This is a clear indication that the majority are exposed to solar ultraviolet radiation. This study has reported a low level of knowledge on attenuation techniques. In Australia, a study conducted among optometrists on solar ultraviolet radiation showed that 76% were aware of the attenuation methods [17]. A similar scenario was reported among optometrists in the United Kingdom, where 75% of the optometrists were aware of the attenuation method [18]. This is seen in developed countries as policies inclined towards solar ultraviolet radiation are well established. In as much as optometrists are well placed to create awareness on the attenuation methods for solar radiation, African context data still misses. In Nigeria, 34% of the general population ware aware of the attenuation methods [14]. However, optometrist's knowledge has not been established. This could be due to lack of policies on solar ultraviolet radiation. In Kenya, nothing has been documented on attenuation awareness by the general public and the optometrist knowledge on solar radiation. In the literature search, little exist on knowledge of optometrists on solar ultraviolet radiation. Therefore this study will be the first in Africa to report knowledge of optometrists on solar ultraviolet radiation.

Prolonged exposure to solar ultraviolet radiation is a risk factor for cataract. A study in Australia reported no significant association between solar ultraviolet radiation and pinguecula, pterygium and keratopathy ($p = 0.67$) [19]. However, there was a significant association between solar ultraviolet radiation and cortical cataract ($p = 0.002$). The study results are concurrent to our study in which there was a significant association between cortical cataract and solar radiation ($p = 0.014$). This is a great risk to blindness as cataract contributes to Kenyan blindness by 43% [4]. In this study, most optometrists did not have the knowledge of cortical cataract as attributed to solar ultraviolet radiation. In Nigeria, most optometrists 65% are aware of cortical cataract to be attributed to solar radiation [7]. In general, optometrists need to engage in a more comprehensive diagnosis and proper history taking to ascertain the causes of the ocular conditions. Based on literature such, this will be the first study relating optometrists and solar ultraviolet radiation. The World Health Organization recommends certain measures to apply in curbing solar radiation. A study in Tanzania showed that 90% of the most affected by solar radiation are people with albinism [12]. Other studies reported that whites are more prone to skin diseases attributed to solar radiation than blacks. In Kenya, albinism exists however, little is known on solar ultraviolet radiation effects to the eye. The optometrists are well placed to assess this and come up with conclusive information. Therefore, a global investigation of optometrist's knowledge needs to be established so as to reduce the incidences of solar ultraviolet radiation effects.

Acquiring a filter to curb solar ultraviolet radiation goes at a cost. This may influence the optometrist's scope of advice as they may pre judge a patient. In the United States, filters to curb solar radiation are affordable while in Kenya only Photochromatic lenses are affordable. A study conducted in Tanzania showed that 22% were wearing absorbing filters against solar ultraviolet radiation [11]. This was the contrary in Kenya where 60% wear photochromatic lenses for fashion purposes [4]. Most optometrists based in Mombasa Kenya reported that 45% wear sunglasses due to the hot conditions. Due to climate change, in Canada, it was reported that 90% wear filters during hot seasons [20].In as much this happens globally, little is known on the practice of optometrist on solar ultraviolet radiation. Attention on attenua-

tion and practice on solar radiation is significant, however, it is the responsibility of optometrists to facilitate this.

The study had certain limitation. Firstly other eye care providers were not included in the survey. Therefore the results of the study may not be generalized to other eye care providers. Secondly, other stakeholders were not included in the survey and this influenced the government to take and stand on solar ultraviolet radiation.

The strength of the present study was it first investigated the personnel who see the general population. Involving optometrists in the study was a baseline in first getting whether the exports understand the situation before moving to the general population.

CONCLUSION

Solar ultraviolet radiation exists. Therefore there is need of public health policy on solar radiation to provide disease burden associated with overexposure and in exposure. There is need for solar radiation protection programmes to raise awareness of the health hazards. A global solar radiation index should be integrated so as to enhance a long term public health protection approach. A global investigation of optometrist's knowledge and practice on solar ultraviolet radiation should be determined. This will ensure that continuous update to the general population on solar radiation reaches the general public.

Ethics approval

Ethical approval was obtained from the institution review board of Maseno University. Participation was voluntary, and the respondents could withdraw from the survey at any time during the study period. The responses were kept confidential, and the data were de-identified before data analysis. The study adhered to the tenets of the Declaration of Helsinki.

Consent for publication

N.A.

Availability of data and materials

The dataset is available from corresponding author.

Competing interests

No competing interest.

Funding

No funding received.

Author contribution

S.M developed the proposal and conducted the study.

Acknowledgement

Thanks to participants.

REFERENCES

1. Bishop KD, Olszewski AJ. Epidemiology and survival outcomes of ocular and mucosal melanomas: a population-based analysis. Int J Cancer. 2014; 134(12): 2961–2971, doi: 10.1002/ijc.28625, indexed in Pubmed: 24272143.
2. Brandberg Y, Sjödén PO, Rosdahl I. Assessment of sun-related behaviour in individuals with dysplastic naevus syndrome: a comparison between diary recordings and questionnaire responses. Melanoma Res. 1997; 7(4): 347–351, doi: 10.1097/00008390-199708000-00011, indexed in Pubmed: 9293486.
3. Moise AF, Gies HP, Harrison SL. Estimation of the annual solar UVR exposure dose of infants and small children in tropical Queensland, Australia. Photochem Photobiol. 1999; 69(4): 457–463, indexed in Pubmed: 10212577.
4. Rosmini F, Stazi MA, Milton RC, et al. Italian–American Cataract Study. Group A dose-response effect between a sunlight index and age-related cataracts. Ann Epidemiol. 1994; 4(4): 266–270, doi: 10.1016/1047-2797(94)90081-7, indexed in Pubmed: 7921315.
5. Luande J, Henschke CI, Mohammed N. The Tanzanian human albino skin. Natural history. Cancer. 1985; 55(8): 1823–1828, doi: 10.1002/1097-0142(19850415)55:8<1823::aid-cncr2820550830>3.0.co;2-x, indexed in Pubmed: 3978567.
6. Raasch BA, Buettner PG. Multiple non-melanoma skin cancer in an exposed Australian population. Int J Dermatol. 2002; 41(10): 652–658, doi: 10.1046/j.1365-4362.2002.01573.x, indexed in Pubmed: 12390187.
7. Parisi AV, Kimlin MG. Comparison of the spectral biologically effective solar ultraviolet in adjacent tree shade and sun. Phys Med Biol. 1999; 44(8): 2071–2080, doi: 10.1088/0031-9155/44/8/316, indexed in Pubmed: 10473215.
8. Hersey P, Bradley M, Hasic E, et al. Immunological effects of solarium exposure. Lancet. 1983; 1(8324): 545–548, doi: 10.1016/s0140-6736(83)92808-8, indexed in Pubmed: 6131254.
9. McCarty CA. Epidemiology of pterygium in Victoria, Australia. Br J Ophthalmol. 2000; 84(3): 289–292, doi: 10.1136/bjo.84.3.289, indexed in Pubmed: 10684840.
10. Norn M. Spheroid degeneration, keratopathy, pinguecula, and pterygium in Japan (Kyoto). Acta Ophthalmol. 1984; 62(1): 54–60, doi: 10.1111/j.1755-3768.1984.tb06756.x, indexed in Pubmed: 6720277.
11. Nwosu SN. Ocular problems of young adults in rural Nigeria. International Ophthalmology. 1998; 22(5): 259–263, doi: 10.1023/a:1006338013075, indexed in Pubmed: 10826540.
12. Panchapakesan J, Hourihan J, Mitchell P. Prevalence of pterygium and pinguecula: the Blue Mountains Eye Study. Aust N Z J Ophthalmol. 1998; 26(Suppl 1): S2–S5, doi: 10.1111/j.1442-9071.1998.tb01362.x, indexed in Pubmed: 9685008.
13. Rasanayagam RT. The incidence and racial distribution of pterygium in West Malaysia. Trans Ophthalmol Soc NZ. 1973; 25: 56–59, indexed in Pubmed: 4519231.
14. Sasaki H, Asano K, Kojima M, et al. [Epidemiological Survey of Ocular Diseases in K Island, Amami Islands Prevalence of Cataract and Ptery-

gium]. Nippon Ganka Gakkai Zasshi. 1999; 103(7): 556–563, indexed in Pubmed: 10443131.
15. Sebban A, Hirst LW. Pterygium recurrence rate at the Princess Alexandra Hospital. Aust NZJ Ophthalmol. 1991; 19(3): 203–206, doi: 10.1111/j.1442-9071.1991.tb00661.x, indexed in Pubmed: 1958364.
16. Singh MM, Murthy GV, Venkatraman R. A study of ocular morbidity among elderly population in a rural area of central India. Indian J Ophthalmol. 1997; 45(1): 61–65, indexed in Pubmed: 9475015.
17. Duncan DD, Muñoz B, Bandeen-Roche K, et al. Assessment of ocular exposure to ultraviolet-B for population studies. Salisbury Eye Evaluation Project Team. Photochem Photobiol. 1997; 66(5): 701–709, doi: 10.1111/j.1751-1097.1997.tb03210.x, indexed in Pubmed: 9383994.
18. Garssen J, Nowal M, Loveren HV. UV-B induced immunomodulation: a health risk. Polar Research. 2017; 18(2): 339–343, doi: 10.3402/polar.v18i2.6593.
19. Moise AF, Gies HP, Harrison SL. Estimation of the Annual Solar UVR Exposure Dose of Infants and Small Children in Tropical Queensland, Australia. Photochem Photobiol. 1999; 69(4): 457–463, doi: 10.1111/j.1751-1097.1999.tb03312.x, indexed in Pubmed: 10212577.
20. Parisi AV, Kimlin MG. Comparison of the spectral biologically effective solar ultraviolet in adjacent tree shade and sun. Phys Med Biol. 1999; 44(8): 2071–2080, doi: 10.1088/0031-9155/44/8/316, indexed in Pubmed: 10473215.

CASE REPORT
DOI: 10.5603/OJ.2020.0030

Retinoblastoma and prune belly syndrome: the first described association in literature

Rafat Turki[1], Ibrahim Alnawaiseh[1], Ewa Jasińska[2], Agata Pietras-Baczewska[2], Mustafa Mehyar[1], Yacoub A. Yousef[1], Robert Rejdak[2], Rashed Mustafa Nazzal[3]

[1]Ophthalmology Department, King Hussein Cancer Center, Amman, Jordan
[2]Ophthalmology Department, Medical University of Lublin, Lublin, Poland
[3]Shami Eye Center, Amman, Jordan

ABSTRACT

BACKGROUND: Retinoblastoma is the most common primary intraocular tumor in children. Prune belly syndrome is a rare congenital disease affecting newborns. The combination of the two diseases has never been reported before. In this article, we present a case of a male infant diagnosed with prune belly syndrome (PBS) at birth.

CASE REPORT: Patient underwent many surgeries to manage the resulting consequences of PBS. At the age of 7 months, he presented with left eye leukocoria. He was examined and diagnosed with retinoblastoma. The eye was enucleated, and the diagnosis was confirmed histopathologically. This is the first case to be described in the literature of such an association to the best of our knowledge.

KEY WORDS: prune belly syndrome; retinoblastoma; Eagle-Barrett syndrome

Ophthalmol J 2020; Vol. 5, 143–145

INTRODUCTION

Retinoblastoma is the most common intraocular primary malignancy in children, with an estimated incidence of 1 in 15,000 to 1 in 18,000 live births. There is no racial or gender predisposition for the tumor. It can be unilateral, bilateral, or even trilateral; in the latter case, the pineal gland is featuring a tumor as well. The average age at diagnosis is 18 months; unilateral retinoblastomas are diagnosed at an older age than bilateral tumors [1]. The genetic bases for the tumor were identified early on. The retinoblastoma gene (RB1) was the first tumor suppressor gene cloned. It is a negative regulator of the cell cycle through its ability to bind the transcription factor E2F and repress transcription of genes required for the S phase. The gene is located on chromosome 13q14 [2].

On the other hand, prune belly syndrome (PBS), which is also known as Eagle-Barrett syndrome, is a rare congenital disorder characterized by the triad of deficient abdominal musculature, cryptorchidism, and urinary tract abnormalities [3, 4]. Prune belly syndrome has an incidence of 3.6 to 3.8 per 100,000 live male births [5]. It has a wide range of presentations from being incompatible with life to an almost normal child [6, 7]. The severity of renal dysplasia largely determines the prognosis of this disease [8]. While PBS mainly affects the genitourinary tract, including different degrees of renal dysplasia, hydronephrosis, enlarged bladder, and urethral obstruction, multisystem involvement has been frequently reported [9].

Indeed, various gastrointestinal, cardiac, pulmonary, skeletal manifestations have been associated with PBS, including pulmonary hypoplasia, patent ductus arteriosus, imperforated anus, club foot, and congenital hip dislocation [10]. Given the very low incidence of each disease alone, statistically

CORRESPONDING AUTHOR:
Ibrahim Al Nawaiseh, King Hussein Cancer Center, Amman, Jordan, Queen Rania Al Abdullah Street (next to Jordan University)
P.O. Box 1269, Amman 11941, tel: (+962-6) 53 00 460; e-mail: i_nawaiseh@hotmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

speaking, the probability of both conditions to exist together is exceedingly rare. This article is by far the first case to be reported with such association. Whether this simultaneous occurrence is causative or by chance still to be elucidated.

CASE REPORT

The patient is a male, born from nonconsanguineous parents, and delivered vaginally. Antenatal ultrasound revealed oligohydramnios and a large fetal bladder. The neonate has prune-like abdominal skin wrinkles, bilateral cryptorchidism, and developmental hip dysplasia (Fig. 1). He was admitted to the neonatal intensive care unit for multiple urinary tract infections and underwent vesicostomy due to severe bilateral hydronephrosis, chronic kidney disease, and vesicoureteral reflux stage V. By the age of 7 month, his mother noticed left eye leukocoria. Fundus examination of the left eye, performed under anesthesia, showed intraocular mass occupying the vitreous cavity (endophytic growth) with total exudative retinal detachment and subretinal seeds. The right eye was normal. B-scan ultrasound of the left eye showed numerous hyperechoic calcifications within the mass (Fig. 2). Magnetic resonance imaging (MRI) revealed a large left intraocular mass, measuring around 1.3 x 1.3 cm on axial images and around 1.6 cm craniocaudally. There was an intermediate signal on the T1-weighted sequence, an intermediate to slightly hypointense signal on the T2-weighted sequence, and a deep hypointense T2 signal on the short T1-inversion recovery (STIR) sequence. The patient was diagnosed with left eye retinoblastoma group D and underwent left eye enucleation. Histopathologic assessment of the enucleated eye confirmed the diagnosis of retinoblastoma with massive choroidal invasion.

DISCUSSION

Both retinoblastoma and prune belly syndrome can take place as an isolated event or as a familial disease. In familial cases, both conditions could have a genetic background. Initially, a possible genetic basis for PBS was discounted mainly due to reports of monozygotic twins discordant. Nevertheless, few publications have suggested the possibility that this syndrome can have a genetic background when case reports of familial PBS primarily affecting brothers have suggested a possible autosomal or X-linked recessive mode of inheritance. Thus, a genetic basis for PBS is highly suggested [5].

Further studies have currently identified *HNF1β* as the only candidate PBS gene based on two published PBS cases with chromosome 17q12 microdeletions encompassing the *HNF1β* gene [11]. Although some authors have reported an ocular association to be present in some cases of PBS, these features are usually part of Potter's faces, which might be present secondary to oligo-hydramnios rather than being genuine associated features. These include: micrognathia, wide-set eyes, flattened palpebral fissures, prominent epicanthus, flattened nasal bridge, low-set ears lacking cartilage, and skeletal deformities [12].

Nevertheless, few reports described genuine associations: micro-cornea, primary optic atrophy, persistent pupillary membrane, and congenital mydriasis [13, 14]. Although 13q deletion syndrome can sometimes be associated with retinoblastoma and urological problems, it has never been reported as a PBS cause. It is a rare genetic disease caused by

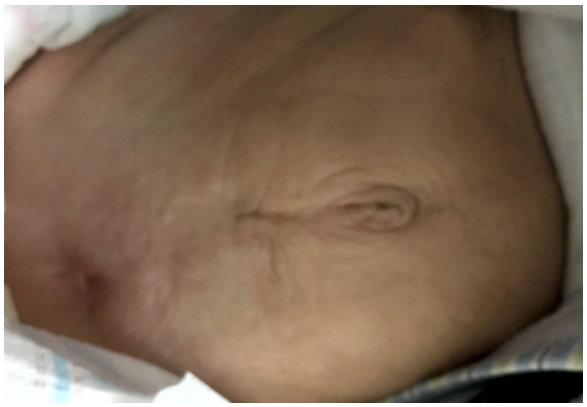

FIGURE 1. Abdominal image showing scar of previous surgeries to manage the urological consequences of the disease

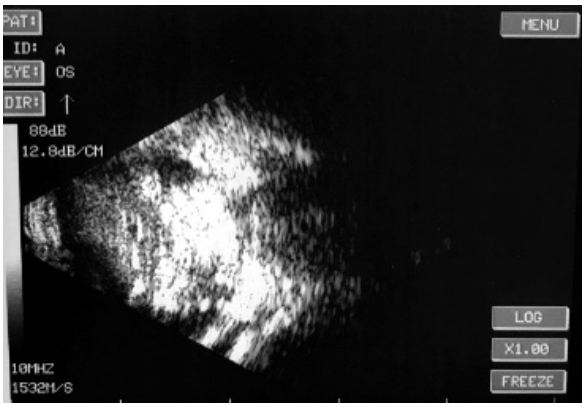

FIGURE 2. Ocular B-scan ultrasonography illustrating the intraocular mass with calcifications

the deletion of some or the entire large arm of human chromosome 13. Different areas of deletion are associated with various symptoms, including: mental retardation, broad prominent nasal, bridge, hypertelorism, microphthalmia, epicanthus, ptosis, colobomata, retinoblastoma, micrognathia, protruding maxilla, low set ears, facial asymmetry, congenital heart disease, imperforate anus, Hypospadias or epispadias, undescended testes, bifid scrotum, pelvic girdle anomalies, and foot and toe anomalies [15].

CONCLUSION

Retinoblastoma and PBS have never been reported in the literature, and to the best of our knowledge, this is the first case report to register such an association. Whether this has a causative relationship or not is unclear.

Acknowledgments

None.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Ethics

This article adheres to the World Medical Association Declaration of Helsinki.

Consent

The patient's written informed consent and images were provided by the patient's legally authorized representative (father).

Funding

None.

REFERENCES

1. Shields JA. Intraocular tumors — a text and atlas. WB Saunders Company, Philadelphia 1992.
2. Hanahan D, Weinberg R. The Hallmarks of Cancer. Cell. 2000; 100(1): 57–70, doi: 10.1016/s0092-8674(00)81683-9, indexed in Pubmed: 10647931.
3. Seidel NE, Arlen AM, Smith EA, et al. Clinical manifestations and management of prune-belly syndrome in a large contemporary pediatric population. Urology. 2015; 85(1): 211–215, doi: 10.1016/j.urology.2014.09.029, indexed in Pubmed: 25444629.
4. Eagle JF, Barrett GS. Congenital deficiency of abdominal musculature with associated genitourinary abnormalities: A syndrome. Report of 9 cases. Pediatrics. 1950; 6(5): 721–736, indexed in Pubmed: 14797335.
5. Granberg CF, Harrison SM, Dajusta D, et al. Genetic basis of prune belly syndrome: screening for HNF1 gene. J Urol. 2012; 187(1): 272–278, doi: 10.1016/j.juro.2011.09.036, indexed in Pubmed: 22114815.
6. Diao B, Diallo Y, Fall PA, et al. [Prune Belly syndrome: epidemiologic, clinic and therapeutic aspects]. Prog Urol. 2008; 18(7): 470–474, doi: 10.1016/j.purol.2008.04.003, indexed in Pubmed: 18602609.
7. Zugor V, Schott GE, Labanaris AP. The Prune Belly syndrome: urological aspects and long-term outcomes of a rare disease. Pediatr Rep. 2012; 4(2): e20, doi: 10.4081/pr.2012.e20, indexed in Pubmed: 22802998.
8. Hillman RT, Garabedian MJ, Wallerstein RJ. Pregnancy outcome in a woman with prune belly syndrome. BMJ Case Rep. 2012; 2012, doi: 10.1136/bcr-2012-006490, indexed in Pubmed: 23203170.
9. Sutherland RS, Mevorach RA, Kogan BA. The prune-belly syndrome: current insights. Pediatr Nephrol. 1995; 9(6): 770–778, doi: 10.1007/BF00868740, indexed in Pubmed: 8747124.
10. Grimsby GM, Harrison SM, Granberg CF, et al. Impact and frequency of extra-genitourinary manifestations of prune belly syndrome. J Pediatr Urol. 2015; 11(5): 280.e1–280.e6, doi: 10.1016/j.jpurol.2015.06.005, indexed in Pubmed: 26231776.
11. Murray PJ, Thomas K, Mulgrew CJ, et al. Whole gene deletion of the hepatocyte nuclear factor-1beta gene in a patient with the prune-belly syndrome. Nephrol Dial Transplant. 2008; 23(7): 2412–2415, doi: 10.1093/ndt/gfn169, indexed in Pubmed: 18411231.
12. Woods AG, Brandon DH. Prune belly syndrome. A focused physical assessment. Adv Neonatal Care. 2007; 7(3): 132–43; quiz 144, doi: 10.1097/01.anc.0000278211.95767.05, indexed in Pubmed: 17844777.
13. Brodsky MC, Turan KE, Khanna CL, et al. Congenital mydriasis and prune belly syndrome in a child with an ACTA2 mutation. J AAPOS. 2014; 18(4): 393–395, doi: 10.1016/j.jaapos.2014.02.010, indexed in Pubmed: 24998021.
14. Shorey P, Lobo G. Ocular anomalies in abdominal muscle deficiency syndrome. Am J Ophthalmol. 1989; 108(2): 193–195, doi: 10.1016/0002-9394(89)90019-6, indexed in Pubmed: 2757102.
15. Grace E, Drennan J, Colver D, et al. The 13q- deletion syndrome. J Med Genet. 1971; 8(3): 351–357, doi: 10.1136/jmg.8.3.351, indexed in Pubmed: 5097142.

CASE REPORT
DOI: 10.5603/OJ.2020.0029

Multifocal serpiginous-like choroiditis revealing mediastinal lymph node tuberculosis

Imane Chabbar, Louai Serghini, Zakia Hajji, Abdelkrim Boulanouar, Amina Berraho

Ophthalmology B Department, Ibn Sina University Hospital, Rabat, Morocco

ABSTRACT

Serpiginous-like choroiditis is a rare manifestation of intraocular tuberculosis. It most often occurs in the context of suspected or latent tuberculosis. The diagnostic confirmation remains a real challenge. We report a case of a young patient presented with rapid bilateral visual acuity decrease. The diagnosis of tuberculous serpiginous-like choroiditis associated with mediastinal lymph node tuberculosis was established based on anamnestic, clinical, radiographic, and histological arguments. Anti-tuberculosis drugs have been recommended in combination with corticotherapy. The evolution was marked by significant stabilization of choroidal lesions with an improvement in visual acuity. Given its great clinical polymorphism, ocular tuberculosis should be suspected in any ocular inflammation, even atypical, in order to start early and appropriate treatment and improve the visual prognosis.

KEY WORDS: tuberculosis; multifocal serpiginous-like choroiditis; uveitis; anti-tuberculosis drugs; prognosis

Ophthalmol J 2020; Vol. 5, 146–149

INTRODUCTION

Tuberculosis is a systemic infectious disease caused by Mycobacterium Tuberculosis, which is mainly transmitted by air [1]. It is the first cause of infectious morbidity in endemic underdeveloped countries. A remarkable resurgence of this disease was observed in industrialized countries in parallel with HIV infection prevalence increase [2]. Tuberculosis mainly affects the lungs. However, ocular involvement is not uncommon [3]. There are various intraocular manifestations of tuberculosis, which include: choroiditis, anterior or intermediate uveitis, retinal vasculitis, panuveitis, and endophthalmitis [4]. Serpiginous-like choroiditis represents a rare clinical form of this disease. We report an observation of serpiginous-like choroiditis of tuberculous origin, with extraocular localization. In this paper, we analyzed the clinical, therapeutic, and prognostic characteristics of this disease.

CASE REPORT

We present a case report of a 40-year-old male, complaining of a bilateral visual acuity decrease, rapidly progressive, and more marked in the left eye. The interrogation reveals a history of tuberculosis contagion and chronic smoking. On admission, the best-corrected visual acuity was 8/10 in the right eye and 6/10 in the left eye. The ophthalmological examination found a correct anterior segment, bilaterally. The eye fundus examination (Fig. 1) found a moderate bilateral vitreous Tyndall. In the left eye, we noted the presence of multiple choroiditis foci with geographical distribution, located in the nasal region of the optic disc and extending centrifugally, but sparing the macular center. These lesions were yellowish active with fuzzy limits and with a retinal vasculitis opposite. In the right eye, we noted yellowish foci arranged around the macula with papillary hyperemia.

CORRESPONDING AUTHOR:
Imane Chabbar, Ophthalmology B Department, Ibn Sina University Hospital, Rabat, Morocco; e-mail: imana1chab@gmail.com

Copyright © 2020 Via Medica, ISSN 2450–7873

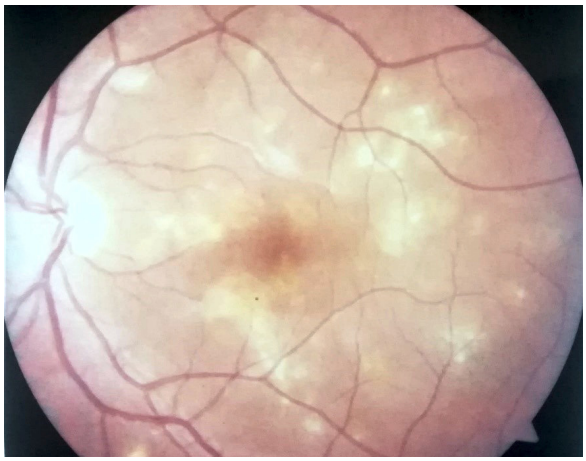

FIGURE 1. Color fundus photography of the left eye showing multiple yellowish lesions with fuzzy limits and geographical distribution, corresponding to choroiditis foci

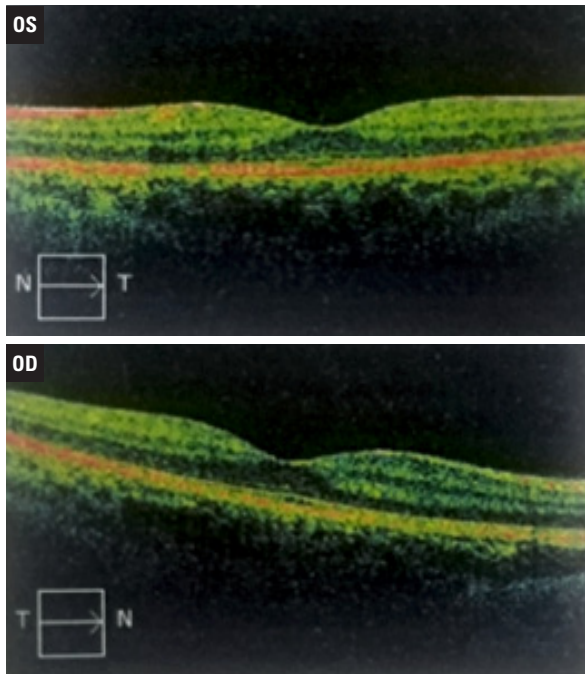

FIGURE 3. Macular OCT shows choriocapillaris hyperreflectivity compatible with choroiditis foci, very marked in the left eye, with thickening of the retinal pigment epithelium

Fluorescein angiography (Fig. 2AB) showed in both eyes an hyperfluorescent character of these foci in early times gradually increasing to become intense in late times with papillary retention in favor of papillitis. Macular OCT revealed a choroidal hyperreflectivity compatible with the choroiditis. It was very marked in the left eye, with retinal pigment epithelium thickening (Fig. 3).

The results of routine blood tests, including full blood count and C-reactive proteins, were in the normal range. The results of serologic tests excluded toxoplasmosis, syphilis, and Lyme disease. The tuberculin intradermal reaction and QuantiFERON test were positive. Chest X-ray showed a mediastinal enlargement. Thoracic CT scan (Fig. 4) revealed multiple mediastinal lymphadenopathies: the largest one contained central necrosis. CT-guided transparietal biopsy revealed a tuberculoid granuloma with caseous necrosis. The diagnosis of mediastinal lymph node tuberculosis with tuberculous choroiditis was thus established. In collaboration with the Pulmonology Department, our patient received anti-tuberculosis treatment based on two-phased chemotherapy; an initial intensive phase, combining four drugs for two months: isoniazid 5 m/kg/d,

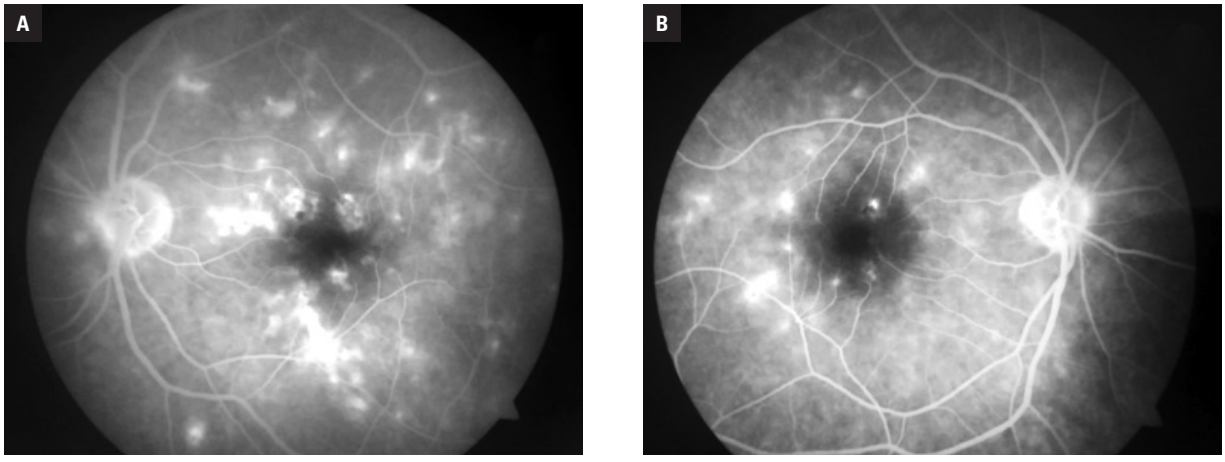

FIGURE 2. Fluorescein angiography of the left (**A**) and the right (**B**) eye, showing hyperfluorescent lesions in early times gradually increasing to become intense in late times with papillary impregnation

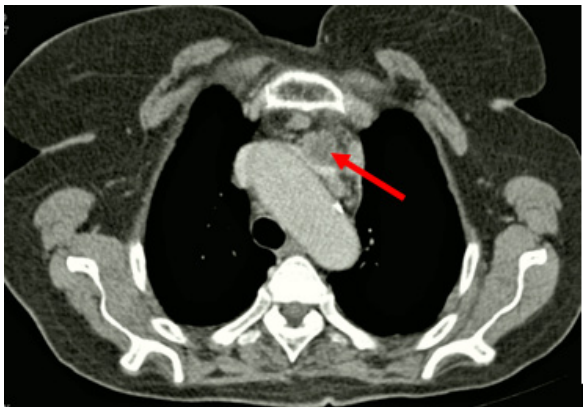

FIGURE 4. Thoracic CT scan showing multiple mediastinal lymphadenopathies, the largest one (arrow) contains central necrosis very suggestive of tuberculous origin

rifampicin 10 mg/kg/d, pyrazinamide 20 mg/kg/d, and ethambutol 15 mg/kg/d, followed by a continuation phase with two drugs: isoniazid and rifampicin at the same dosage for four months. A corticotherapy was administered 48 hours after anti-tuberculosis drugs: a methylprednisolone bolus 1 g/day for three successive days relayed by prednisone *per os* 1 mg/kg/day. The evolution was characterized by a stabilization of choroidal lesions with visual acuity improvement in both eyes reaching 9/10.

DISCUSSION

Bouchut tubercles are the most frequent intraocular manifestation of systemic tuberculosis [4]. Tuberculous uveitis can present as serpiginous-like choroiditis, also called tuberculous multifocal serpiginous choroiditis [5]. Its clinical appearance is similar to serpiginous choroiditis, a condition of undetermined idiopathic etiology. It corresponds to a rare, multifocal, chronic, and recurrent inflammatory disease. The lesions involve a retinal pigment epithelium, the choriocapillaris, and the choroid with irreversible photoreceptors damage, typically extending from the juxta papillary region and following a centrifugal path [4]. Macular forms have also been described. Both eyes are often affected asymmetrically. There is usually no inflammatory reaction of the anterior segment, but very moderate hyalitis may be present. These clinical elements are consistent with the presentation of our patient. The pathogenesis of intraocular tuberculosis remains a controversial subject [6], although many hypotheses have been discussed. In fact, the eye can be the entry route for mycobacteria (primary ocular tuberculosis), although it is very rare. In the majority of cases, the bacteria reach the eye by hematogenous dissemination (secondary ocular tuberculosis). A recent study showed a mycobacteria multiplication within the retinal pigment epithelium which would serve as its reservoir [7]. In addition, many authors consider that the intraocular inflammatory reaction secondary to tuberculosis infection is mainly due to a hypersensitivity reaction against mycobacterial antigens. Fluorescein angiography and indocyanine green angiography can be useful in evaluating the extent and activity of lesions [8]. Optical coherence tomography objectively determines whether or not macular edema is present. The association between serpiginous choroiditis and tuberculosis was reported in 1974 by Laatikainen and Erkkila [9]. In 2003, Gupta and et al. described seven cases of suspected ocular tuberculosis presenting with serpiginous choroiditis. They observed a clinical improvement under a combination of anti-tuberculosis drugs and corticotherapy [10]. Similarly, Mackensen et al. observed that 52% of patients presenting with serpiginous choroiditis had a positive QuantiFERON test result. In this study, the condition of 25% of patients improved after anti-tuberculosis treatment combined with corticotherapy [11]. The diagnosis of ocular tuberculosis is often based on the detection of latent or active systemic infection in patients from endemic regions or having a tuberculosis contagion. Chest X-ray shows mediastinal, pulmonary, and pleural lesions that can be better analyzed on thoracic CT scan.

In our case, the diagnosis was based on clinical and paraclinical arguments: the history of tuberculous contagion, positive tuberculin intradermal reaction, positive QuantiFERON test, mediastinal adenopathies on the CT scan, and finally — the biopsy confirming the histological diagnosis. The treatment of tuberculous choroiditis is based on the combination of anti-tuberculosis drugs and corticosteroids. This therapy considerably reduces recurrence risk. Patients' prognosis is favorable under treatment with stabilization or even improvement of final visual acuity, in the absence of macular involvement [12].

CONCLUSION

Serpiginous-like choroiditis is a rare manifestation of intraocular tuberculosis. It most often oc-

curs in the context of suspected or latent tuberculosis. The diagnostic confirmation remains a real challenge. Given its great clinical polymorphism, ocular tuberculosis should be considered in any ocular inflammation, even atypical, especially in countries with tuberculosis endemic, in order to start early and appropriate treatment and improve the visual prognosis.

Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Forrellad M, Klepp L, Gioffré A, et al. Virulence factors of the Mycobacterium tuberculosis complex. Virulence. 2013; 4: 3–66, doi: 10.4161/viru.22329, indexed in Pubmed: 23076359.
2. Martinson NA, Hoffmann CJ, Chaisson RE, et al. Epidemiology of tuberculosis and HIV: recent advances in understanding and responses. Proc Am Thorac Soc. 2011; 8(3): 288–293, doi: 10.1513/pats.201010-064WR, indexed in Pubmed: 21653530.
3. Shakarchi FI, Shakarchi FI, Shakarchi FI. Ocular tuberculosis: current perspectives. Clin Ophthalmol. 2015; 9: 2223–2227, doi: 10.2147/OPTH.S65254, indexed in Pubmed: 26648690.
4. Willermain F, Makhoul D, Caspers L, et al. Uvéites tuberculeuses. Les Uvéites. 2010: 121–128, doi: 10.1016/b978-2-294-71107-7.50008-1.
5. Nazari Khanamiri H, Rao NA, Nazari Khanamiri H, et al. Serpiginous choroiditis and infectious multifocal serpiginoid choroiditis. Surv Ophthalmol. 2013; 58(3): 203–232, doi: 10.1016/j.survophthal.2012.08.008, indexed in Pubmed: 23541041.
6. Lim WK, Buggage RR, Nussenblatt RB, et al. Serpiginous choroiditis. Surv Ophthalmol. 2005; 50(3): 231–244, doi: 10.1016/j.survophthal.2005.02.010, indexed in Pubmed: 15850812.
7. Rao NA, Saraswathy S, Smith RE, et al. Tuberculous uveitis: distribution of Mycobacterium tuberculosis in the retinal pigment epithelium. Arch Ophthalmol. 2006; 124(12): 1777–1779, doi: 10.1001/archopht.124.12.1777, indexed in Pubmed: 17159041.
8. Bouchenaki N, Cimino L, Auer C, et al. Assessment and classification of choroidal vasculitis in posterior uveitis using indocyanine green angiography. Klin Monbl Augenheilkd. 2002; 219(4): 243–249, doi: 10.1055/s-2002-30661, indexed in Pubmed: 12022010.
9. Laatikainen L, Erkkilä H, Erkkilä H, et al. Serpiginous choroiditis. Br J Ophthalmol. 1974; 58(9): 777–783, doi: 10.1136/bjo.58.9.777, indexed in Pubmed: 4433491.
10. Gupta V, Gupta A, Arora S, et al. Presumed tubercular serpiginouslike choroiditis: clinical presentations and management. Ophthalmology. 2003; 110(9): 1744–1749, doi: 10.1016/S0161-6420(03)00619-5, indexed in Pubmed: 13129872.
11. Mackensen F, Becker MD, Wiehler U, et al. QuantiFERON TB-Gold--a new test strengthening long-suspected tuberculous involvement in serpiginous-like choroiditis. Am J Ophthalmol. 2008; 146(5): 761–766, doi: 10.1016/j.ajo.2008.06.012, indexed in Pubmed: 18718569.
12. Gan WL, Jones NP, Gan WL, et al. Serpiginous-like choroiditis as a marker for tuberculosis in a non-endemic area. Br J Ophthalmol. 2013; 97(5): 644–647, doi: 10.1136/bjophthalmol-2012-302918, indexed in Pubmed: 23449344.

REVIEW
DOI: 10.5603/OJ.2020.0028

The possibilities of pharmacological intervention in myopia

Maciej Czepita[1], Elena N. Iomdina[2]

[1]Private Practice, Szczecin, Poland
[2]Helmholtz National Medical Research Center of Eye Diseases, Russian Ministry of Health, Moscow, Russia

ABSTRACT

This paper presents and discusses the current possibilities of pharmacological intervention in myopia. A review of the latest literature regarding the pharmacological treatment of myopia has been presented.
The results of experimental research on the potential use of: atropine, oxyphenonium, pirenzepine, chlorpyrifos, apomorphine, reserpine, 6-hydroxy dopamine, dextromethorphan, MK-801, APV, bicuculline, SR95531, CACA, TPMPA, dextrophanol, levorphanol, *D*- and *L*-naloxane, *L*-NAME, formoguanamine, b-xyloside, the central and peripheral antagonist of VIP, basic fibroblast growth factor, a solution of the basic amino acid salts in the form of succinates, in the treatment of myopia have been described. The clinical use of pirenzepine,7-methylxanthine, and atropine has been discussed.
The obtained results of experimental and clinical studies give hope that a new effective pharmacological method of myopia treatment can be discovered soon.

KEY WORDS: myopia; treatment; pharmacology

Ophthalmol J 2020; Vol. 5, 150–153

INTRODUCTION

It is believed that currently about 1/4 of adults and 1/3 of children worldwide have myopia. This type of refractive error is the most prevalent in Asian and highly developed countries. The development of myopia is related to genetic predispositions and environmental factors. Among the environmental factors, reading, writing, and computer use have the most influence [1–4].

Although myopia is such a significant social problem, no effective treatment method has so far been developed. Various treatment methods or their combinations have been proposed so far for school myopia and progressive myopia [1, 3].

Due to myopia's high social importance and considerable interest in the latest experimental and clinical results, the authors present a review of the current opinions concerning the issue.

RESULTS OF EXPERIMENTAL STUDIES

Research into experimental myopia was started by Young [5] in 1961. The researcher noticed that monkeys develop myopia if kept in a closed space. In 1975, Hubel and Wiesel from Harvard University, while researching the plasticity of the visual cortex, discovered by chance that suturing of the eyelids in young monkeys leads to an increase in the axial length of the eye. In 1981, Hubel and Wiesel were awarded the Nobel Prize for their research into the visual cortex's structure and function. A substantial enlargement of the eye after tarsorrhaphy was not related to their work. However, they immediately concluded that this finding could be of clinical value. Therefore, they conducted extensive control studies, which they later proved through clinical observations. They observed a higher prevalence of myopia in children with ptosis and corneal scars [6].

CORRESPONDING AUTHOR:
Maciej Czepita, MD, PhD, FEBO, Starkiewicza 5/2 St., 70–112 Szczecin, Poland, tel: (+ 48) 517 453 590; e-mail: maciej@czepita.pl

Copyright © 2020 Via Medica, ISSN 2450–7873

In 1977, intensive work on the role of tarsorrhaphy or occlusion on the development of form-deprivation myopia was started. Many experiments on monkeys, cats, rabbits, guinea pigs, shrews, squirrels, chickens, and kestrels were conducted in almost 25 laboratories worldwide. The research, conducted in this field by Raviola and Wiesel from Harvard University, Laties and Stone from the University of Pennsylvania, Wallman from the City University of New York, and Schaeffel from the University of Tübingen [7, 8] deserve special mention. In 1988, Schaeffel et al. [9] discovered that experimental myopia develops due to diffusing lenses usage. In the same year, Stone et al. [10] observed that tarsorrhaphy induces metabolic changes in the retina and, therefore, initiated research to find substances inhibiting the development of experimental myopia.

SUBSTANCES INHIBITING THE PROGRESSION OF MYOPIA

Based on experimental results, researchers from around the world tried to establish which substances could be used in the treatment of myopia. Currently, the following substances have been found to inhibit the progression of experimental myopia:

- atropine, oxyphenonium — non-selective antagonists of the muscarinic receptors [11–13];
- pirenzepine — an antagonist of the muscarinic M1 receptors [14–16];
- chlorpyrifos — a substance inhibiting acetylcholinesterase [17];
- apomorphine — a non-selective agonist of the dopamine receptors [18, 19];
- reserpine — an alkaloid of rauwolfia hampering the storage of catecholamines and serotonin in both the central and peripheral nervous system [20];
- 6-hydroxydopamine — a substance inhibiting hydroxylase of tyrosine and destroying the structure of the adrenergic endings [21–23];
- dextromethorphan, MK-801, APV — antagonists of the NMDA receptors [24];
- bicuculline, SR95531 — antagonists of the GABAA receptors [25];
- CACA, TPMPA — antagonists of the GABAA-Or receptors [25];
- dextrophanol, levorphanol, *D*- and *L*-naloxane — *D*- and *L*-enantiomers acting at opioid receptors [26];
- *L*-NAME — a nitric oxide synthase inhibitor [27, 28];
- formoguanomine — a substance inhibiting the production of proline and glutamate, leading to the fall of the thickness of the choroid, degenerative changes in the photoreceptors and the pigment epithelium of the retina [29];
- b-xyloside — a proteoglycan synthesis inhibitor [30];
- central antagonist of VIP — a hybrid peptide consisting of the C-terminal of the VIP molecule linked serially to the N-terminal portion of neurotensin [31];
- peripheral antagonist of VIP — 4Cl-D-Phe6, Leu17 [31];
- basic fibroblast of growth factor — a growth factor connected with heparin [32];
- a solution of the basic amino acid salts in the form of succinates [33].

Due to the pathogenesis of experimental myopia, which in many different aspects closely resembles the pathogenetic mechanism of progressive myopia in humans, all the substances listed above can be viewed as potential medications inhibiting myopia's progression in children and adolescents.

RESULTS OF CLINICAL STUDIES

In 2004 Siatkowski et al. [34] from the University of Oklahoma examined 277 US children aged 8-12 with myopia between –0.75 to –4.0 D. These children were given topical 2% pirenzepine gel twice a day. After a year of use, the progression of myopia decreased by 51%.

The results of Siatkowski et al. [34] were reaffirmed in 2005 by Tan et al. [35] from the Singapore Eye Research Institute. They examined 353 children from Singapore, Taiwan, and Hong Kong aged 6 to 12 with myopia between –0.75 to –4.0 D. The authors observed that pirenzepine slowed the yearly progression of myopia by 44%.

In 2008, Siatkowski et al. [36] examined 84 American children aged 8–12 with myopia between –0.75 and –4.0 D. The children received topical 2% pirenzepine gel twice daily. After two years of treatment, the progression of myopia decreased by 41%.

In the same year, Trier et al. [37] from Trier Research Laboratories in Copenhagen examined 107 Danish children aged 8 to 13 with myopia above –0.75 D. The children received an oral dose of 0.4 g of 7-methylxanthine once daily. After three

years of treatment with 7-methylxanthine, they revealed a lower progression of myopia.

In 2012 Chia et al. [38] from the Singapore Eye Research Institute examined 400 children from Singapore aged between 6 and 12 years of age with myopia higher than –2.0 D. After two years of treatment with a topical 0.01% solution of atropine, they noted a decrease of 0.5 D of myopia per year.

Following these studies, a mass-scale use of atropine in myopia treatment in many countries has been observed. It has been found that a 0.01% solution of atropine decreases the development of myopia and does not induce side effects in the anterior segment [39–42]. It has also been observed that 0.02% atropine eye drops had a better effect on myopia progression than 0.01% atropine. However, both showed similar effects on pupil diameter and accommodative amplitude after 12 months of treatment [43]. Over two years, the observed efficacy of 0.05% atropine was twice as high as 0.01% atropine. It remained the optimal concentration among the studied atropine concentrations in slowing myopia progression [44].

In Poland, studies into the role of atropine in myopia's progression were initiated by Koronczewska in the 1980s. Regretfully, the author used 0.5% atropine, which led to severe side effects. Currently, research by Grzybowski is ongoing [45, 46].

Other substances used in the above-mentioned experimental studies to slow down the eye growth during myopia development up to this day have not been attempted in clinical practice.

CONCLUSION

The obtained results of experimental and clinical studies are promising enough and raise hope that a new effective pharmacological method of myopia treatment can be discovered soon.

REFERENCES

1. Czepita D. Myopia: incidence, pathogenesis, management and new possibilities of treatment. Russ Ophthalmol J. 2014; 7(1): 96–101.
2. Czepita M, Czepita D, Lubiński W. The Influence of Environmental Factors on the Prevalence of Myopia in Poland. J Ophthalmol. 2017; 2017: 5983406, doi: 10.1155/2017/5983406, indexed in Pubmed: 29348929.
3. Morgan IG, Ohno-Matsui K, Saw SM, et al. Myopia. Lancet. 2012; 379(9827): 1739–1748, doi: 10.1016/S0140-6736(12)60272-4, indexed in Pubmed: 22559900.
4. Zadnik K, Mutti DO. Incidence and distribution of refractive anomalies. In: Benjamin WJ, Borish IMO. ed. Borish's clinical refraction. Elsevier, Butterworth Heimann, St Louis 2006: 35–55.
5. Young FA. The effect of restricted visual space on the primate eye. Am J Ophthalmol. 1961; 52: 799–806, doi: 10.1016/0002-9394(61)90904-7, indexed in Pubmed: 14009335.
6. Raviola E, Wiesel TN, Raviola E, et al. An animal model of myopia. N Engl J Med. 1985; 312(25): 1609–1615, doi: 10.1056/NEJM198506203122505, indexed in Pubmed: 4000200.
7. Goss DA. Development of the ametropias. In: Benjamin WJ, Borish IM. ed. Borish's clinical refraction. Butterworth Heimann, Elsevier, St Louis 2006: 56–92.
8. Norton TT, Norton TT. Animal Models of Myopia: Learning How Vision Controls the Size of the Eye. ILAR J. 1999; 40(2): 59–77, doi: 10.1093/ilar.40.2.59, indexed in Pubmed: 11304585.
9. Aleman A, Schaeffel F, Tepelus TC, et al. Accommodation, refractive error and eye growth in chickens. Vision Res. 1988; 28(5): 639–657, doi: 10.1016/0042-6989(88)90113-7, indexed in Pubmed: 3195068.
10. Stone RA, Laties AM, Raviola E, et al. Increase in retinal vasoactive intestinal polypeptide after eyelid fusion in primates. Proc Natl Acad Sci U S A. 1988; 85(1): 257–260, doi: 10.1073/pnas.85.1.257, indexed in Pubmed: 2448769.
11. Luft WA, Ming Y, Stell WK, et al. Variable effects of previously untested muscarinic receptor antagonists on experimental myopia. Invest Ophthalmol Vis Sci. 2003; 44(3): 1330–1338, doi: 10.1167/iovs.02-0796, indexed in Pubmed: 12601066.
12. McBrien NA, Moghaddam HO, Reeder AP, et al. Atropine reduces experimental myopia and eye enlargement via a nonaccommodative mechanism. Invest Ophthalmol Vis Sci. 1993; 34(1): 205–215, indexed in Pubmed: 8425826.
13. Stone RA, Lin T, Laties AM, et al. Muscarinic antagonist effects on experimental chick myopia. Exp Eye Res. 1991; 52(6): 755–758, doi: 10.1016/0014-4835(91)90027-c, indexed in Pubmed: 1855549.
14. Cottriall CL, McBrien NA, Cottriall CL, et al. The M1 muscarinic antagonist pirenzepine reduces myopia and eye enlargement in the tree shrew. Invest Ophthalmol Vis Sci. 1996; 37(7): 1368–1379, indexed in Pubmed: 8641840.
15. Leech EM, Cottrial CL, McBrien NA. Pirenzepine prevents form deprivation myopia in a dose dependent manner. Ophthal Physiol Opt. 1995; 15(5): 351–356, indexed in Pubmed: 8524553.
16. Rickers M, Schaeffel F. Dose-dependent effects of intravitreal pirenzepine on deprivation myopia and lens-induced refractive errors in chickens. Exp Eye Res. 1995; 61(4): 509–516, doi: 10.1016/s0014-4835(05)80147-2, indexed in Pubmed: 8549693.
17. Geller AM, Abdel-Rahman AA, Peiffer RL, et al. The organophosphate pesticide chlorpyrifos affects form deprivation myopia. Invest Ophthalmol Vis Sci. 1998; 39(7): 1290–1294, indexed in Pubmed: 9620094.
18. Iuvone PM, Tigges M, Stone RA, et al. Effects of apomorphine, a dopamine receptor agonist, on ocular refraction and axial elongation in a primate model of myopia. Invest Ophthalmol Vis Sci. 1991; 35(5): 1674–1677, indexed in Pubmed: 2016144.
19. Rohrer B, Spira AW, Stell WK. Apomorphine blocks form-deprivation myopia in chickens by a dopamine D2-receptor mechanism acting in retina or pigmented epithelium. Vis Neurosci. 1993; 10(3): 447–453, doi: 10.1017/s0952523800004673, indexed in Pubmed: 8494798.
20. Schaeffel F, Bartmann M, Hagel G, et al. Studies on the role of the retinal dopamine/melatonin system in experimental refractive errors in chickens. Vision Res. 1995; 35(9): 1247–1264, doi: 10.1016/0042-6989(94)00221-7, indexed in Pubmed: 7610585.
21. Li XX, Schaeffel F, Kohler K, et al. Dose-dependent effects of 6-hydroxy dopamine on deprivation myopia, electroretinograms, and dopaminergic amacrine cells in chickens. Vis Neurosci. 1992; 9(5): 483–492, doi: 10.1017/s0952523800011287, indexed in Pubmed: 1360257.
22. Schaeffel F, Hagel G, Bartmann M, et al. 6-Hydroxy dopamine does not affect lens-induced refractive errors but suppresses deprivation myopia. Vision Res. 1994; 34(2): 143–149, doi: 10.1016/0042-6989(94)90327-1, indexed in Pubmed: 8116274.
23. Weiss S, Schaeffel F. Diurnal growth rhythms in the chicken eye: relation to myopia development and retinal dopamine levels. J Comp Physiol A. 1993; 172(3): 263–270, doi: 10.1007/BF00216608, indexed in Pubmed: 8510054.
24. Fisher AJ, Seltner RLP, Stell WK. Opiate and N-methyl-D-aspartate receptors in form-deprivation myopia. Visual Neurosci. 1998; 15(6): 1089–1096, doi: 10.1017/s0952523898156080, indexed in Pubmed: 9839973.

25. Stone RA, Liu Ji, Sugimoto R, et al. GABA, experimental myopia, and ocular growth in chick. Invest Ophthalmol Vis Sci. 2003; 44(9): 3933–3946, doi: 10.1167/iovs.02-0774, indexed in Pubmed: 12939312.
26. Seltner RL, Rohrer B, Grant V, et al. Endogenous opiates in the chick retina and their role in form-deprivation myopia. Vis Neurosci. 1997; 14(5): 801–809, doi: 10.1017/s0952523800011548, indexed in Pubmed: 9364719.
27. Fujikado T, Kawasaki Y, Fujii J, et al. The effect of nitric oxide synthase inhibitor on form-deprivation myopia. Curr Eye Res. 1997; 16(10): 992–996, doi: 10.1076/ceyr.16.10.992.9021, indexed in Pubmed: 9330850.
28. Fujikado T, Tsujikawa K, Tamura M, et al. Effect of a nitric oxide synthase inhibitor on lens-induced myopia. Ophthalmic Res. 2001; 33(2): 75–79, doi: 10.1159/000055647, indexed in Pubmed: 11244351.
29. Westbrook AM, Crewther SG, Beresford JA, et al. Formoguanamine-induced inhibition of deprivation myopia in chick is accompanied by choroidal thinning while retinal function is retained. Vision Res. 1995; 35(14): 2075–2088, doi: 10.1016/0042-6989(94)00282-q, indexed in Pubmed: 7660611.
30. Rada JA, Johnson JM, Achen VR, et al. Inhibition of scleral proteoglycan synthesis blocks deprivation-induced axial elongation in chicks. Exp Eye Res. 2002; 74(2): 205–215, doi: 10.1006/exer.2001.1113, indexed in Pubmed: 11950231.
31. Seltner RL, Stell WK. The effect of vasoactive intestinal peptide on development of form deprivation myopia in the chick: a pharmacological and immunocytochemical study. Vision Res. 1995; 35(9): 1265–1270, doi: 10.1016/0042-6989(94)00244-g, indexed in Pubmed: 7610586.
32. Roher B, Stell WK. Basic fibroblast growth factor (bFGF) and transforming growth factor (TGF-beta) act as stop and go signals to modulate postnatal ocular growth in the chick. Exp Eye Res. 1994; 58(5): 553–562, doi: 10.1006/exer.1994.1049, indexed in Pubmed: 7925692.
33. Iomdina N, Tarutta P, Semchishen V , et al. [Experimental realization of minimally invasive techniques of scleral collagen cross-linking]. Vestn Oftalmol. 2016; 132(6): 49–58, doi: 10.17116/oftalma2016132649-56, indexed in Pubmed: 28121299.
34. Siatkowski RM, Cotter S, Miller JM, et al. US Pirenzepine Study Group. Safety and efficacy of 2% pirenzepine ophthalmic gel in children with myopia: a 1-year, multicenter, double-masked, placebo-controlled parallel study. Arch Ophthalmol. 2004; 122(11): 1667–1674, doi: 10.1001/archopht.122.11.1667, indexed in Pubmed: 15534128.
35. Tan DTH, Lam DS, Chua WH, et al. Asian Pirenzepine Study Group. One-year multicenter, double-masked, placebo-controlled, parallel safety and efficacy study of 2% pirenzepine ophthalmic gel in children with myopia. Ophthalmology. 2005; 112(1): 84–91, doi: 10.1016/j.ophtha.2004.06.038, indexed in Pubmed: 15629825.
36. Siatkowski RM, Cotter SA, Crockett RS, et al. U.S. Pirenzepine Study Group. Two-year multicenter, randomized, double-masked, placebo-controlled, parallel safety and efficacy study of 2% pirenzepine ophthalmic gel in children with myopia. J AAPOS. 2008; 12(4): 332–339, doi: 10.1016/j.jaapos.2007.10.014, indexed in Pubmed: 18359651.
37. Trier K, Munk Ribel-Madsen S, Cui D, et al. Systemic 7-methylxanthine in retarding axial eye growth and myopia progression: a 36-month pilot study. J Ocul Biol Dis Infor. 2008; 1(2-4): 85–93, doi: 10.1007/s12177-008-9013-3, indexed in Pubmed: 20072638.
38. Chia A, Chua WH, Cheung YB, et al. Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1%, and 0.01% doses (Atropine for the Treatment of Myopia 2). Ophthalmology. 2012; 119(2): 347–354, doi: 10.1016/j.ophtha.2011.07.031, indexed in Pubmed: 21963266.
39. Azuara-Blanco A, Logan N, Strang N, et al. Low-dose (0.01%) atropine eye-drops to reduce progression of myopia in children: a multicentre placebo-controlled randomised trial in the UK (CHAMP-UK)-study protocol. Br J Ophthalmol. 2020; 104(7): 950–955, doi: 10.1136/bjophthalmol-2019-314819, indexed in Pubmed: 31653669.
40. Cheng J, Yang Y, Kong X, et al. The Effect of 0.01% Atropine Eye Drops on the Ocular Surface in Children for the Control of Myopia-The Primary Results from a Six-Month Prospective Study. Ther Clin Risk Manag. 2020; 16: 735–740, doi: 10.2147/TCRM.S265945, indexed in Pubmed: 32848404.
41. Guo L, Fan L, Tao J, et al. Use of Topical 0.01% Atropine for Controlling Near Work-Induced Transient Myopia: A Randomized, Double-Masked, Placebo-Controlled Study. J Ocul Pharmacol Ther. 2020; 36(2): 97–101, doi: 10.1089/jop.2019.0062, indexed in Pubmed: 31800355.
42. Li FF, Kam KaW, Zhang Y, et al. Differential Effects on Ocular Biometrics by 0.05%, 0.025%, and 0.01% Atropine: Low-Concentration Atropine for Myopia Progression Study. Ophthalmology. 2020; 127(12): 1603–1611, doi: 10.1016/j.ophtha.2020.06.004, indexed in Pubmed: 32525048.
43. Fu A, Stapleton F, Wei Li, et al. Effect of low-dose atropine on myopia progression, pupil diameter and accommodative amplitude: low-dose atropine and myopia progression. Br J Ophthalmol. 2020; 104(11): 1535–1541, doi: 10.1136/bjophthalmol-2019-315440, indexed in Pubmed: 32086237.
44. Yam JC, Li FF, Zhang X, et al. Two-Year Clinical Trial of the Low-Concentration Atropine for Myopia Progression (LAMP) Study: Phase 2 Report. Ophthalmology. 2020; 127(7): 910–919, doi: 10.1016/j.ophtha.2019.12.011, indexed in Pubmed: 32019700.
45. Grzybowski A, Armesto A, Szwajkowska M, et al. The Role of Atropine Eye Drops in Myopia Control. Curr Pharm Des. 2015; 21(32): 4718–4730, doi: 10.2174/1381612821666150909095403, indexed in Pubmed: 26350533.
46. Grzybowski A, Sobolewska B. Dobrowolsky from St. Petersburg and Hosch from Basel reported improvement of myopia after atropine use in 1868 and 1871. Strabismus. 2018; 26(1): 46, doi: 10.1080/09273972.2017.1421675, indexed in Pubmed: 29293393.