Journal of Health Study and Medicine

2021, No. 1

Redaktor naczelny / Editor in chief
dr n. med. Joanna Sułkowska

Skład / Adjustment, Typesetting
Witold Kowalczyk

ISSN 2451-1471

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Wersja elektroniczna publikacji jest wersją podstawową, dostępną na stronie:
jhsm.san.edu.pl
E-version is the original version of the article, available:
jhsm.san.edu.pl

Artykuły recenzowane / All the articles published are subject to reviews.

Journal of Health Study and Medicine
2021, No. 1
pp. 5-25
DOI 10.36145/JHSM2021.01

Implementation of Smoke Free-homes Rules in the Homes of Smokers with Low Socioeconomic Status

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Abstract

Introduction: *Private places such as homes are common places of exposure to secondhand smoke. Currently, more and more attention is being paid to reducing general and residential exposure to ETS (environmental tobacco smoke). The voluntary introduction of smoke-free homes (SFH) is a promising preventive measure in this regard. Most smoking households don't implement comprehensive anti-smoking policies, and exposure to secondhand smoke (SHS) is still common among low socioeconomic populations and children.*

Aim: *The aim of the study was to assess exposure to passive smoking and to assess compliance with the rules of a smoke-free home in the homes of smokers with low socioeconomic status.*

Material and methods: *117 smokers in Piotrków County were examined in 2015. The research tool was a questionnaire. The study received a positive opinion from the Bioethics Committee of the Medical University of Lodz (RNN/243/15/KE).*

Results: *People who respect the implementation of smoke free-homes rules in their homes accounted for 48.7% of the total number of respondents, of which 58% were women and 42% were men.*

They were mostly people aged 50 and more (54.3%), married (60%), with secondary education (33.3%), employed persons (70.2%), living at home with one adult (43.8%). 68.4% of the respondents advocating smoke-free homes have ever tried to quit, usually 1–2 times (38.6%). Fear of the disease (36.8%) and the wish of the family (29.8%) were the most frequently mentioned reasons that prompted the respondents to quit smoking in tobacco-free homes. In smoke-free homes, 82.5% of the guests complied with the accepted rules for smoking.

Conclusions: *There is a need for interventions to encourage a smoking ban in homes. Primary care interventions, public health programs, and media campaigns should promote the health benefits of having a smoke-free home.*

Key words: *smoke free-homes, smoking tobacco, passive* smoking.

Introduction

Private places such as homes are common places of exposure to second--hand smoke. Although there are laws prohibiting smoking in public places, the issue of passive exposure to tobacco smoke in homes still remains unresolved [1]. Many countries (including Poland) have implemented anti--smoking policies in workplaces and public places to reduce the impact of exposure to SHS (second-hand smoke) on the health of non-smokers; which resulted in a reduction of exposure to SHS after their implementation [2, 3].

More and more attention is now also being paid to reducing general and residential exposure to the ETS (environmental tobacco smoke). The voluntary introduction of smoke-free homes (SFH) is a promising preventive measure in this regard. Owning SFH (smoke-free homes) means that both family members and visitors are not allowed to smoke anywhere in the home [4]. Although the prevalence of smoke-free homes has increased in the past two decades, nearly half of all smokers still allow smoking in the home [5, 6, 7, 8, 9].

Smoke-free homes can reduce exposure to second-hand smoke (SHS), encourage smoking cessation among active smokers, and discourage teenagers from taking up smoking [5, 10].

Households remain the main source of children's exposure to SHS [11, 12]. Children exposed to passive smoking in homes have an increased risk of lower respiratory tract infections, asthma, and are at increased risk of sudden infant death syndrome [13]. Households with children use the regulations banning smoking at home more often, while households, where adults are older have lower income, have a lower education or smoke, use these regulations less frequently [14, 15].

Most smoking households do not implement comprehensive anti-smoking policies, and exposure to second-hand smoke (SHS) is still common among low socioeconomic status (SES) populations and children [16].

Few studies have assessed smoke-free home (SFH) rules outside the context of protecting young children from SHS, and none have focused on families [17, 18].

Smokers are the people with the lowest incidence of completely bans on smoking at home.

The aim of the study was to assess exposure to passive smoking and to assess compliance with the rules of a smoke-free home in the homes of smokers with low socioeconomic status.

Materials and methods

The study was approved by the Bioethics Committee of the Medical University of Lodz (RNN/243/15/KE). A detailed description of the study has been published elsewhere [19, 20]. A cross-sectional study was conducted in 2015 and included smokers from the Piotrków district who gave their written consent to participate in the study. The subjects were referred to a doctor to encourage them to quit smoking.

The research tool was a questionnaire. The questions included in the survey concerned: socio-demographic data, smoking, intentions regarding smoking, exposure to passive smoking.

The no-smoking policy in homes was measured by the following questions: „Does your home have policies that restrict smoking in the home? If so, please specify these rules". People with smoking restriction policies in their homes were included in the group representing smoke free-homes. People who have no rules limiting smoking in their homes to the group representing a home without a smoking ban.

Results

The study involved 117 people smoking cigarettes in the Piotrków district, 44% were men and 56% women. 90.6% of all respondents are daily smokers. A detailed description of the respondents is presented in Table 1. Smokers were most often people in the age group 50–59 (32.5%), married (47.9%), with secondary education (38.5%), employed (60.7%), and with a monthly net income per person in the family above PLN 1000 to PLN 1500 (25.6%).

Among smokers, the most frequently used cigarettes were filtered cigarettes (68.4%) and slim cigarettes (32.9%). Every second test person smoked more than 10 to 20 cigarettes a day. The number of years of regular daily smoking (after subtracting any abstinence breaks) for 31.6% of the subjects was 10–20 years, and for 25.6% it was 21–30 years. 58.1% of respondents have ever tried to quit smoking, most often 3–4 and 5–6 times (31.6% and 27.3%). 70.1% of the respondents have not tried to quit smoking in the last 12 months. Every fifth respondent (20.5%) tried to quit smoking within the last 12 months, most often 1–2 times (41.9%).

When asked which of the statements best describes your intentions to quit smoking, 65.8% of respondents replied that they intend to quit smoking within the next month. 37.6% of respondents are currently definitely convinced of the success of quitting smoking, while 47.0% are rather convinced of success. When asked what prompted you to try to quit smoking, the most important reason for 25.6% of respondents was the fear of illness, and for 19.6% the current health problems.

Smokers most often lived in a home with one adult (18 and over) (47.0%) and one child (under 18) 15.4%. To the question of whether tenants at home smoke, 48.0% answered that none of the tenants smoked, and 36.3% that at least one person smoked.

48.7% of respondents indicated that there are rules in force in their home that limit smoking. For 25.6%, smoking was forbidden in any closed room, 30.8% smoking was allowed in some rooms, and for 23.9% smoking was allowed everywhere (Table 2).

In the event that smoking was forbidden in every enclosed space in 37.6%, this rule was strictly followed. 47.0% of respondents indicated that guests comply with the rules of smoking at home.

70.1% of people currently work outside the home, most often indoors (60.7%), only 4.3% work outside. In more than half of the respondents (53.8%) smoking is prohibited in all rooms in the workplace, and 20.5% of respondents only in some rooms. 70.1% of the respondents stated that in the last 30 days no one smoked indoors in the workplace where the respondent worked.

For this study, two groups were distinguished: people who promote the principles of a smoke-free home and people who represent houses without a smoking ban.

People who respect the principles of a smoke-free home in their homes accounted for 48.7% of the total number of respondents, of which 58% were women and 42% were men. They were mostly people aged 50 and more (54.3%), married (60%), with secondary education (33.3%), employed persons (70.2%), living at home with one adult (43.8%).

People with no smoking ban in their homes accounted for 47.8% of the respondents, 55.4% were women, and 44.6% were men. The most numerous group were people aged over 50 (57.2%). They were mostly married (39.3%), with secondary education (44.6%), employed persons (53.6%), living at home with one adult (50.0%).

Table 3 presents a detailed description of the respondents with the rules of a smoke-free home in their homes and the respondents with no smoking ban in their homes, taking into account socio-demographic features.

68.4% of the respondents propagating smoke-free homes have ever tried to quit, usually 1–2 times (38.6%). In the group of respondents who do not have a smoking ban in their homes, 48.2% have tried to quit smoking, usually 1–2 times (26.8%).

In both analyzed groups, the majority of respondents (66%) intend to quit smoking within the next month and their current approach to quitting smoking is equated with the belief that it will rather be a success (45.6% of respondents promoting smoke-free homes and 50.0% in homes without a smoking ban). The fear of illness (36.8%) and the wish of the family (29.8%) were the most common reasons that prompted the respondents to quit smoking in tobacco-free homes; in the group of respondents in homes without a smoking ban, current health problems (28.6%) and financial considerations (23.2%) were the most frequently mentioned. The majority of respondents in both groups (over 70%) did not live with children under 18 (Table 3). In smoke-free homes, 82.5% of the guests complied with the accepted rules for smoking.

In the group of respondents in homes without a smoking ban, 33.9% of guests did not follow the rules of household smoking.

Implementation of smoke free-homes rules in the homes of smokers with low socioeconomic status.

Table 1. Characteristics of the studied population (N = 117)

Variable	N	%
Sex		
• female	65	56.0
• man	52	44.0
Age (years)		
• < 30	14	12.0
• 30–39	28	23.9
• 40–49	10	8.5
• 50–59	38	32.5
• ≥ 60	27	23.1
Marital status		
• bachelor/miss	28	23.9
• married	56	47.9
• divorced	18	15.4
• widower/widow	15	12.8
Education		
• basic	2	1.7
• basic vocational	21	17.9
• average	45	38.5
• post-secondary	14	12.0
• higher (bachelor's degree)	10	8.5
• higher (master's)	25	21.4
Professional status in the last 12 months		
• salaried employee	71	60.7
• self-employed person	11	9.4
• pupil/student	3	2.6
• housewife	2	1.7
• annuitant	15	12.8
• pensioner	8	6.8
• unemployed	7	6.0
Monthly net family income per person		
• up to 500 PLN	11	9.4
• over 500 to 700 PLN	9	7.7
• over 700 to 1000 PLN	18	15.4
• above 1000 to 1500 PLN	30	25.6
• above 1500 to 2000 PLN	26	22.2
• above 2000 to 2500 PLN	13	11.1
• above 2500 PLN	10	8.6

Do you currently smoke tobacco every day, less often than every day or does not smoke at all?		
• every day	106	90.6
• less often than every day	8	6.8
• he doesn't smoke at all	3	2.6
What kind of cigarettes do you smoke most often?		
• with filter	80	68.4
• unfiltered	1	0.9
• slim	28	23.9
• menthol	6	5.1
• other	2	1.7
How many cigarettes do you smoke in total during the day? (pieces)		
• < 1	4	3.4
• 1–5	6	5.1
• above 5 do 10	27	23.1
• above 10 do 20	61	52.1
• above 20 do 30	18	15.4
• above 30	1	0.9
Number of years of regular daily smoking? (after deducting any interruptions for abstinence)		
• < 10	19	16.2
• 10–20	37	31.6
• 21–30	30	25.6
• 31–40	20	17.2
• > 40	11	9.4
Have you ever tried to quit smoking?		
• No	49	41.9
• Yes	68	58.1
If you have ever tried to quit smoking it how many times?		
• 0	2	1.7
• 1–2	37	31.6
• 3–4	32	27.3
• 5–6	7	6.0
• 6+	3	2.6
• No data	36	30.8
In the last 12 months, have you tried to quit smoking?		
• No	82	70.1
• Yes	24	20.5
• No data	11	9.4

If he has tried in the last 12 months quit smoking, how many times?		
• 0	7	6.0
• 1–2	49	41.9
• 3–4	6	5.1
• 5–6	4	3.4
• 6+	2	1.7
• No data	49	41.9
Which of the following best describes your intention to quit smoking?		
• I'm going to quit smoking within the next month	77	65.8
• I'm considering quitting in the next 12 months	27	23.1
• I'll quit smoking, but not in the next few months	5	4.2
• I'm not going to quit, I don't know	1	0.9
• I don't know	6	5.1
• No data	1	0.9
Which of the following best describes your current approach to quitting smoking?		
• I'm definitely convinced of your success	44	37.6
• I'm rather convinced of success	55	47.0
• I'm not convinced of success	18	15.4
What prompted you to now try to quit smoking? (please indicate only one, most important reason):		
• current health problems	23	19.6
• fear of disease	31	26.5
• doctor's recommendations	7	6.0
• family wishes	22	18.8
• belief in the harmful effects of smoking	11	9.4
• financial considerations	20	17.1
• no smoking in the workplace	2	1.7
• other reason, what?	1	0.9

Table 2. Rules limiting smoking in homes in smokers

Variable	N	%
Number of adults (18 and over) with whom the smoker lives		
• 0	34	29.1
• 1	55	47.0
• 2	21	17.9
• 3	3	2.6
• 4	2	1.7
• 5	2	1.7
Number of children (under 18) she lives with a smoker at home		
• 0	85	72.6
• 1	18	15.4
• 2	14	12.0
• 3	0	0
Do tenants smoke?		
• Yes, at least one is smoking	43	36.3
• No, none of them smoke	56	48.0
• I don't know	17	14.5
• No data	1	0.9
Total number of smoking tenants		
• 0	70	59.0
• 1	28	24.0
• 2	17	14.5
• 3	2	1.7
Are there any policies in your home that restrict smoking in the home?		
• Yes	57	48.7
• No	56	47.8
• I don't know	3	2.6
• No data	1	0.9
If so, please specify these rules:		
• Smoking is not allowed in any closed room	30	25.6
• Smoking is allowed in some rooms	36	30.8
• Smoking allowed everywhere	28	23.9
• No data	23	19.7
If smoking is prohibited in all enclosed spaces, is this rule strictly followed?		
• Yes	44	37.6
• No	36	30.7
• I don't know	12	10.3
• No data	25	21.4

Do guests follow the smoking policy in your home?		
• Yes	55	47.0
• No	26	22.2
• I don't know	11	9.4
• No data	25	21.4
If smoking is prohibited in any enclosed space in your home, how long does this rule apply?		
• Up to 1 year	2	6.7
• 2–5	6	20.0
• 6–10	11	36.7
• > 10	1	3.3
• No data	10	33.3
How often does someone (anyone) smoke in your home? Whether it is daily, weekly, or once in a while a month or less than once a month?		
• Every day	82	70.1
• Once a week	3	2.6
• Once a month	6	5.1
• Less often than once a month	22	18.8
• No data	4	3.4
Do you currently work outside the home?		
• Yes	82	70.1
• No, I don't work	35	29.9
Do you usually work inside (indoors) or outdoors?		
• Inside	71	60.7
• Outside	5	4.3
• Both	17	14.5
• No data	24	20.5
Are there closed rooms in your workplace?		
• Yes	74	63.2
• No	16	13.7
• No data	27	23.1
Which of the following statements best describes approach to smoking indoors at your workplace:		
Allowed everywhere	2	1.7
Only allowed in certain rooms	24	20.5
Prohibited in all rooms	63	53.8
I don't know	5	4.3
No data	23	19.7
In the past 30 days, has anyone smoked in closed rooms in which you works?		
• Yes	12	10.3
• No	82	70.1
• No data	23	19.6

Table 3. Characteristics of respondents in smoke-free homes and in home without smoking ban

Variable	Smoke-free home (rules to limit smoking at home) N (%)	Home without smoking ban (no rules to limit smoking at home) N (%)
Sex		
• female	33 (58%)	31 (55.4%)
• man	24 (42%)	25 (44.6%)
Age (years)		
• < 30	7 (12.3%)	7 (12.5%)
• 30–39	14 (24.6%)	12 (21.4%)
• 40–49	5 (8.8%)	5 (8.9%)
• 50–59	16 (28.0%)	20 (35.7%)
• ≥ 60	15 (26.3%)	12 (21.5%)
Marital status		
• bachelor/miss	12 (21%)	13 (23.2%)
• married	34 (60%)	22 (39.3%)
• divorced	5 (9%)	12 (21.4%)
• widower/widow	6 (10%)	9 (16.1%)
Education		
• basic	2 (3.5%)	-
• basic vocational	6 (10.5%)	13 (23.2%)
• average	19 (33.3%)	25 (44.6%)
• post-secondary	5 (8.8%)	8 (14.3%)
• higher (bachelor's degree)	7 (12.3%)	3 (5.4%)
• higher (master's)	18 (31.6%)	7 (12.5%)
Professional status in the last 12 months		
• salaried employee	40 (70.2%)	30 (53.6%)
• self-employed person	4 (7%)	7 (12.5%)
• pupil/student	2 (3.5%)	1 (1.8%)
• housewife	-	2 (3.6%)
• annuitant	7 (12.3%)	8 (14.3%)
• pensioner	3 (5.3%)	4 (7.1%)
• unemployed	1 (1.7%)	4 (7.1%)
Monthly net family income per person		
• up to 500 PLN	2 (3.5%)	8 (14.3%)
• over 500 to 700 PLN	6 (10.5%)	3 (5.35%)
• over 700 to 1000 PLN	8 (14.0%)	9 (16.1%)
• above 1000 to 1500 PLN	16 (28.1%)	12 (21.4%)
• above 1500 to 2000 PLN	11 (19.3%)	15 (26.8%)
• above 2000 to 2500 PLN	7 (12.3%)	6 (10.7%)
• above 2500 PLN	7 (12.3%)	3 (5.35%)

How many cigarettes do you smoke in total during the day? (pieces)		
• < 1	3 (5.3%)	1 (1.8%)
• 1–5	4 (7.0%)	2 (3.6%)
• above 5 do 10	14 (24.6%)	11 (19.6%)
• above 10 do 20	30 (52.6%)	28 (50.0%)
• above 20 do 30	6 (10.5%)	13 (23.2%)
• above 3	-	1 (1.8%)
Have you ever tried to quit smoking?		
• No	18 (31.6%)	29 (51.8%)
• Yes	39 (68.4%)	27 (48.2%)
If you have ever tried to quit smoking it how many times?		
• 1–2	22 (38.6%)	15 (26.8%)
• 3–4	17 (29.8%)	13 (23.2%)
• 5–6	6 (10.5%)	1 (1.8%)
• 6+	-	3 (5.4%)
• No data	12 (21.1%)	24 (42.8%)
In the last 12 months, have you tried to quit smoking?		
• No	40 (70.2%)	39 (69.7%)
• Yes	12 (21.0%)	12 (21.4%)
• No data	5 (8.8%)	5 (8.9%)
Which of the following best describes your intention to quit smoking?		
• I'm going to quit smoking within the next month	38 (66.7%)	37 (66.1%)
• I'm considering quitting in the next 12 months	13 (22.8%)	13 (23.2%)
• I'll quit smoking, but not in the next few months	2 (3.5%)	3 (5.35%)
• I'm not going to quit, I don't know	1 (1.75%)	-
• I don't know	2 (3.5%)	3 (5.35%)
• No data	1 (1.75%)	-
Which of the following best describes your current approach to quitting smoking?		
• I'm definitely convinced of your success	24 (42.1%)	18 (32.1%)
• I'm rather convinced of success	26 (45.6%)	28 (50.0%)
• I'm not convinced of success	7 (12.3%)	10 (17.9%)
What prompted you to now try to quit smoking? (please indicate only one, most important reason):		
• current health problems	7 (12.3%)	16 (28.6%)
• fear of disease	21 (36.8%)	9 (16.1%)
• doctor's recommendations	2 (3.5%)	5 (8.9%)
• family wishes	17 (29.8%)	5 (8.9%)
• belief in the harmful effects of smoking	4 (7.0%)	6 (10.7%)
• financial considerations	5 (8.8%)	13 (23.2%)
• no smoking in the workplace	1 (1.8%)	1 (1.8%)
• other reason, what?	-	1 (1.8%)

Number of adults (18 and over) with whom the smoker lives		
• 0	16 (28.1%)	17 (30.3%)
• 1	25 (43.8%)	28 (50.0%)
• 2	14 (24.6%)	6 (10.7%)
• 3	2 (3.5%)	1 (1.8%)
• 4	-	2 (3.6%)
• 5	-	2 (3.6%)
Number of children (under 18) she lives with a smoker at home		
• 0	40 (70.2%)	42 (75.0%)
• 1	10 (17.5%)	7 (12.5%)
• 2	7 (12.3%)	7 (12.5%)
• 3	-	-
Do guests follow the smoking policy in your home?		
• Yes	47 (82.5%)	6 (10.7%)
• No	6 (10.5%)	19 (33.9%)
• I don't know	4 (7.0%)	7 (12.5%)
• No data	-	24 (42.9%)

Discussion

Our study complements the literature on voluntary smoke-free housing rules. In our study, the prevalence of tobacco-free homes was 48.7%. The results obtained are lower than in other countries such as Scotland (51.8%) or the USA, where the percentage was 53% in states with loose tobacco control regulations and higher in states with comprehensive policies [11, 7]. In the USA, 83.7% of households are smoke-free nationally, and smoke-free homes are much more common among non-smokers (90.8%) than among smokers (53.7%) [21]. Our survey results are higher than those of the Eurobarometer, where the incidence was 44% [22].

The Eurobarometer considers completely smoke-free homes to be households where smoking is prohibited, without distinguishing between indoor and outdoor areas [22]. The incidence of smoke-free home admission among non-smoking households was 23.5% in the United Kingdom, 39.2% in the USA, 39.1% in Canada and, 44.3% in Australia [23]. Another study found that 28.4% of smokers used a total ban on smoking indoors [24]. The prevalence of a total smoking ban in the home observed among

smokers in other European countries was 16% in Ireland, 25% in France, 38% in Germany, 17% in the Netherlands, and 25% in the UK [25].

In the Parks et al. study, the majority of adult smokers have implemented no smoking policy in the home only (43%) and 31% have not implemented any no smoking policy [15]. In our study, for 25.6%, smoking was forbidden in any closed room, for 30.8%, smoking was allowed in some rooms, and for 23.9%, smoking was allowed everywhere. The results of our study show that smoke-free homes are more often promoted by people with low socioeconomic status, married, living with one adult.

In the Parks et al. study, comprehensive anti-smoking policies were more common among people of high socioeconomic status (SES), married people who did not live with a smoker; people with a child at home more often introduced smoke-free homes [15]. Low-income and low-educated people were less likely to implement comprehensive smoke-free laws [15].

In a cross-sectional study in Barcelona, 57.4% of households used a total smoking ban. The frequency of households with total indoor bans was higher among non-smokers, women, married people, and in households where minors lived [24].

Other studies have also shown that voluntary adoption of total anti--smoking rules at home was more frequent among people who agree that inhaling tobacco smoke from smokers is dangerous for non-smokers [24]. In the study by Helgertz et al., current smokers less frequently than non--smokers declared compliance with the rules of the smoking ban (70.0%; vs. 96.2%) [26]. The percentage of smokers who declared that their home was non-smoking was higher among those who lived with children (82.0%). In our study, 70.2% of smokers promoting smoke-free rules did not live with children under the age of 18.

In our study in smoke-free homes, 68.4% of respondents have ever tried to quit smoking. The respondents cited fear of illness (36.8%) and family wish (29.8%) as the reason that made them stop smoking. Other studies support the finding that the habit of smoking at home is hard to break [27, 28, 29]. In a study by van Wijk et al., smoking parents struggled or still struggled with changing the habit of smoking indoors to smo-

king outdoors. In the absence of adequate outdoor space, the study found that parents could quit smoking, rather than setting stricter home smoking policies [30]. Smokers with lower SES find it very difficult to quit [31], and SFH interventions should always be accompanied by an offer to quit smoking attempt [30].

Heck et al. demonstrated that the introduction of a complete ban on smoking at home is correlated with the smoking status of household members and with the demographic characteristics of respondents [32]. In Poland, Kaleta et al. showed a nearly two-fold higher risk of not introducing a complete smoking ban in a home inhabited by smokers in relation to non-smokers [3].

Our analysis has strengths that have been described elsewhere [19]. For the first time, the study was conducted among the socially disadvantaged adult rural population. The limitation of the study is a small group of the population. The study also used a cross-sectional design that tends to be observable at one point in time, making it impossible to observe changes over longer periods of time.

Our results demonstrate the need for increased interventions to encourage tobacco-free homes and increased awareness of the health risks associated with SHS in private settings, especially among smokers.

Conclusions

There is a need for interventions to encourage a smoking ban in homes. Primary care interventions, public health programs, and media campaigns should promote the health benefits of having a smoke-free home. Also, measures should be taken to reduce the social acceptance of smoking in homes in the presence of children, pregnant women, and non-smokers.

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Journal of Health Study and Medicine
2021, No. 1
pp. 27-41
DOI 10.36145/JHSM2021.02

Rehabilitation Procedure in People with Degeneration of the Intervertebral Disc

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Abstract

Introduction: *The International Association for the Study of Pain (IASP) defines pain as a subjective sensory and emotional sensation resulting from the action of stimuli that disturb the tissue. Pain significantly impacts the quality of our lives, mainly if it concerns the spine. In Poland, more than half of the population experiences pain in the spine, while as much as 44% of spine disorders concern the lower segment. Back pain is currently one of the most common reasons for contacting a GP, which makes it a medical and socio-economic problem.*

Purpose of the study: *Subjective evaluation of the effectiveness of rehabilitation in people with degeneration of the intervertebral disc.*

Material and methods: The study was carried out in a group of 153 patients. A self-constructed questionnaire was the study tool.

Results and conclusions: *The patients were asked to carry out activities of daily living. At the beginning, they reported the occurrence of pain, and thus the ordered activities were carried out by them carefully and slowly. At the end of rehabilitation, a control analysis was carried out, which showed an improvement in the quality of life of the patients (the pain rating on the scale decreased from 3.33 points to 2.36 points). The activities were carried out naturally. Properly selected and conducted rehabilitation causes both the improvement of the patients' quality of life and the reduction of pain associated with degenerative spine disease.*

Key words: *rehabilitation, degenerative disease, intervertebral disc.*

Introduction

Pain in the spine is one of the main reasons for a patient to visit a GP. This is a key issue in terms of patients' quality of life, which is deteriorating significantly over time. Both in the acute and chronic period, back pain contributes to lowering the quality of life in every population [1].

In some cases, the problem is to isolate the main causative factor causing back pain. In these cases, both medical and socio-economic factors are considered [2, 3]. Most of the patients believe that the level of quality of life is influenced by the low socio-economic status, which can significantly impact on the physiological functioning of the organism or intensify the development of ageing processes [4, 5].

In 2014, the researchers showed a relationship between allostatic overload and reduced skeletal mineralization. A group of over 700 people was analysed in terms of the mineralization of the femur and spine was examined [6]. Disrupting the homoeostasis of the system causes a number of changes in the body, as a result of which allostatic loads develop. Even a condition that lasts for a short period of time can cause disorders that provoke, inter alia: headaches or pain in the spine [2].

The degeneration of the intervertebral disc in the elderly patients results mainly from changes within the structure itself. However, in the case of people at the reproductive age, any modifications within the intervertebral disc are a consequence of an incorrect lifestyle [7]. The dynamic progress of civilization contributes to the development of civilization diseases. Chronic disorders appearing in the body, including in the form of pain in the spine due to the degeneration of the intervertebral disc, can significantly impact on the occurrence of depression [8].

Human evolution over the ages did not create adaptive mechanisms that could counteract the long-term factors impacting the human body, as a result of which the change of the human body posture from four-legged to two-legged has negative consequences. Weakening of the body's antigravity muscles, repeatability of everyday activities, incorrect ergonomics of work and rest cause pain in the spine [9, 10].

The development of technology contributes to the reduction of physical activity and improper diet, which results in an obesity epidemic among both adults and children. Overweight people often complain of pain in the spine. The main reason for this involves changes in the disc as a reduction in muscle stabilisation, as a result of which the remaining structures are forced to increase activity [11].

Material and methods

The research was conducted among 153 patients of the rehabilitation surgery. The study was carried out in a group of 87 women (56.9%) and 66 men (43.1%). The average age of the subjects did not exceed 43.9 years ± 14.94 years. Body weight was 44–110 kg, mean 75.69 kg ± 12.15 kg. The BMI index was 18.08 kg/m^2 – 37.77 kg/m2, on average 25.8 ± 3.55 kg/m^2. The BMI of half of the patients was normal and was not higher than 24.91 (Me).

All patients were diagnosed with the degenerative disease of the intervertebral disc. The study involved own questionnaire.

Statistical analysis was carried out in the Statistica 13.1 program. The Wilcoxon pair order test was used for the analysis. The Mann-Whitney U test was used to verify the data between the independent variables. The level of statistical significance in the study was 5% ($p < 0.05$).

Results. The largest group of the patients involved people who started rehabilitation no earlier than 12 months after the first pain ailments (N = 49; 32.0%), while the second largest group involved the patients (N = 38; 24.8%) who started rehabilitation in the period from 7 to 12 months. Only a small group of people managed to implement the therapy in the first months of pain. In the remaining groups, the patients declared the commencement of rehabilitation from 2 to 6 months after the occurrence of pain (Table 1).

Table 1. The time from the occurrence of the first pain to the start of rehabilitation

The time from the occurrence of the first pain to the start of rehabilitation	N	%
Up to one month from the occurrence of pain	13	8.5
From 2 to 3 months from the occurrence of pain	27	17.6
From 4 to 6 months from the occurrence of pain	26	17.0
From 7 to 12 months from the occurrence of pain	38	24.8
More than 12 months from the occurrence of pain	49	32.0
Total	153	100.0

n – number of observations; % – percent

Pain complaints most often concerned the lumbosacral section (N = 60; 39.2%) or only the lumbar spine (N = 50; 32.7%). The smallest group consisted of questionnaires with pain complaints in the cervical and thoracic sections (Table 2).

Table 2. The occurrence of pain symptoms depending on the spine section

Section of the spine	N	%%
Cervical section	30	19.6
Thoracic section	13	8.5
Lumbar section	50	32.7
Lumbosacral section	60	39.2
Total	153	100.0

n – number of observations; % – percent

Most patients described pain as radiating and acute. The remaining patients described pain as girdling, shooting and pressing. Pulling pain was declared by 12.4% of the patients, while continuous pain was declared by 11.8% of them. Pain related to tingling, numbness and burning was declared by 11.1% of the patients, while similar results were recorded in the patients with prickly pain. Intermittent pain occurred only in a small percentage of the reported pain (Table 3).

Table 3. Nature of the pain

Nature of the pain	N	%%
Acute	65	42.5
Radiating	68	44.4
Shooting	34	22.2
Girdling	35	22.9
Prickly	17	11.1
Pulling	19	12.4
Pressing	20	13.1
Continuous	18	11.8
Intermittent	14	9.2
Combined with tingling, numbness, burning etc.	17	11.1

n – number of observations; % – percent
* multiple question; ∑ ≠ 100% Manner of pain symptoms

In the studied group, pain symptoms appeared suddenly the most often (N = 57; 37.3%) or there was a gradual intensification of symptoms (N = 55; 35.9%). Pain appeared and disappeared among 23.3% of respondents. The smallest group involved the patients whose pain occurred in a different way than presented above (Table 4).

Table 4. Manner of the occurrence of pain symptoms

Manner of the occurrence of pain symptoms	N	%
Sudden pain	57	37.3
Pain gradually intensified	55	35.9
Pain appeared and disappeared	36	23.5
Pain appeared in a different way	5	3.3
Total	153	100.0

n – number of observations; % – percent

The patients stated that the main cause of pain involved pressing and overloading the spine. They indicated another factor causing pain, namely the movement of bending, leaning and walking (N = 17; 11.1%). On the other hand, a large group of the patients (N = 35; 22.9%) described the source of pain as spontaneous, not preceded by a previous causative stimulus (Table 5).

Table 5. Circumstances in which the pain occurred

Circumstances in which the pain occurred	N	%%
It occurred during certain movement	17	11.1
It occurred during pressing	43	28.1
It occurred as a result of an overload on the spine	57	37.3
It was spontaneous; the occurrence of pain was not immediately preceded by anything	35	22.9
Other	1	0.7
Total	153	100.0

n – number of observations; % – percent

The patients used massage (N = 121; 79.1%) and exercise (N = 121; 79.1%) in analgesic therapy the most often. Physical procedures were also used extensively: magnetotherapy, electrotherapy, laser therapy and iontophoresis. The use of the kinesiotaping method was declared by 9.8% of the patients. The least amount of hydrotherapy was used: underwater baths, acid-carbon baths and brine baths (Figure 1).

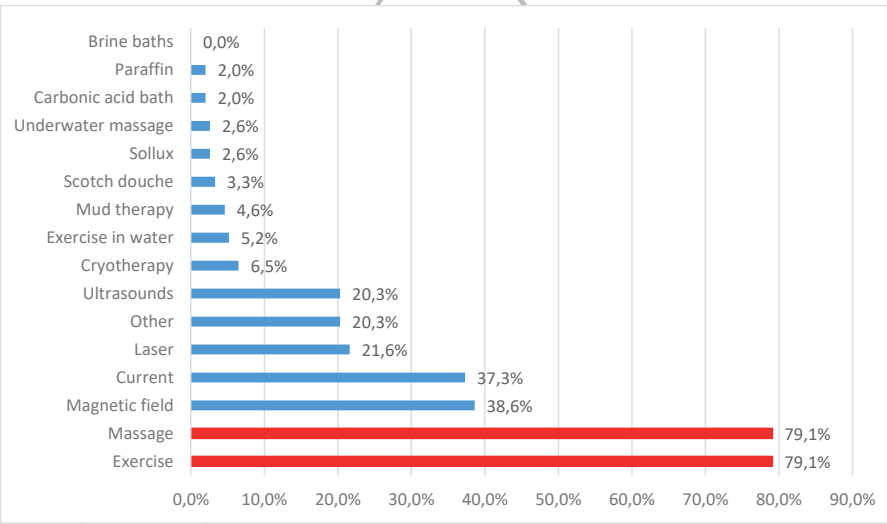

Figure 1. The type of physiotherapeutic procedures applied for the patients

Most patients used outpatient rehabilitation (N = 141; 92.2%). The remaining patients declared the use of outpatient health resort

rehabilitation (N = 36; 23.5%) and health resort rehabilitation (N = 32; 20.9%).

All people declared the need to use painkillers as a result of back pain in the period before rehabilitation. After rehabilitation, the number of the patients using painkillers decreased to 39.9%. The analysis confirms a significant reduction in the number of the patients taking pharmacological means after the applied rehabilitation ($p < 0.001$) (Table 6).

Table 6. The need to take painkillers for back pain in the period before and after treatment in the study group

Need to take painkillers for back pain	Before rehabilitation		After rehabilitation	
	N	%	N	%
Yes	153	100.0	61	39.9
No	0	0.0	92	60.1
Total	153	100.0	153	100.0
p	Z = 8.32 p < 0.001			

n – number of observations; % – percent; Z – result of the Wilcoxon pair order test; p – level of significance of differences

The patients assessed the intensity of the perceived pain on a 5-point scale. The measurement was carried out twice - before and after the therapeutic procedure. Before the implementation of rehabilitation, the average level of perceived pain was 3.33 ± 1.26 points. After the implementation of therapeutic treatment, the average pain level decreased significantly and amounted to 2.36 ± 1.2 points ($p < 0.001$) (Table 7; Figure 2).

Table 7. Assessment of back pain intensity before and after rehabilitation in the study group

Pain intensity Scale 1-5 points	N	$\bar{x}$	Me	Min.	Max.	Q1	Q3	SD
Before rehabilitation	153	3.33	3.00	1.00	5.00	3.00	4.00	1.26
After rehabilitation	153	2.36	2.00	1.00	5.00	1.00	3.00	1.20
p	Z=6.23 p<0.001							

n – number of observations; x – arithmetic average; Me – median; Min. – minimum; Max. – maximum; Q1 –lower quartile; Q3 – upper quartile; SD – standard deviation; Z – result of the Wilcoxon pair order test; p – level of significance of differences

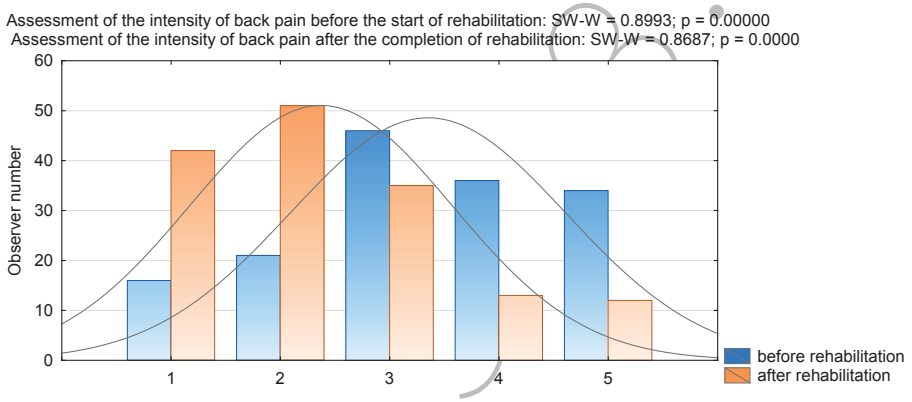

Figure 2. Assessment of back pain intensity before and after rehabilitation in the study group

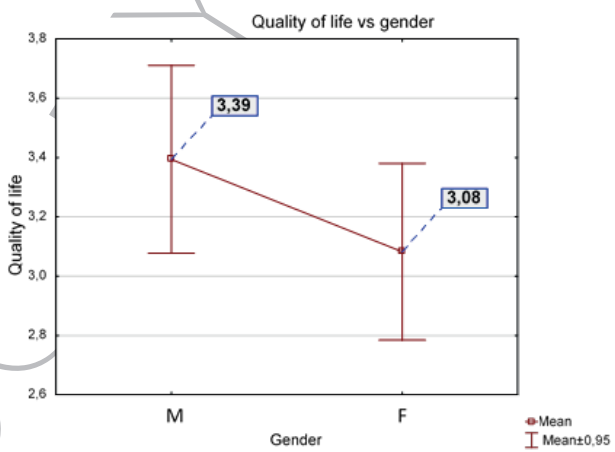

Figure 3. Average quality of life of the patients considering gender

Men assessed the average quality of life better ($\bar{x}$ = 3.39) compared to the group of women, where the mean value was 3.08 points. The difference in the mean quality of life in both compared groups was not statistically significant ($p > 0.05$).

Discussion

The lesion of the intervertebral disc affects young people more and more often. The main causes of these changes involve the lack of physical activity, a sedentary lifestyle, obesity and overload accumulating over time. According to Kremer Juergen, the most important "determinant" where the risk of the first pain symptoms occurs is the period from the occurrence of changes in the spine movement segments [12]. It is extremely important, because the time of rehabilitation by the patients should not be too long, due to the possibility of stopping the disease or minimising its effects.

Considering their own studies, a low part of the patients reported to a doctor in the first months from the first pain incident. This may mainly mean that the problem is being neglected by the society, due to the still insufficient awareness among the population. The secondary reason for the long waiting time for rehabilitation can involve difficulties related to the excessive waiting time for the implementation of therapeutic treatment reimbursed under the National Health Fund.

Prevention and prophylaxis are the most important, which mean, inter alia, lifestyle changes or weight reduction. In addition, one can successfully use physical treatments in the treatment of pain. A significant proportion of the patients report to a doctor at all when the pain is unbearable. Long-term delay in diagnosis consequently causes permanent complications in the movement segment of the spine. In the secondary procedure, rehabilitation is used the most often, which mostly includes massage, kinesiotherapy, physical therapy and patient health education.

According to the analysis of the carried-out studies, the largest number of the patients reported pain only 12 months after the first incident

(N = 49; 32%). Gasik and Styczyński received similar studies, where the time from the occurrence of a pain episode to reporting to a doctor ranged from 0 to 45 years. According to the patients, the mean duration was up to 12 years [13].

Basing on the results of own studies, a significant part of the patients declared the presence of acute and radiating pain. According to Milanow's study, pain of a similar nature is known as neuropathic pain [14].

The patients most used massage and exercise the most often, which is confirmed by the studies of other authors, including Sapuła, Lesiak or Mataczyński. They showed that the rehabilitation program was based on physical therapy and kinesiotherapy. According to Sidor and Kubińska, most patients are referred to laser (N = 122; 22.8%) and ultrasound (N = 99; 18.5%) [15]. According to Garczyński and Lubkowska, a significant proportion, as many as 63% of the patients, are referred for physical treatments. According to the patients, they choose treatments in the field of: cryotherapy, magnetotherapy and electrotherapy, as well as ultrasound, the most often. The main task of physical therapy is to completely reduce or decrease pain, and thus remove the resulting inflammation [17].

The respondents most often reported pain during pressing and overloading the spine. According to people studies by Klimaszewska and Krajewska-Kułak, women (N = 35; 22.44%) reported complaints during work performed while moving, while in men (N = 31; 19.87%) pain increased in a sitting position [16].

The study on the group of the patients showed that rehabilitation significantly reduced pain, thanks to which the amount of taken pharmacological agents decreased significantly. Among people studied by Klimaszewska and co-authors, only 20 people did not use painkillers, which constituted 12.8% of the entire group. The assessed subjective quality of life among women was lower than among men by 0.31 points.

The years 2000–2010 were declared as the Decade of Bones and Joints by the World Health Organization and the United Nations. This clearly proves the importance of the problem [18]. Summing up, the cur-

rent lifestyle contributes significantly to pain in the lumbar spine. It is mainly influenced by the decreasing level of physical activity and leading a sedentary lifestyle, and thus the inappropriate ergonomics of work and rest.

The correct rehabilitation program and early measures aim at removing or reducing pain in the lumbar spine. The results of the carried-out study proved that kinesitherapy used in the course of pain reduces the perception of pain [19].

According to Garczyński and Lubkowska, early education of the patient is an effective method that could bring the expected results. This would reduce the percentage of the population that is at risk of developing degenerative changes in the spine. The authors' comments are important because back pain can sometimes be eliminated from professional, family and social life for a certain period.

Conclusions

1. The main percentage of the patients underestimated the first symptoms, and as a result they most often report to a GP at least one year after the first pain symptoms occurred.
2. The patients declared that the most often used therapeutic procedures were therapeutic massage and kinesiotherapy.
3. The number of people taking painkillers significantly decreased after the rehabilitation procedure was implemented.
4. According to the patients, pain was caused by pressing or overloading the spine the most often.
5. The patients considered pain as acute and radiating the most often.
6. Men subjectively assessed the quality of life at a slightly higher level than women. On a five-point scale, the average level of perceived quality of life in men was 3.39 points, and in women 3.08 points.

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Journal of Health Study and Medicine
2021, No. 1
pp. 43-64
DOI 10.36145/JHSM2021.03

EN ISO 9001:2015 Quality Management System for Health Care Sector in Accordance with PN-EN 15224:2017-02 Standard and Accreditation Standards of the Minister of Health – Comparative Analysis

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Abstract

The aim: *The aim of this article is to indicate similarities and differences between EN ISO 9001:2015 quality management system in accordance with PN-EN 15224:2017-02 standard and the accreditation standards of the Minister of Health.*

Material and methods: *A comparative analysis of two documents describing requirements of the quality management system EN ISO 9001:2015 in accordance with PN-EN 15224:2017-02 and accreditation standards of the Minister of Health issued by the Quality Monitoring Centre was performed.*

Results: This comparative analysis concerns individual aspects/quality requirements of the PN-EN 15224-02 standard with reference to thematically analogous accreditation standards. According to the following analysis designation of both the PN-EN 15224:2017-02 standard and accreditation for health care sector causes natural, very high convergence and similarity between both systems. For specialist and expert on discussed subject, there is no bigger problem with connecting mutual reference of requirements of individual quality aspects described in the standard and accreditation standards. The PN-EN 15224:2017-02 standard, similarly to accreditation standards, pays particular attention to obligation to manage clinical risk during planning, implementation and control of individual process which becomes the key element of quality management system for clinical activities. In both cases, data related to significant events connected with hospitalization should be analyzed and assessed, and conclusions and observations should be used to conduct improvement projects in important health care areas in accordance with the E. Deming quality improvement methodology (PDCA cycle). However, they can`t be said to be identical. Differences result from the very structure of the documents. Accreditation standards are divided into 15 subject areas, gathering a total of 221 standards. The PN-EN 15224:2017-02 standard, in accordance with the ISO/ IEC Directives, Part 1, Consolidated ISO Supplement, Annex SL, contains common, consistent structure of new revised management system standards. Another difference between discussed systems concerns scope of both documents, the standard has international dimension and the set of standards is definitely national.

There are, of course, many more similarities as well as differences, which this article deals with in full.

Conclusions: *Carried out analysis shows clearly that, despite formal differences, there are numerous connections and analogies between requirements of individual quality aspects of the PN-EN 15224:2017-02 standard and requirements of the accreditation standards. Effective implementation of both requirements of the ISO standard in question and accreditation standards can constitute the basis for creating a single, consistent and effective management system for treatment entity as a whole.*

Key words: *ISO, accreditation, certification, quality, safety.*

Introduction

The quality providing process in treatment entities requires a holistic and interdisciplinary approach. Health services provided in health care units should be realized not only in accordance with specific standards but also based on current medical knowledge and values that are important from patient`s perspective [1]. Quality management systems based on international ISO standard and accreditation granted by the Minister of Health are the basic instruments which guarantee the highest quality of health services. Both systems impose on the treatment entity number of actions which, by reducing risk associated with provision of health services and standardizing of medical and organizational procedures, in significant way impact on increase of the knowledge about the entity and possible irregularities, enabling initiation of appropriate improvement actions led directly to improve safety of provided health care.

One of the most popular management systems implemented and maintained in medical entities, which constitutes basis to build integrated management systems, is the quality management system according to ISO 9001. However, if we think of system influencing the process of improving quality and safety of patients, there is the accreditation of the Minister of Health, whose holistic nature and explicit purpose for assessment of health care allows collecting information about global health system and its real problems [2].

In the environment dealing with implementation of quality guarantee systems (including representatives of the Center of Quality Monitoring in Health Care (CMJ), employees of individual certification bodies in accordance with ISO standard, management of medical entities) there is a clear lack of compliance: if the accreditation granted by the Minister of Health and certification according to ISO standards are competing or rather complementary systems for assessing functioning of medical facilities [3]. Supporters of ISO management systems emphasize that current standards regulate the requirements in such way that all organizations can use them to measure effectiveness of their activities and are definitely more likely

to indicate compatibility of the requirements of accreditation standards and only implementation of accreditation is insufficient mechanism to achieve a significant improvement in the quality of services [4]. However, supporters of accreditation indicate its orientation in key areas related to improvement of quality and safety of care, without finding too many connections with the requirements of ISO standards where, in their opinion, scope of the assessment is too general and arbitrary, often fragmentary, or even agreed with the interested party. However, there is no doubt that the accreditation of the Minister of Health and certification for compliance with ISO standard are methods of review and evaluation of medical entities. However, the approach to ISO has been changing, especially since management standard in medical entities in accordance with PN-EN 15224:2017-02 was adopted and implemented. "EN ISO 9001:2015 quality management system for health care sector" (first edition of the standard in Poland, 2013 – PN-EN 15224:2013-04) [5].

The aim of this article is to indicate similarities and differences between EN ISO 9001:2015 quality management system in accordance with PN-EN 15224:2017-02 standard and the accreditation standards of the Minister of Health.

Material and methods

A comparative analysis of two documents describing requirements of the quality management system EN ISO 9001:2015 in accordance with PN-EN 15224:2017-02 and accreditation standards of the Minister of Health issued by the Quality Monitoring Centre was performed [6]. Due to the length of both documents, only some part of assumptions and requirements which were considered the most important in the quality improvement process in medical entity were analyzed in detail. The element enriching the analysis and conclusions presented in the article are observations and thoughts of two of co-authors of the article who have many years of experience in implementing and maintaining these systems in medical entities.

Results

This comparative analysis concerns individual aspects/quality requirements of the PN-EN 15224-02 standard with reference to thematically analogous accreditation standards. The first quality aspect of the PN-EN 15224:2017-02 standard is proper/adequate care. As it is indicated in Table 1, related elements can be found among accreditation standards of at least four areas: Patient Rights (PP), Patient Condition Assessment (OS), Care of Patient (OP) and Improvement of Patient Quality and Safety (PJ).

Firstly, according to the PP 1 standard, each patient is informed about their rights and obligations, these rights should be written down, legible and made available in the places where patients stay. In Poland the patient rights are defined in the Act of November 6, 2008 on patient rights and the Patient Rights Ombudsman (Journal of Laws 2009, No 52, item 417), where at the very beginning in Chapter 2 we read about the right to health services provided with proper diligence, in conditions which correspond to professional and sanitary requirements [7]. With regard to accreditation standards in the area of OS, it fully refers to comprehensive and team assessment of condition of the patient as the basis for establishing a care plan including diagnostic and therapeutic activities.

There is definitely an analogy to this qualitative aspect in the form of the rank and importance of the interview and physical examination, nursing assessment and daily medical assessment, as well as in accordance with the requirements of accreditation standards in the area of PJ, the need to identify and assess the risk of adverse events. Undoubtedly, we can also find a connection among the accreditation standards in the area of Care of Patient, such as OP 1 and OP 1.1, regarding the development of a care plan and its modification depending on needs.

The subject of *availability of services*, *equal treatment* or *timeliness*, referred to in the following quality requirements of the PN-EN 15224:2017-02 standard, was included by the authors of the accreditation standards both in the area of Patient Rights (PP) and in the area of Improvement

of Patient Quality and Safety (PJ). As before, compliance with rights and obligations of patient obliges medical entities to provide patients, when possibilities to provide appropriate health services are limited, right to transparent, objective, based on medical criteria procedures which determine order of access to these services. Moreover, according to Art. 7 sec. 1 of the Act, patient has right to immediate medical services due to threat to their health or life [7]. The part of Improvement of Patient Quality and Safety in PJ 1 accreditation standard indicates obligation to develop program of activities for quality improvement and, in accordance with the indicated explanation, a written program can also include improvement of service availability, while in PJ 5 *Patient Safety* standard, among adverse events requiring monitoring and analysis untimely provided care was included.

Continuity of care is another qualitative aspect and similarly named CO accreditation standards department, definitely in both cases emphasizing need to perceive individual services provided to patient during hospitalization as elements of comprehensive medical care, where successive phases of medical care require continuity and guarantee of continuation of treatment [6].

The greatest number of connections between quality aspects indicated in quality standards for health care sectors and individual areas of requirements of accreditation standards can be found with regard to effectiveness and efficiency of undertaken activities and patient safety. In fact, true will be statement that they are the most important areas to the provision of health services. Therefore it is not difficult to find existing analogies. The connection of quality aspects of the PN-EN 15224:2017-02 standard – effectiveness and efficiency with individual areas of accreditation standards can be successfully found in following parts: (1) Care of Patient (OP); (2) Infection Control (KZ), (3) Treatments and anesthesia (ZA), (4) Pharmacotherapy (FA), (5) Laboratory (LA), (6) Improvement of Patient Quality and Safety (PJ), (7) General Management (ZO), (8) Human Resource Management (ZZ), (9) Information Management (ZI), (10) Management of Care Environment (ŚO).

References to aspects of patient safety, which in both systems have been called very similarly and both refer to the concept of quality improvement of E. Deming (PDCA cycle: plan/ do/check/ act) [8] as an effective tool to improve quality of clinical processes and management processes, we can find among the following accreditation areas: (1) Care Continuity (CO), (2) Improvement of Patient Quality and Safety (PJ), (3) Human Resource Management (ZZ), (4) Information Management (ZI), (5) Management of Care Environment (ŚO). In fact, practically each of 11 quality aspects or 221 accreditation standards has an element aimed at directly or indirectly ensuring safety of patients, their families and health care staff.

Considering another quality aspect of the PN-EN 15224:2017-02 standard – care based on evidence/ knowledge, you can again find similarities to accreditation standards in such areas as: Patient Rights (PP), Care of Patient (OP), Improvement of Patient Quality and Safety (PJ) and Human Resource Management (ZZ). Similarly to the aspect of adequate/ proper care, obligatory observance of patient`s rights obliges medical entities, in accordance with the Act on Patient Rights and Patient`s Rights Ombudsman of November 6, 2008, to provide health services in accordance with current medical knowledge, provided with due care and in conditions which meet professional and sanitary requirements [6]. Among OP standards, care based on evidence and knowledge is indicated by, for example, OP 2 standard. In the hospital, Standard Operating Procedures (SOP) work, including in emergency life-threatening situations. SOP should be developed in each ward and based on clinical practice guidelines. Undoubtedly, provision of health services based on evidence and knowledge will also be influenced by actions taken and implemented as part of meeting the requirements of accreditation standards in area of PJ, such as PJ 2. Regular analyses of important events related to hospitalization (extended stays/ deaths/ readmissions/ reoperations) or PJ 5 are performed in the hospital. Patient safety (identification, collection and analysis of data on adverse events, use of conclusions from conducted analyzes), which properly reported and, above all, thoroughly analy-

zed, provide the most valuable knowledge about the organization and its processes, capture areas for improvement, provide opportunity to learn from possible mistakes. Also very important for care based on evidence and knowledge is taking up policy of continuous improvement of staff qualifications, i.e. the accreditation standard ZZ 5, along with defining educational needs of individual professional groups ZZ 5.1, planning and implementation of training ZZ 5.2 – ZZ 5.5

Patient-centered care is another one of qualitative aspects of the PN--EN 15224:2017-02 standard, focusing on personal preferences and needs as well as on physical, mental and social integrity of the patient. Such an approach can be found in at least several areas of accreditation standards, with particular emphasis on Care Continuity (CO), Patient Rights (PP), Patient Assessment (OS), Care of Patient (OP), Improvement of Patient Quality and Safety (PJ). Exactly as indicated in the discussed qualitative aspect, the PP 6 accreditation standard concerns he patient`s conscious agreement for performed procedures, preceded by gaining understandable information on proposed treatment method, expected benefits, risk, long-term effects and other possible ways of acting [7]. In the case of accreditation standards, approvals are also connected with following requirements:

- CO 1 Patient admission procedures (including method of obtaining patient`s consent for hospitalization) has been developed and implemented in the hospital,
- PP 5 List of procedures requiring additional patient consent has been defined,
- PP 7 Patients give their conscious consent to anesthesia,
- PP 8 Patients give their conscious consent to participate in medical experiment.

Comprehensive approach to the patient, focusing on his physical, mental and social integrity we can also find among accreditation standards in area of Patient Condition Assessment, such as OS 1. Scope of medical interview and physical examination OS 2 has been defined in the hospital. The hospital defined scope of nursing assessment, OS 5.3 results of

physical examination, OS 5.4 assessment of patient mental state and OS 5.5 assessment of patient social status, in which family and environmental interview is integral part of holistic assessment of the patient health. Based on interview, physical examination and preliminary test results, a care plan is developed, which was also referred to earlier, it concerns OP 1 accreditation standard in the area of Care of Patient (OP).

The last analyzed quality requirement of the PN-EN 15224:2017-02 standard is patient involvement. Mentioned above accreditation standards related to patient consent to either hospitalization or individual medical procedures are consistent with subject of the matter because the patient involvement, referred to discussed norm, is primarily his active participation, first in making decisions and then in implementation of individual medical procedures related to treatment process. Analyzing on, elements which engage the patient, and even more, his family, can be found in accreditation area of Care Continuity (CO), Patients Rights (PP) and Nutrition (OD).

Table 1 shows quality aspects/ requirements of the PN-EN 15224:2017-02 standard with thematically relevant areas of accreditation standards which have been discussed in detail in this part of the article.

Table 1. Connection of quality aspects/ requirements of the PN-EN 15224:2017-02 standard with thematically relevant areas of accreditation standards

	Quality aspect/ requirement in the standard PN-EN 15224:2017-02							
Accreditation standards (areas)	Proper, adequate care	Availability; Own Capital/ equal treatment; Timeliness (punctuality)/ availability	Care continuity	Effectiveness, Efficiency	Care based on knowledge evidence	Patient--centered care, including physical, mental and social integrity	Patient involvement	Patient safety
Care Continuity (CO)			+			+	+	+
Patient Rights (PP)	+	+			+	+	+	
Patient Condition Assessment (OS)	+					+		
Care of Patient (OP)	+			+	+	+		
Infection Control (KZ)				+				
Treatments and anesthesia (ZA)				+				
Pharmacotherapy (FA)				+				
Laboratory (LA)				+				

Image Diagnostics (DO)								
Nutrition (OD)			+				+	
Improvement of Patient Quality and Safety (PJ)	+	+		+	+			+
General Management (ZO)				+				
Human Resource Management (ZZ)				+	+			+
Information Management (ZI)				+				+
Management of Care Environment (ŚO)				+				+

According to the above analysis designation of both the PN-EN 15224:2017-02 standard and accreditation for health care sector causes natural, very high convergence and similarity between both systems. For specialist and expert on discussed subject, there is no bigger problem with connecting mutual reference of requirements of individual quality aspects described in the standard and accreditation standards. However, they can`t be said to be identical. Differences result from the very structure of the documents. The PN-EN 15224:2017-02 standard, in accordance with the ISO/ IEC Directives, Part 1, Consolidated ISO Supplement, Annex SL, contains common, consistent structure of new revised management system standards in form of following points (universal structure):

1. Scope of the standard
2. Normative references
3. Terms and definitions
4. Context of the organization
5. Leadership
6. Planning
7. Support
8. Operational activities
9. Assessment of effects of the activities
10. Improvement

Reaching specific qualitative, discussed above, aspects requires thorough understanding and exploring entire content because information about them is included both in the introduction and in operational activities, and descriptions and explanations of requirements from other sections of the standard in question constitute a complement of holistic approach to quality management in health care.

Accreditation standards are divided into 15 subject areas, gathering a total of 221 standards. Subject accreditation areas (strictly defined structure):

1. Continuity of Care (CO).
2. Patient Rights (PP).

3. Assessment of Patient Condition (OS).
4. Patient Care (OP).
5. Infection Control (KZ).
6. Treatment and Anesthesia (ZA).
7. Pharmacotherapy (FA).
8. Laboratory (LA).
9. Medical imaging (DO).
10. Nutrition (OD).
11. Quality Improving and Safety of the Patient (PJ).
12. General Management (ZO).
13. Human Resource Management (ZZ).
14. Information Management (ZI).
15. Care Environment Management (ŚO).

Another difference between discussed systems concerns scope of both documents, the standard has international dimension and the set of standards is definitely national. In the case of the PN-EN 15224:2017-02 standard, obtaining the certificate takes place if all requirements of the standard are met (it is acceptable to exclude requirements which don`t apply, from scope of the system, such exclusion should be justified and proved that it doesn`t affect the medical entity`s ability to ensure compliance of provided services). Accreditation system assumes granting of certificate after meeting at least 75% of the standards.

Moreover, the PN-EN 15224:2017-02 standard establish periodic audits of system compliance in 3-year certification cycle – usually in form of 2 surveillance audits, accreditation in present form doesn`t provide for such solutions.

Method of compliance assessment is also different. In the case of the standard, assessment is the most often performed by a certification body chosen by a given medical entity, in accreditation system only CMJ. In the standard compliance with given requirement is assessed, accreditation standards differ in importance assigned to them (4-point scale: 1.0, 0.75, 0.5, 0.25), and the final result is component of importance and assessments of standards for which a three-point scale was adopted, points

1, 3 or 5, where 1 means non-compliance with the standard, 3 is a partial compliance and 5 confirms full compliance with a given requirement, or two-degree scale, points 1 or 5, in the case of even partial non-compliance the standard is rated 1.

Discussion

Providing high quality services should be priority value for each medical entity, because quality translates to health, trust, safety and also patient life [9]. Along with progress of science and technology, nowadays certification becomes one of the most important tools supporting further development of both production companies and service sector [10]. Obtaining accreditation is a proof of implementation of adopted standards of conduct by a given entity, including medical entity, element increasing prestige and confirmation of readiness for further development and continuous improvement of implemented processes [11]. The system compliant with ISO standards is system of general requirements which relate to establishment, documentation, implementation and maintenance of quality management system and continuous improvement of its effectiveness [1]. Accreditation, unlike ISO 9001 certification, which has industrial origin, has been dedicated since the very beginning to health care system – initially it was developed on basis of experience of hospitals, and then it was used in all medical entities [12].

According to the subject literature review, opinion on reasonability and effectiveness of implementation of management systems in medical entities in accordance with ISO reference standards and accreditation of the Minister of Health is clearly divided. As Budgol [13] notes, there are no ideal systems, pointing out that in typically medical areas the ISO quality management system allows to order patient service processes, strengthen documents supervision, raises quality awareness and contributes to its further improvement, improving organizational culture. According to Golinowska, accreditation is a mechanism insufficient for achieving a significant improvement in quality of services but it is a good

"tool" for assessing quality of provided services [4]. However, Niżankowski emphasizes that characteristic feature of accreditation is that assessment is made by specialists in a given field. Inspection I carried out by accreditation commission which focuses on a comprehensive and reliable assessment of activity of the entity. Essence of assessment is level of compliance of actual state with standards which the medical entity should meet [2]. The expert also points out that management systems compliant with ISO are "industrial systems" which are more effective in typical production activities than in health care entities [13]. However, it should be emphasized that in the analyzed quality management system EN ISO 9001:2015 according to the PN-EN 15224:2017-02 standard, basis and background for the concept of "health" were based on five health components of the International Classification of Functioning, Disability and Health (ICF) prepared by WHO [14, 15].

Interest of medical entities in implementation of individual ISO management systems or accreditation of the Minister of Health has shown a clear upward trend for many years [16] and may result from: (1) awarding additional points by the National Health Fund (NFZ) as part of offering and contracting process [17]; (2) possibility of obtaining additional funds [18], (3) willingness to direct treatment activities to needs and expectations of the patient.

Most of accreditation standards focus on areas related to patient safety and those elements of care which have high risk of error and adverse events. For this reason, accreditation visit means not only meeting with top level management or documentation review, but also direct visiting over 50% of area of care provision (e.g. wards, operating theatres, laboratories and diagnostic facilities) as well as care environments (e.g. sterilization point, pharmacy, archives, staff, economic department, technical department or medical equipment department). Standards which are dynamic and subject to periodic modification, are of fundamental importance for accreditation process. Thanks to that, the assumption that accreditation will constantly stimulate to achieve optimum level which is determined by accreditation standard, is met. Each time requirements of

standards must be on as high level as possible but realistically achievable [16]. Undoubtedly, it is noteworthy that accreditation is granted by only one center in Poland – CMJ, and this certainly allows to include entity with accreditation certificate among medical entities in which health care safety is manifested in practically every aspect of its activities. All medical entities with accreditation are closely monitored, and information about them is available on the CMJ website. Moreover, accreditation doesn`t give possibility to exclude any of 221 accreditation standards grouped into 15 subject areas. In the case of ISO management systems, things are a little different. First of all, there are many accredited certification bodies which grant ISO certificates. Additionally, justified exclusions of individual requirements of standards are allowed if they aren`t referenced in the scope of the entity activity. There is also possibility to certify only selected locations or a narrow scope of activities without need for holistic management of all implemented processes.

On one hand we have accreditation, proven and recognized in the world health care assessment system, created from the beginning on basis of experience of hospitals [13], and on the other hand universal guidelines of international ISO standards which originally were not created for the purposes of health care. Nevertheless, due to the PN-EN 15224:2017-02 standard as dedicated to health care sector, they should become a part of process of difficult but effective management of medical entities.

The performed analysis clearly shows that, despite formal differences, there are numerous connections and analogies between requirements of individual quality aspects of the PN-EN 15224:2017-02 standard and requirements of accreditation standards, yet, neither one nor the other approach should be discredited, because in both cases, reliable preparing the entity for very complex system implementation process is a guarantee of success. It is very important to be aware that rank and value of accreditation or selected and implemented management system for a given medical entity largely depends on approach, knowledge, skills and commitment of the board and top management. The PN-EN 15224:2017-02 standard, similarly to accreditation standards, pays particular attention

to obligation to manage clinical risk during planning, implementation and control of individual process which becomes the key element of quality management system for clinical activities. In both cases, data related to significant events connected with hospitalization should be analyzed and assessed, and conclusions and observations should be used to conduct improvement projects in important health care areas in accordance with the E. Deming quality improvement methodology (PDCA cycle) [8]. Only continuous improvement and systematic monitoring of level of fulfillment of individual requirements in both systems guarantee implementation of process in friendly and safe environment for patients, their families and health care staff.

Conclusions

According to the above discussion the most important conclusions from the conducted comparative analysis are as follows:

1. Despite formal differences, there are numerous connections and analogies between requirements of individual quality aspects of the PN-EN 15224:2017-02 standard and requirements of accreditation standards.
2. Implementation and maintenance of one system should not exclude the other one, on the contrary, it can constitute basis for creating single, coherent system for managing the medical entity as a whole.
3. Due to costs, implementation and maintenance of the system compliant with requirements of the ISO standard as the first one can be more advantageous for the medical entity, and at the same time providing basis for effective implementation of further accreditation standards.
4. If only purpose of implementation process is to gain certificate for benefits connected with contracting or obtaining additional funds, both accreditation and individual management systems (including these compatible with the standard in question) become only a labor consuming and bureaucratic obligation.

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Journal of Health Study and Medicine
2021, No. 1
pp. 65-83
DOI 10.36145/JHSM2021.04

Cognitive Screening Tests as an Early Method of Detecting Cognitive Dysfunctions

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Abstract

Cognitive impairment is an increasingly common problem in aging societies. With age, cognitive functions are naturally weakened. However, this process may lead to more serious deficits such as mild cognitive impairment (MCI) and dementia. Identification of patients at high risk, early diagnosis of cognitive impairment and monitoring of the patient's condition, as well as taking appropriate action is very important. Cognitive impairment is detected using neuropsychological screening tests that enable the detection of cognitive impairment in the early stages. The most commonly used tools for the initial assessment of cognitive functioning are: Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Clock Drawing Test (CDT), Addenbrooke's Cognitive Examination (ACE III). Early detection of MCI gives the opportunity to quickly implement appropriate interventions, which can slow down or limit the development of cognitive impairment. Early diagnosis allows to find the cause and reduce the adverse effects of modifiable factors that contribute to the development of dementia. Among these factors, there are: reduced levels of folic acid, diabetes and depression. Early diagnosis also gives the opportunity to plan the patient's care appropriately, including the patient's conscious participation in making such decisions. Cognitive screening tests are also used to monitor the progress of the disease, which allows you to respond appropriately and modify the treatment plan adequately to the patient's condition and cognitive deficits.

Key words: *the elderly, cognitive impairment, memory impairment, cognitive screening tests.*

Definition and epidemiology

The growing number of elderly people in the society and the prolongation of life lead to the increasing incidence of cognitive disorders. Aging of the human organism causes certain changes in cognitive functioning, including natural age-associated memory impairment (AAMI), mild cognitive impairment (MCI) and early forms of dementia (including stages of Alzheimer's disease) [6, 7]. The natural process of aging is associated with the impairment of cognitive functioning, the speed of information processing decreases, memory, visual-spatial functions and executive functions deteriorate. The most noticeable for patients is memory impairment, with age the ability to encode new information in memory and access to new information decreases. In a naturally aging organism, not all cognitive functions are impaired, e.g. vocabulary may even improve with age. Important elements of strengthening memory are preventive measures to maintain the best functioning of cognitive processes [8].

Mild cognitive impairment (MCI) is characterized by a deterioration in cognitive functioning with an increased severity than expected in regards to the given age and educational level of the patient. The presence of MCI increases the risk of future dementia [9, 10], which is defined as a complex of chronic and progressive mental disorders, most often occurring in the course of brain diseases with undifferentiated etiology [7]. Dementia is characterized by memory impairment and a decline in intellectual performance compared to a patient's previous state [11]. The occurrence of cognitive dysfunctions may be influenced by modifiable (e.g.: lifestyle, mental activity, education, and cardiovascular stress) and non-modifiable (e.g. age) risk factors [12]. The prevalence of dementia in the elderly population is estimated at about 10% [14]. In 2011, McKhann et al. estimated the global incidence of dementia at around 30 million, with an upward trend to 60 million in 2030, and even up to 114 million in 2050 [13]. It is also estimated that 47 million people worldwide currently suffer from dementia, and by 2050 this number could triple [15]. As it can be seen, it is estimated that the number of people suffering from dementia

syndromes will increase year by year, which makes them not only a significant medical problem, but also a social and economic problem.

Criteria for diagnosis by cognitive screening tests

In order to detect cognitive functioning disorders in the elderly, neuropsychological cognitive screening tests are used, which allow to initially assess the level of cognitive activity of the patient. The tests in a simple and quick way give a numerical result, which assesses the general condition of the patient in regard to cognitive functioning. The most popular are: Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Clock Drawing Test (CDT), California Verbal Learning Test (CVLT), Trail Making Test (TMT) and becoming more and more popular among clinical neuropsychologists Addenbrooke's Cognitive Examinations (ACE III) [19, 20, 21].

Conducting neuropsychological tests is often hard work not only for the examiner, but above all for the tested person. The test results are influenced by, among others: disturbances in the senses such as vision or hearing (therefore it is important that the test subjects have reading glasses and hearing aids, if they use them every day), medications taken, mood, and willingness to participate in research. If the patient is subjected to several tests, those are performed day after day in order not to tire the patient. It is important that each test is performed by the same person, in the same room and at the same time of the day [22].

The most commonly used test is MMSE. This tool is used not only in the clinical diagnosis of patients, but also widely used in research in the field of neuropsychology. The obtained numerical result of this test shows the level of cognitive functioning of the patient. The final result is the sum of points from all subtests, in which the following are evaluated: orientation in time and place, remembering, attention with counting, word recall, and language functions: naming and repeating, writing and also construction praxia, i.e. copying 2 figures [23]. 30 points is the maximum score that can be obtained on this test. The norm is considered to be

a result equal to or greater than 28 points. A score in the range of 24–27 indicates mild cognitive impairment and below 24 may indicate an ongoing dementia process. The test result is influenced by factors such as age and level of education. Therefore, if the patient obtains 24 points from the test or less, further diagnostics is required to verify the cognitive test result: confirm or exclude dementia [23, 24]. Research clearly shows that approximately 51% of primary healthcare entities use the MMSE test in practice [25]. Another cognitive screening test is the Montreal Cognitive Assessment (MoCA). It was developed by Nasreddine in Montreal for the detection of mild cognitive impairment (MCI). The following are assessed: visual-spatial, executive and linguistic functions, attention, fluency, naming, memory, and orientation [26, 27]. Similarly as in the MMSE test, patients can score a maximum of 30 points. A result equal to or greater than 26 is considered correct. A score between 25 and 18 is evidence of MCI and less than 18 of dementia. At the end of the test, the number of years of study of the patient must be taken into account. If the examined person has 12 or less years of education, an additional point is awarded [27, 28]. The studies validating this test clearly show the high sensitivity and specificity of this scale in the detection of MCI in the early stages of Alzheimer's disease. At the same time, the research shows the advantage of MoCA over the MMSE test, which is the most common screening test used as a screening tool by clinicians [26, 29]. The Clock Drawing Test has in recent years become a very popular screening tool in many clinical areas for a wide range of cognitive impairment and severity. CDT is used not only to detect mild cognitive impairment [30, 31]. It is also useful for the early detection and prediction of dementia, diagnosis of disorders in this area of neurological origin (e.g. in Parkinson's disease), post-accident brain trauma, in the course of mental disorders (depression, schizophrenia), metabolic diseases and due to hospitalization of general diseases. Although earlier CDT was used simultaneously for screening purposes, the current research suggests using this tool to monitor the course of dementia of varying severity [31]. Four variants of CDT are used in cognitive screening: two Shulman variants, one Watson modification and one

Sunderland modification. Each of these versions is characterized by high sensitivity and specificity in detecting cognitive disorders in the elderly. There is an error classification for each variation of this test. After the completion of the examination, the degree of cognitive impairment is determined using this error classification [31, 32].

The ACE III scale is an extended tool for cognitive screening and detecting cognitive dysfunctions at an early stage. It is also used for the differential assessment of dementia syndromes and (similarly as MoCA and CDT) helpful in monitoring the disease progression [33]. The ACE-III test is a short examination that takes 15–20 minutes and assesses basic cognitive functions [34]. The test examines five domains, each of which is assessed separately, and the sum of the points scored gives the final result. The examined person may receive a maximum of 18 points for attention, 26 points for memory and language, 14 points for fluency, and 16 points for visual-spatial functions. A maximum of 100 points can be obtained by a test subject, which distinguishes this test from other cognitive screening tests (for an example in the MoCA test and the MMSE test, a maximum of 30 points can be scored). The higher the test result is achieved by the patient, the better his cognitive functioning [35]. ACE-III is a test that is easy to carry out, both for the subject and the examiner, and most importantly, it demonstrates high utility and accuracy in detecting MCI and dementia of varying severity [35, 36]. Research shows that the ACE-III test is a reliable tool for the detection of cognitive dysfunction and dementia [35], it shows high sensitivity and specificity. Compared to MMSE, the ACE-III test is more sensitive in detecting dementia [34].

The California Verbal Learning Test (CVLT) by Delis et al. [37] is one of the most popular tests used in the world for the diagnosis of learning and various dimensions of verbal memory [38]. It was adapted for use in Polish with a full psychometric study by Łojek and Stańczak [39]. Only the examiner and the test subject should be in the room at the time of the examination. The entire test must be performed during one meeting. The California Language Learning Test should only be performed and evaluated by psychologists, including clinical neuropsychologists. Persons tested

during the CVLT test at a steady pace are read a list of 16 words related to each other into 4 semantic categories. Before each reading of the word list, the test subject is told to remember as many words as possible on the shopping list for the day. The Monday shopping list is read five times. Before each reading, the test subject is asked to remember as many words as possible and repeat them in any order after the tester has read the list. In the further part of the test, the Tuesday shopping list is read out once with different words (representing intentional interference). Before reading the Tuesday list of words, the test subject is asked again to remember and repeat as many items from this list as possible. Then the examined person is asked to recall the Monday list (short postponement), and then again after a longer postponement (after a break of about 20 minutes). In the last stage of the examination, the test subject is presented with a list of words to be recognized. From among 44 items, the examined person has to indicate words from the Monday list. In addition to the main indicators, which include: the number of recalled words after each reading, the number of recalled words after the short and long delay and the number of words recognized from the last part of the test. The CVLT also counts the error rates for each reminder and word recognition [39, 40]. The individual indicators of the CVLT test allow for the analysis of neuropsychological functions such as: general verbal memory performance, verbal short-term memory, long-term memory, resistance to interference, effectiveness of learning strategies, mechanical learning, creating a learning plan, learning using semantic categorization of stimuli, differentiation the verbal material being prepared [38].

Trail Making Test (TMT) is one of the most widely used and popular neuropsychological tests in clinical trials. This may be due to the fact that it is one of the few instruments that is sensitive to, for example, brain injuries. TMT provides information on: mental flexibility, visual scanning, executive functions, visual search and processing speed [41, 42]. It also studies the field search function, and in particular the interhemispheric functioning. TMT consists of two separately assessed parts (Part A and Part B). The Trail Making Test aims to assess psychomotor speed – part

A, and in part B – cognitive flexibility and visual-spatial working memory [43]. In TMT part A the test subject is to draw a line as quickly as possible, which continuously and sequentially connects 25 digits circled and placed on a sheet of paper. In TMT part B, the requirements are similar, with a small difference: the test subject must connect alternating numbers with letters of the alphabet as quickly as possible with a continuous line in the following order: (1 – A – 2 – B – 3 – C etc.) [41, 42, 43].When assessing the test results, one should take into account the time measured in seconds as well as the number of errors made by the examined person. The cut-off time for TMT part A is 40 seconds and for TMT part B is 92 seconds [41]. In order to accurately assess the correctness of executive functions, scientists propose to pay attention to the ratio of test execution time B – A; this will allow to exclude the so-called psychomotor component tested in TMT part A. Summing up, the longer the relative time of TMT part B in relation to TMT part A, the automatically worse the result evaluating the so-called cognitive flexibility [43]. And when the time of performing part B is twice as long as part A, it indicates a dysfunction of the frontal cortex [41].

Importance of cognitive screening tests in the elderly

Epidemiological studies show that even 15–30% of people over 60 years of age are affected by mild cognitive impairment (MCI). This percentage increases with age and amounts to: 18.7% in people aged 60–70 years, 21% in people between 71–80 years of age and as much as 29.4% in people aged over 81 [44, 45]. As previously mentioned, MCI increases the risk of developing dementia in the future. Overall, about half of people diagnosed with MCI will develop dementia within the next 3 years. From the moment of diagnosis of mild cognitive dysfunction, 6–15% of patients develop dementia every year [46]. In the light of the above statistics, early detection of MCI becomes more and more important. Despite the limited treatment options for dementia, the need for early diagnosis and diagnosis of the onset of the disease in the asymptomatic phase is

emphasized. Diagnosis is often made too late or not made at all, to the detriment of the patient. Fast and early diagnosis enables early implementation of interventions that may slow down or limit the progression of cognitive disorders [47]. Research has shown that there are modifiable factors, such as diabetes mellitus, decreased levels of folic acid, which, if not controlled, may lead to the development of dementia (though there is no clear evidence that eliminating these factors completely protects against this) [48, 49]. One of the modifiable factors is also depression, which affects an increasing percentage of the population and promotes the occurrence of cognitive disorders, both in acute depressive episodes and in remission [50]. It is recommended that after the diagnosis is made, the information about MCI should be communicated to the patient carefully, so that it does not cause fear and anxiety [50, 51]. It is recommended in the conversation with the patient to discuss the prognosis for the development of the disease, as well as the long-term treatment plan. Moderate physical exercise and cognitive training should be recommended [52]. Patients should be advised that mild cognitive impairment does not necessarily progress to dementia. Early diagnosis of MCI gives the opportunity, especially for the immediate family, to plan the care over the patient accordingly as the dementia will progress. It also allows the patient to consciously participate in making such decisions. People suffering from dementia are not able to function independently and need (often round the clock) care of third parties [46]. Many clinicians recommend monitoring patients with MCI for cognitive functioning over time, preferably every 6 months [52, 53, 54]. In people over 60 years of age, despite the increasing risk of mild cognitive disorders, they are often not correctly diagnosed [55], and even 4 years pass from the first symptoms appearing in a senior to the moment of obtaining a correct diagnosis [56]. The scary fact is that as many as 81% of patients with symptoms of cognitive dysfunction are not diagnosed at all [57]. The fundamental challenge in European countries (including Poland) is the implementation of the mechanism of performing neuropsychological screening tests by primary care physicians during follow-up visits to the office in a group of

patients over 60 years of age in order to increase the detection of MCI. A big issue is that most of these doctors underestimate the importance of early diagnosis in this area. Another obstacle in the implementation of the aforementioned standards is the lack of adequate preparation of family doctors to diagnose MCI and dementia [57]. As already mentioned, screening testing should use neuropsychological tests with high psychometric properties, and at the same time the duration of which would be a maximum of 15 minutes [58].

Conclusion

Aging of the population is an increasing problem for today's society. Along with this, the number of people suffering from cognitive dysfunction increases. Although it is a physiological process and it progresses with age, it can turn into more serious deficits, such as MCI and dementia. Mild cognitive impairment (MCI) increases the likelihood of dementia, is characterized by cognitive decline, and is not always properly diagnosed. Dementia, on the other hand, leads to a decline in intellectual performance and memory impairment. Early recognition of these conditions can protect an elderly person from complications caused by cognitive dysfunction. Neuropsychological testing is one of the fastest screening methods for detecting these disorders. Great emphasis should be placed on screening tests by primary care physicians during the control examinations of elderly people in the office. This would increase the detectability of the MCI at an early stage. We can distinguish tests such as: MMSE, MoCA, Clock Drawing Test, ACE III. Additionally, the popular tests that are used in extended neuropsychological diagnostics are: CVLT and TMT A and B. Early detection of any abnormalities allows for modifying factors that may contribute to the development of MCI and dementia, including Alzheimer's disease. The modification of incorrect factors may also affect the patient's treatment process as well as improve their efficiency and functioning in everyday life. The modifiable factors include, for an example, depression, diabetes, and reduced levels of folic acid. Cogniti-

ve screening tests may also be used for monitoring the progress of the disease, and thus the patient's condition and deficits. Tests should be performed every six months to efficiently and professionally monitor the possible deterioration of the patient's condition and the development of dementia. It is estimated that in 2050 the number of people suffering from dementia will triple. This growth will bring with it major challenges for all areas of medicine, as well as for the economy and society as a whole.

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Journal of Health Study and Medicine
2021, No. 1
pp. 85-100
DOI 10.36145/JHSM2021.05

Onasemnogene Abeparvovec as New Gene Therapy in Patients with Spinal Muscular Atrophy – a Review of the Literature

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Abstract

Introduction: *Spinal muscular atrophy is an autosomal recessive neurodegenerative disease that mainly affects children. It is caused by mutation in the SMN1 gene, which results in degeneration and loss of alpha motor neurons innervating skeletal muscles. Without any intervention, spinal muscular atrophy progresses and leads to disability or even early death.*

Material and methods: *The latest available literature accessible on the PubMed database was reviewed. Thirty papers, which were published in English, available as full-text publications, and published since 2015, were selected for analysis.*

Results: *Depending on the level of motor development and the age of onset, spinal muscular atrophy is divided into 4 or 5 subtypes. Onasemnogene abeparvovec is a gene replacement therapy and consists of a vector of the serotype 9 adeno-associated virus, which delivers a functional copy of the SMN1 gene to the cells of the motor neuron. Important advantage of the drug is single administration via an intravenous route. The limitation is the high price and the lack of studies in older children. Several studies confirmed the efficacy and safety of using onesamnogene abeparvovec in children who afterward made progress in respiratory functions, swallowing, and motor milestones, like head control and sitting independently.*

Conclusions: *Onasemnogene abeparvovec is an innovative and effective drug with great potential for present and future use. Therapy in spinal muscular atrophy should be implemented as early as possible to avoid muscle cell loss. It is important to conduct universal screening tests of newborns to detect the disease before the first symptoms appear.*

Key words: *gene therapy, spinal muscular atrophy.*

Introduction and objective

Spinal muscular atrophy (SMA) is a group of severe inherited neurodegenerative diseases caused by a mutation in the *SMN1* gene (survival of motor neuron) on chromosome 5q13. It results in degeneration and loss of alpha motor neurons of the spinal cord innervating skeletal muscles, which is manifested by progressive muscle weakness and atrophy [1, 2]. The gene codes SMN protein, without which it is impossible to survive. Patients with SMA live due to the small amount of SMN protein produced from the *SMN2* gene. SMA is an autosomal recessive disease that mainly affects children. Depending on the level of motor development and the age of onset, spinal muscular atrophy is divided into 4 subtypes [3]. Sometimes type 0 is also enumerated or classified as 1A by some authors [4]. The incidence of SMA in the population is estimated at 1 in 10,000 live births [5]. Patient support consists of the symptomatic treatment of the disease in order to prevent further deterioration of health [1]. Without any intervention, spinal muscular atrophy progresses and leads to disability or even early death [1, 5].

The first disease-modifying drug approved for the treatment of spinal muscular atrophy was nusinersen. It consists of antisense oligonucleotides and interacts with the *SMN2* gene, resulting in increased production of the SMN protein and requires multiple for life intrathecal administration [6]. There are trials of treatment with other drugs possible for use in SMA therapy, for example, risdiplam [7].

In recent years, scientists have been looking for other, more effective, safe, and easier to administer drugs in the treatment of spinal muscular atrophy. In May 2019, new gene therapy was approved in the United States for the treatment of paediatric patients under 2 years old [8]. It appeared on the market as the most expensive drug currently in the world – onasemnogene abeparvovec. In 2020 the European Medicine Agency approved it for the treatment of patients with the clinical presentation of SMA type 1 or SMA with up to three copies of the *SMN2* gene [9].

The aim of the study is to present the current state of knowledge on the effectiveness of the new gene therapy with the use of onasemnogene abeparvovec in the treatment of SMA.

Material and methods

The latest available literature was reviewed. The materials accessible in the PubMed database were used. The following inclusion criteria were applied: papers published in English, available as full-text publications, and published since 2015. Original and review papers were chosen whereas letters to the editor were not included. The literature review was carried out on 7 November 2020, using the following keywords: "gene therapy" and "spinal muscular atrophy", from which 150 results were received. Using the brand name of the drug "Zolgensma" 49 results were obtained, while using the pharmaceutical name of the preparation "onasemnogen abeparvovec" – 33 publications. After reading abstracts, 30 papers, which met the adopted criteria, were selected for analysis.

Results

SMA as a genetic disease with a different clinical picture

The clinical picture of the disease varies depending on the type of disease and includes problems such as general motor muscle weakness, limited mobility, muscle contractures, and respiratory failure [2]. Intellectual development is normal. Type 0 of spinal muscular atrophy is recognized prenatal or at birth, in which profound hypotension and respiratory distress are present soon after birth, and life expectancy in the absence of treatment is up to one month [4]. In infants with type 1 SMA, the first symptoms appear before the age of 6 months and include respiratory problems, hypotonia, and motor delays. Patients never sit up. It is the most severe form and the most common genetic disease with high mortality even before the age of 2. Children with SMA type 2 are able to sit, but they cannot walk. Symptoms of the disease appear later and before the

age of 18 months. In patients with type 3 SMA, symptoms of the disease are relatively mild and begin after 18 months of age. Children can walk independently, but there is a risk of losing this ability later. The symptoms of type 4 SMA appear in adults and are characterized by slow progress. It is the mildest form of the disease, in which patients walk, and their life expectancy is usually normal [10]. The strongest genetic modifier of SMA severity is the *SMN2* gene copy number. The more copies of the gene, the milder the course of SMA. However, this inversely proportional relationship is not absolute, and we cannot always predict the course of the disease [2, 11].

Molecular basis of gene therapy in SMA

Gene therapy is a very effective method of treating neurodegenerative diseases, which also includes disorders of the motor neuron. It involves the introduction of nucleic acids into cells and enables treatment at the molecular level [12, 13]. SMA is a result of a single gene defect, therefore gene therapy can be extremely effective in the treatment of this disease [14]. It prevents the death of neuronal cells and inhibits the progression of SMA [6]. Onasemnogene abeparvovec is a one-time gene replacement therapy. It consists of a vector of the serotype 9 adeno-associated virus (AAV9) [6]. AAV is a non-enveloped small virus of the *Dependovirus* genus of the *Parvoviridae* family. The length of a single-stranded, linear DNA genome is ~ 4.7 Kb. It is encased in a 25-nm icosahedral capsid. This virus cannot replicate itself, but can infect dividing and non-dividing host cells. The AAV genome then integrates with the host cell's DNA and remains hidden there [15]. AAV9 crosses the blood-brain barrier allowing a single intravenous infusion, which is a significant advantage of the drug [14, 16]. The dose is selected strictly according to the patient's weight. Multiple dosing cannot be used, because the patient might develop the AAV antibodies [17]. The advantage of the AAV vector is efficacy, safety, and the induction of a limited immune response [13]. Its task is to deliver a functional copy of the *SMN1* gene to the cells of the motor neuron directly. This replaces the faulty or missing *SMN1* gene. DNA self-com-

plementation technology enables the rapid formation of a functional episome by a vector delivered in the form of double-stranded DNA [14]. Administration of the drug increases protein expression in the central and peripheral nervous system [18]. As a result, onasemnogene abeparvovec has a very fast onset of action [14].

The effectiveness of gene therapy in the treatment of SMA in research

Numerous studies confirm the effectiveness of onasemnogene abeparvovec therapy in children. Waldrop et al. assessed the safety and early outcome data from 21 children aged 1–23 months and proved that in this population, due to screening and careful post-gene transfer management, replacement therapy with onasemnogene abeparvovec-xioi was efficient and safe. An asymptomatic drop in platelets in the first week after treatment was experienced by 19 out of 21 children. Two patients experienced stabilization and 17 experienced improvements in motor function in a group of 19 children with repeated outcome assessments. Due to the hepatotropic properties of the drug vector adenovirus, post-drug liver enzyme levels should be monitored and steroids administered. Gene transfer was well tolerated in children below 6 months. In this group, serum aspartate aminotransferase and alanine aminotransferase elevations were modest and an association with γ glutamyl transpeptidase elevations was not seen. Initial prednisolone was administered. In children over 6 months, a higher dose of prednisolone was required due to more common elevations in serum transaminases and γ glutamyl transpeptidase, but all patients did not present clinical symptoms [19].

Al-Zaidy et al. evaluated the effectiveness of onasemnogene abeparvovec therapy (previously known as AVXS-101) in infants with spinal muscular atrophy type 1 (n = 12) and compared the results with a cohort of healthy infants (n = 27) and a prospective natural history cohort of SMA1 infants (n = 16) from the NeuroNEXT (NN101) study. Event-free survival, CHOP-INTEND scores (scale for assessing neuromuscular efficiency of infants), compound muscle action potential, motor milestone achievements, and adverse events were compared. All onasemnogene

abeparvovec treated infants survived by 24 months of follow-up. In the NN101 study, the percentage was 38%. Independent sitting and walking were achieved by infants receiving AVXS-101. SMA1 infants from NN101 study presented the average baseline CHOP-INTEND score 20.3, which worsened to 5.3 by age 24 months. In patients receiving AVSX-101 the average baseline score was 28.2 and improved to 56.5 by age two years. AVXS-101-treated infants at 6 and 24 months had improvements in compound muscle action potential peak area (means of 1.1 and 3.2 millivolts/second) [20].

In another study, Al-Zaidy et al. assessed the effectiveness of AVXS-101 gene replacement therapy among twelve SMA1 infants with homozygous deletions of the *SMN1* gene and two *SMN2* gene copies. Patients received a one-time intravenous AVXS-101 between December 2014 and 2017 and were followed for 2-years post-treatment for outcomes. Eleven children were able to swallow, which allows orally feeding. Seven patients did not require noninvasive ventilation and eleven achieved the ability to speak. Eleven patients were able to control the head position and sit independently. Two of them could walk without help. The mean length of hospitalization was assessed as 6.7 days. The mean unadjusted annualized hospitalization rate was 2.1. The mean proportion of time hospitalized was 4.4%, which showed the decline and contributed to the improvement of the quality of life of patients and their parents [21].

Lowes et al. conducted a study on the effect on motor function of onasemnogene abeparvovec administration in one-time gene replacement therapy in infants with severe spinal muscular atrophy type 1. The therapeutic dose of AVXS-101 was administered to 12 infants. The infants were grouped according to age at the time of AVXS-101 administration and baseline values from the Philadelphia Children's Hospital neuromuscular disorder test. The first group of children was less than 3 months old, with a score < 20 (n = 3) and weak motor skills. Early dosing was used which resulted in a mean increase of 35 points from a mean baseline value of 15.7. The next group consisted of children aged 3 months or older (n = 6). Late dosing was performed which resulted in a mean increase of

23.3 points compared to a mean starting value of 26.5. The last group consisted of children under 3 months of age with a score of ≥ 20 (n = 3) and strong motor skills. As a result of early dosing compared to a mean baseline of 44.0, a mean score of 60.3 was rapidly achieved. Children with strong motor skills who received early dosing with AVXS-101 were the earliest of the 3 groups tested to start sitting up alone. The group of children with lower motor skills who used the dosing earlier despite a lower value of the initial motor score started to sit up faster than the group of children who used the latter dosing. The results of these studies have shown that early treatment is important and that improvement in the quality of life is independent of baseline motor function [22].

The concern issue of combining molecular therapies in patients with SMA1 was addressed by Yohei Harada et al. Five patients (age: 17––29 months) who had homozygous *SMN1* deletions and two copies of *SMN2* were tested. All received nusinersen and onasemnogene abeparvovec-xioi and four of them (1, 2, 4, 5) had received nusinersen prior to onasemnogene. Nusinersen was continued in three of them. The treatment of the fifth patient was sequential, but not concurrent. As a result of the increase in liver enzymes, the first and second patients had to stay in the hospital and undergo longer corticosteroid therapy. The second patient had a liver biopsy, and his symptoms indicated a liver failure. In the fourth and fifth patients, the increase in liver enzymes was found to be milder, they were normalized after treatment with corticosteroids. In addition, transient thrombocytopenia was observed in both of these patients. The third patient was taking onasemnogene abeparvovec-xioi, which was the first drug, and then he was given nusinersen. No side effects were observed. Improvement was seen in all patients with SMA1 after combination therapy [23].

Paul et al. highlighted in their review that the level of improvement in muscle strength and respiratory health differs depending on SMA genotype, treatment applied, the timing of the first dose, and intensity of baseline neuromuscular and pulmonary impairment. The authors after analyzing data from several studies claimed that although some patients

might still require escalation of respiratory support during illnesses, overall pulmonary morbidity might have decreased after a single intravenous infusion of onasemnogene. The number of patients who acquired the ability to safe swallow function to allow partial oral feeding increased from 58% to 92%, assessed in video-fluoroscopy. Percentage of children able to drink thin liquids increased from 33% before treatment to 83% after it [24].

In the study conducted by Dabbous et al., treatment efficacy of onasemnogene abeparvovec (AVXS-101) relative to nusinersen for the treatment of SMA type 1 was evaluated. The possibility of preventing death was 20% higher for children treated with onesamnogene abeparvovec than nusinersen (risk ratio (RR) = 1.2). Among symptomatic infants with SMA type 1, the number needed to treat to prevent (NNT) one more death with AVXS-101 instead of nusinersen was 6.2. For event-free survival, the NNT to prevent one more event was 2.6 (RR = 1.6). For improvement in motor function, NNT was 3.5 (RR = 1.4). For milestone achievements, the NNTs were 1.4, 1.5, and 1.2 (RR = 4.2, 7.8, and 11.2) for head control, rolling over, and sitting independently, respectively. Each outcome was reported with 95% confidence intervals. Results suggest that AVXS-101 may have an efficacy advantage in comparison to nusinersen for independence from permanent assisted ventilation, motor function, milestones, and overall survival [25].

In the study by Waldrop et al., several case reports of patients with SMA were presented. In one of them, the patient received onasemnogene abeparvovec-xioi at 6 months of age, and nusinersen was stopped. His general gross and fine motor development has improved to be at the appropriate time or even early. Patients' CHOP-INTEND score has stabilized at 64 about 2 months after gene transfer (5 months since the last dose of nusinersen). The second patient with CHOP-INTEND = 37 received onasemnogene abeparvovec-xioi at 10 months of age. Her clinical outcomes have improved, with a CHOP-INTEND score of 54 at 13 months. Onasemnogene abeparvovec-xioi performs very well with minimal liver toxicity, but the sample size in research is much smaller compared to

nusinersen and the data are only in infants. Due to possible side effects throughout the body after systemic administration (an ability of AAV9 to transduce also other than neurons cells types and use a promoter in all types of cells in the body) and possible higher exposure of the motor neurons to the delivered *SMN1* directly to central nervous system, the intrathecal administration may be considered in clinical trials [26]. A lower dose would be sufficient with such a method of administration and the drug potentially might be used in older patients.

Rashnonejad A. et al. assessed the efficacy of human SMN gene expression after delivering gene therapy in SMA mouse embryos in the context of possibilities of fetal treatment for early-onset SMA. Intrauterine intracerebroventricular injection of AAV9-EGFP led to the vast expression of EGFP protein in the central nervous system with a huge amount of transduced neural stem cells. Mouse fetuses received a single intracerebroventricular injection of a single-stranded or self-complementary AAV9-SMN vector that led to a lifespan of 93 (median of 63) or 171 (median 105) days for ill mice. In both study groups, the muscle pathology and number of the motor neurons improved. Little better results come from self-complementary AAV treatment [27]. In the study conducted by Hinderer et al., three juvenile nonhuman primates and three piglets were treated with an intravenous injection of an AAVhu68 vector (an AAV9 variant) which carried a human SMN transgene. In both species, wide transduction of spinal motor neurons was achieved after administration of $2x10^{14}$ genome copies/kilogram of body weight. The dose was close to that used in the SMA clinical trials. Nonhuman primates exhibited increased transaminases. All animals presented with features of degeneration of dorsal root ganglia sensory neurons. Authors conclude that research involving high systemic doses of AAV vectors should include precise control for toxicity [28]. However, among children under the age of two, onesamnogene abeparvovec visibly changes the natural history of spinal muscular atrophy with minimal side effects [26].

Limitations of the drug therapy

Unfortunately, onasemnogene abeparvovec is not refunded by the National Health Fund now in 2020 in Poland. Its cost makes it impossible to use in any child with SMA who would be qualified for the therapy. Onasemnogene abeparvovec treatment costs (brand name – Zolgensma) were estimated at $2.1 million per one dose or an annualized cost of $425,000/year for 5 years [29]. Nevertheless, the 5-year costs for Zolgensma, which is a one-time treatment, are lower in comparison to nusinersen, which is the only approved therapy for SMA and costs $750,000 in the first year of treatment and $375,000 annually thereafter for life [29].

Future perspectives

There is presently no treatment that can revive muscle cell loss due to the disease, because currently used drugs can only increase the availability of the SMN protein in motor neurons and prevent them from dying further. The early diagnosis of the disease and the use of the drug help to stop the progression of the disease. Australian experience with the introduction of wide-ranging newborn screening for SMA between 1 August 2018 and 31 July 2019 shows that in the first year of the program, 10 out of 103,903 newborns were screened positive for SMA using polymerase chain reaction (PCR). The median time for ending the screening and diagnostic process was 13.5 days (from 8 to 21 days) and therapeutic intervention was implemented by the median of 26.5 days after birth (from 16 to 37 days). Early commencement of treatment with nusinersen offers the best prognosis for survival and clinical outcomes, particularly treatment within the presymptomatic period [30]. If children were early detected, the implementation of onasemnogene abeparvovec treatment as well would be more effective than using the drug after the onset of symptoms. There is a need for conducting further analyses on the efficacy of screening in newborns prior to onasemnogene abeparvovec treatment.

Conclusions

Gene therapy with the use of onasemnogene abeparvovec is an innovative and effective method of treating spinal muscular atrophy, which is confirmed by clinical observations. It is extremely important to implement therapy in spinal muscular atrophy as early as possible and introduce universal screening tests of newborns for mutations in the SMN gene in order to detect the disease before the first symptoms appear. Onesamnogene abeparvovec has great potential to make significant progress in clinical outcomes among patients with spinal muscular atrophy in the future. Due to the novelty of the described gene therapy, further depth research in its field should be conducted.

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Journal of Health Study and Medicine
2021, No. 1
pp. 101-116
DOI 10.36145/JHSM2021.06

Small Intestinal Bacterial Overgrowth: Diagnosis, Pathophysiology and Treatment Methods

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Abstract

Small intestinal bacterial overgrowth (SIBO) is the excessive abundance of nonpatogenic microbes in the small bowel, which are characteristic to the large intestine. It is often referred to as dysbiosis. Typical symptoms include: immoderate flatulence, abdominal pain, steatorrhea or micronutrient deficiencies that may cause conditions like anemia or general fatigue associated with it. The dysfunction of the intestinal mucosal barrier and chronic inflammation, caused by SIBO, are the causes of many diseases, for example fatty liver disease and autoimmune diseases, which also act as predispositions to bacterial overgrowth. The diagnosis is based mainly on the breathing tests. The therapy is comprehensive and relies on pharmacological treatment, adequate diet (usually low-FODMAP diet is recommended) as well as preventive measures in order to avoid the relapse. The key to complete recovery is correct identification of the core cause and its removal, which is often not so clear as SIBO manifests itself with many nonspecific symptoms and therefore, may be misidentified as irritable bowel syndrome, celiac disease or other GI tract diseases.

This article reviews and summarizes the current state of knowledge about the bacterial overgrowth in the small intestine.

Key words: *Small Intestine Bacterial Overgrowth, SIBO, Irritable bowel syndrome, IBS, rifaximin, microbiome, dysbiosis, acne*

Introduction

Research, carried out as part of the Human Microbiome Project, contributed to the discovery and analysis of microbes inhabiting the human gastrointestinal tract. It indicated a great qualitative and quantitative diversity of bacteria, as well as individual variability of gut flora – that is, between people. Bacterial intestinal composition is dynamic and fine-tuned, meaning it undergoes changes depending on one's lifestyle as well as previous and ongoing diseases [1]. For this reason, changes in the level of specific strains are already being used as a diagnostic tool directed for disease detection and may also be used in the development of potential therapies based on probiotic bacterial strains [2]. However, despite many beneficial functions, an imbalanced composition of the intestinal microflora may lead to undesirable conditions. One of these digestive system disorders is SIBO – Small Intestinal Bacterial Overgrowth, which is characterized by an excessive number of bacteria in the small intestine that are specific to the large intestine. Many patients with this condition suffer from general disorders such as bloating, diarrhea or abdominal pain, and because of that, they are often misdiagnosed for IBS (Irritable Bowel Syndrome). However, some authors suggest that SIBO may also be the underlying cause of IBS [3].

Due to many common, nonspecific symptoms, it is possible that bacterial overgrowth in the small intestine is mistakenly categorized as a food allergy, inflammatory bowel disease, or a result of chronic stress, and therefore patients with mentioned conditions live with bothersome disorders for many years. However, the cause of this disease is the overgrowth of bacteria that naturally inhabit the large intestine. This lack of harmony leads to malabsorption of valuable nutrients, such as fats and vitamins. In extreme, untreated cases, this disease can lead to weight loss, major deficiencies or even osteoporosis [4, 5].

Definition

The main characteristic of SIBO is an excessive amount of bacteria in the small intestine. The disease is diagnosed when the number of bacterial populations exceeds 105–106 organisms per mL of collected sample [6]. It is worth noting that the average number of organisms in equilibrium state should not exceed 10^3 organisms per mL of sample [7, 8].

The qualitative composition of the microbes inhabiting the intestine is also taken into account during the diagnosis. For example, one of the indicators of dysbiosis is the prevalence of bacteria metabolizing bile salts to insoluble compounds. This leads to impaired fat absorption and, consequently, steatorrhea. Too abundant amount of microorganisms that are responsible for the conversion of carbohydrates to SCFAs (Short-Chain Fatty Acids) and gases can cause abdominal distension without diarrhea, fatty acids are absorbed by the intestinal epithelial cells, whereas gases are responsible for the feeling of bloating or even lower abdominal pain. Other bacterial species, such as *Klebsiella*, can produce toxins that damage the mucosa, contributing to its inflammation and impaired absorption [9, 10].

Clinical picture

The symptoms of SIBO are very nonspecific and overlap with those assigned to IBS, lactose or fructose intolerance [11]. For this reason, the disease has been rarely diagnosed. Moreover, indicators of bacterial overgrowth in the small intestine vary in intensity between patients. The most common ones are:

- abdominal distension
- diarrhea or, on the contrary, constipation; may occur alternately,
- nausea,
- indigestion
- lower abdominal pain and discomfort

- malabsorption, which causes deficiencies of nutrients, vitamins (i.e. A, D, E, K, B vitamins), micro- and macro- elements (i.e. iron, omega-3 fatty acids)
- headaches and fatigue
- depressive and anxiety states

Typically, about 60% of patients report the presence of listed symptoms. Distended Stomach is often the most troublesome symptom. Gaseous accumulation in the initial section of the intestine can lead to reflux, as well as pain and discomfort [10]. Vitamin deficiencies (mainly from group B) contribute to the development of, among others, acne. Moreover, one study found that people with SIBO were 10 times more likely to suffer from *acne vulgaris* than healthy people [4, 12, 13].

Due to the excessive uptake of vitamin B12 by microbes, anemia can also occur. On the other hand, damage of the enterocytes in the intestine disturbs the digestion and absorption of for example disaccharides, which may be manifested by lactose and fructose intolerance [12, 13]. Additionally, the malabsorption of fats and vitamins soluble in them, is the result of improper metabolism of bile salts. However, it is worth noting that symptoms caused by hypovitaminosis of fat-soluble vitamins are rarely manifested. Therefore, night blindness, hypocalcaemia, neuropathies and retinopathies, immunodeficiencies or blood coagulation disorders occur only in extreme cases [10].

Etiology

The cause of bacterial overgrowth in the small intestine is the disturbance of microbial homeostasis. The most frequently mentioned conditions that predispose patients to this disease are associated with changes in the motility of the GI tract as well as enzymatic functions of digestive system. Hypochlorhydria increases the risk of bacteria being transferred from food and settling in the small intestine. The deficiency of hydrochloric acid, secreted by the parietal cells of the mucosal layer, allows these bacteria to survive [15]. Another major predisposition is believed to be

lying in the damage of the MMC – Migrating Myoelectric Complex, causing chyme - partially digested food, to accumulate. This promotes the growth of bacteria in the small intestine. Other factors are immune-related disorders, like congenital and secondary immunodeficiencies characterized by excess of immunoglobulin A (IgA) in the lumen of the gut, as well as anatomical abnormalities of GI tract, for example - small intestine constriction or the formation of 'blind loops' , diabetes, celiac disease, neurodegenerative diseases [10, 17, 18]. Some researchers imply that immunosuppresive therapy can also cause SIBO, although the data is quite ambiguous. The study conducted by Siniewicz-Luzeńczyk and Tkaczyk has shown that children suffering from steroid-dependent idiopathic nephritic syndrome, who underwent cyclosporine therapy (second line immunosuppressive agents), do not develop SIBO. Nevertheless, some of the children indicated having symptoms characteristic to SIBO, such as abdominal discomfort [16].

Research [7, 19, 20, 26] has shown that there are several risk factors predisposing to SIBO, including:

i. anatomical tendencies (diverticula of the small intestine, strictures, fistulas, obstructions)
ii. intestinal motility disorders (celiac disease, gastroparesis)
iii. irritable bowel syndrome
iv. metabolic disorders (diabetes, hypochlorhydia)
v. organ dysfunctions (cirrhosis, conductors, pancreatitis, immunodeficiency, Crohn's disease, malnutrition)
vi. certain medical treatments (excessive intake of antibiotics, gastric acid secretion suppressors)
vii. alcoholism
viii. age-related complications and diseases, including Parkinson's disease

Overgrowth of microbes may also contribute to the development of inflammatory state in the intestinal mucosa, further aggravating the typical symptoms of SIBO [22]. According to Miazga et al., inflammation causes changes in the patterns of expression of genes involved in the production and secretion of mucus, thus creating correlations between

such disease entities as SIBO, IBS, cystic fibrosis or chronic abdominal pain [23].

Diagnostics

SIBO diagnosis is mainly based on breathing tests and the roman criteria IV [24]. It measures the amount of hydrogen separately, or both methane and hydrogen in the exhaled air. The unit is ppm - parts per million [25]. This method is proceeded under two conditions – first measure is done after fasting and another after ingestion of a fermentable product (usually 10 grams of lactulose or 75 grams of glucose, in the form of 200 mL of solution), as these gases are produced during bacterial fermentation reactions. These measurements are taken at intervals of 15–20 minutes. Thus, the amount of gases is proportional to the size of microbial proliferation, while the time when the increase in hydrogen/methane concentration is detected, indicates the section of the intestine occupied by the questioned pathology [26].

Interpretation of the test for determination of SIBO is based on an increase of ≥ 20 ppm above the baseline in exhaled hydrogen, up to 120 minutes from the start of the measurement [19, 26]. It is worth adding that this technique is nearly noninvasive and easy to carry out. However, before testing, patients should prepare themselves by eating a low-fermenting diet for 1–2 days prior the testing, and fasting for 12 hours before coming in for the test [28].

Another method is to take a liquid aspirate from the small intestine and culture it. Although this test is considered to be the gold standard [29], it is rarely performed due to the higher invasiveness, possible complications in sampling and contamination of the sample. In addition, some species of microbes that colonize the intestines cannot be cultured *ex vivo*, which makes it impossible to accurately determine the number of bacteria. This issue is made even more difficult by the dispersed distribution of bacteria in the intestine. Thus, the sample taken may not be representative [17].

Drug treatment and diet

The first step in getting rid of SIBO is antibiotic treatment. The most commonly recommended is a course of rifaximin – typically 1200 milligrams per day for 10–14 days. Its action is particularly helpful in this disease, because as an eubiotic it has a protective effect on the beneficial microflora as well as its anti-inflammatory activity has been confirmed. Antibiotic therapy with the use of two antibiotics is also possible. This possibility is advised in the presence of severe, chronic constipation. The additional antibiotics used are metronidazole or neomycin. An important aspect is also the stimulation of intestinal motility by prokinetics and eating a properly balanced diet [30, 31].

Patients affected by SIBO should follow the diet recommended during antibiotic therapy, which facilitates the treatment process and eliminates troubling symptoms by reducing inflammation. The first step is to remove simple sugars that are rapidly broken down by bacteria, which increases their proliferation rates and enhances inflammation. Products rich in fiber cause adherence of undigested carbohydrates to the intestinal wall causing bloating or diarrhea. Therefore, the most frequently proposed diet is a low FODMAP diet, meaning low in Fermentable Oligo-, Di-, and Monosaccharides and Polyols. This diet was developed by researchers at Monash University in Australia. Therefore, food categories abundant in fructose, glucose (i.e. honey, agave syrup, many fruits), as well as lactose, galactans (found in legumes) should be eliminated [19, 23]. Recommended low-FODMAP products are listed in Table 1.

In some cases, intake of histamine-rich foods (i.e. tomatoes, peppers, red wine) should also be temporarily reduced. Intolerance to the these foods can cause allergy-like symptoms due to the lack of access to the enzyme - diamine oxidase, in the brush border of apical surface of some intestinal epithelial cells. This enzyme's activity is to break down excess of histamine [14].

A 2010 study found that incorporating probiotic-rich foods into the diet reduces the symptoms of SIBO. In addition, under certain circum-

stances, it is also important to include supplementation during therapy, because patients suffering from dysbiosis and subsequent malabsorption are prone to deficiencies of micronutrients, including omega-3 acids and vitamins, especially A, D, E, K. Impaired absorption of vitamins from food, in severe cases may cause several disorders linked to disturbed haematopoiesis , digestive functions, or the metabolism of bone tissue and skin. Thus, not treating SIBO could lead to additional complications such as anemia, acne, osteoporosis, night blindness or chronic fatigue syndrome [10, 34].

Table 1. Example products classified into the low-FODMAP group – with a low content of fermentable oligosaccharides, disaccharides, monosaccharides and polyols [32, 33]

Food category	low-FODMAP product
Vegetables	carrot, cucumber, lettuce, tomato, ginger, kale, okra, olives, pumpkin, algae, chicory, potatoes, spinach, eggplant, beetroot
Fruits	banana, orange, mandarins, grapes, clementines, pineapple, strawberries, rhubarb, papaya, blueberries, melon, kiwi
Milk products	lactose-free milk and yoghurt, hard cheeses
Protein sources	white and red meat, fish and seafood, tofu
Grains	gluten-free sourdough bread, spelled, rice, oats, gluten-free pasta, quinoa
Nuts and seeds	almonds, macadamia nuts, peanuts, Brazilian nuts, pumpkin seeds, poppy seeds, sesame seeds, sunflower seeds
Other	herbs (basil, coriander, mint, oregano, parsley, thyme, rosemary), natural spices, tea (black, green)

In addition to modifying the diet, probiotics are also tested as means in the treatment of SIBO. However, current studies are inconclusive [20]. A meta-analysis made by Zhong et al. [35] suggests that probiotics may suppress the proliferation of gut bacteria that are the source of SIBO, giving better breath test results and reducing abdominal pain. It is worth noting, however, that the studied sample was not very representative and heterogeneous, meaning that further research is required [35]. Whereas research conducted by Chedid [37] has shown that herbal therapies

apparently maybe be as effective as treatment with rifaximin for resolution of SIBO and because of that, can be used as a replacement for antibiotics. In the experiment, herbal therapies increased the response rate for normalizing breath hydrogen testing by over 10%, compared to SIBO patients treated with rifaximin. These commercial, herbal preparations, among others, consisted of: *Thymus vulgaris*, *Salvia officinalis*, *Glycyrrhiza uralensis*, *Origanum vulgare*, *Melissa officinalis*. Although substances derived from such plants are known to have antibacterial and anti-inflammatory activities, more research in this field is needed as cited study needs more validation, as it was not a prospective, randomized controlled trial. However, it broadens current knowledge and possible therapies that do not necessarily base on antibiotics [37].

Nevertheless, it is worth emphasizing that an adequate, elimination diet is only able to reduce some symptoms, and not remove the core cause of SIBO. Its implementation should be preceded by a recommendation from a specialist, and after the symptoms of SIBO have subsided, gradually switch to a standard, diverse diet [7]. Additionally, treatment of SIBO also requires the right amount and quality of sleep, stress reduction and physical activity, which all also stimulate metabolism.

Summary

Research indicates that up to 15% of the population might suffer from Small Intestine Bacterial Overgrowth. Middle-aged and elderly people are more prone to it, as well as those diagnosed with irritable bowel syndrome (IBS) [10]. Prevalence of SIBO is more frequent in the lower socioeconomic strata of developing countries and children from families with smaller income, thus contributing to poor carbohydrate absorption, malnutrition and worse oral vaccine results [38, 39]. These facts contribute to the improvement of current diagnostic tools and therapies, as well as raising awareness concerning the problem. It is crucial to identify the cause of SIBO, remove its cause or at least mitigate the symptoms. A significant part of the current knowledge about the pathogenesis of discussed

disease, comes from studies conducted in developed countries, where the research sample consisted of patients with co-occurring pathologies of the gastrointestinal tract. Thus, it would be important to understand what is the etiology and pathophysiology of SIBO and whether it differs between children in developing countries, who have not been diagnosed with multimorbidities, and patients from highly industrialized countries.

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