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ORIGINAL PAPER

PROBLEM OF FATIGUE IN PATIENTS WITH MULTIPLE SCLEROSIS

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Abstract

Aim: The aim of the study was to determine the frequency of the incidence of fatigue, and its impact on the performance of activities of daily living in patients with the diagnosis of multiple sclerosis (MS), regarding their cognitive, physical, and psychosocial functioning, and also to identify differences in the frequency of its occurrence in patients diagnosed with the disease for up to five years, and in those diagnosed for more than five years. *Design:* A quantitative cross-sectional study. *Methods:* A total of 94 MS patients with the mean age of 38.70 ± 11.20, and average disease duration of 6.5 ± 4.7, were included in the sample. An adapted version of a self-assessed questionnaire, the *Modified Fatigue Impact Scale* (MFIS), was used to collect empirical data. *Results:* Fatigue had the greatest incidence and impact on activities in the physical subscale of the used tool (19.98 ± 8.71). We identified statistically significant differences between the first group of MS patients with disease duration of up to five years, and the second group with disease duration of over five years in the physical ($p = 0.019$) and psychosocial subscales ($p = 0.006$). The group of respondents with MS for more than five years reported higher incidence of fatigue on both subscales. No significant differences were identified on the cognitive subscale. *Conclusion:* Objectification of the frequency of fatigue incidence – a burdensome symptom of the disease – and the monitoring of its impact on activities of daily living by means of suitable measuring instruments, such as the MFIS, contribute to a better understanding of the issue in diagnostics. It also opens up possibilities for its effective management. In terms of further research, it would be valuable to conduct validation studies of this instrument in the Slovak sociocultural environment.

Keywords: fatigue, patients, multiple sclerosis, Modified Fatigue Impact Scale.

Introduction

Multiple sclerosis manifests itself in the clinical picture by a range of symptoms which often vary between patients, but which generally intensify in each patient in the first ten years after diagnosis, "with the main negative effects centering on physical decline" (Basak, Unver, Demirkaya, 2015). Fatigue is one of the so-called non-specific symptoms of the disease. It is defined as a subjectively evaluated lack of physical and/or mental energy in the patient, which interferes with common activities of daily living (Johansson et al., 2009). According to scientific studies, the incidence of symptoms in patients is in the range of 75–90%. About 50% of all patients consider fatigue to be the most negative and burdensome symptom of MS (Forwell et al., 2008; Jakubíková, Klímová, 2010).

It is a dynamic multidimensional symptom. The dynamics means that fatigue may occur at any time of day, and may equally quickly subside, irrespective of stimuli (Mills, 2012). Some patients may feel permanently tired or tired for much of the day, intensifying the impact of the clinical symptoms of MS (Brañas et al., 2000). Scientific terminology published in the literature describes the multidimensional nature of MS-related fatigue, as, for example, general fatigue, sleepiness, lack of energy, mental fatigue, physical fatigue, cognitive fatigue, increased fatigability, lassitude, and asthenia (fatigue at rest) (Kos et al., 2008). Progressive fatigue during the day is typical for the given group of patients. It starts immediately on waking after night sleep and worsens with various factors, e.g., temperature, acute illness, pain, and physical activity (Schwid et al., 2002). It can also occur without being triggered by any other factor, and its occurrence can affect mobility, make physical activity impossible, including normal functioning at home and at work, and cause many other difficulties (Kos et al., 2003).

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In the given groups of patients, the emergence and persistence of fatigue is conditioned by many factors. So-called pathological fatigue, which is not linked to any physical and/or neurological impairment (deficit) objectified by magnetic resonance imaging, occurs in 80–85 % of MS patients. Pathological fatigue occurs even without the presence of diseases such as anemia, thyroid function disorders, depression, diseases of the heart and blood vessels, and chronic infections (Giovannoni, 2006; Braley, Chervin, 2010). The onset of fatigue is therefore related directly to the actual pathophysiology of MS. In this case it is known as primary fatigue (Forwell et al., 2008). Primary fatigue is caused by the presence of inflammatory cytokines, the diffuse distribution of antibodies in the central nervous system, and neurotransmission performed by chronically demyelinated nerve fibers, in reduced numbers (Giovannoni, 2006; Mills, 2011). In addition, there are other factors influencing feelings of tiredness in MS patients, one of which is problems connected with sleeping, for example insomnia, which prevent the build up of energy reserves during night sleep, which are required during the day. Similarly, there are mobility problems which cause rapid depletion of energy reserves, and worsen fatigue. Another cause of fatigue may be pain associated with the presence of contractures, as well as side effects of pharmacotherapeutic treatment for pain or depression, and the side effects of muscle relaxants, sedatives and hypnotics (Schwid et al., 2002; Forwell, 2011). Other factors involved in the formation and increasing intensity of fatigue in MS patients are stress, sudden temperature fluctuations (interior and exterior), humidity, and exercise. All the above mentioned factors cause the onset of nonprimary (secondary) fatigue (Forwell et al., 2008). Symptoms of fatigue in patients may differ. Patients describe them as increased fatigability, need for more frequent rest periods, and sleepiness (Schwid et al., 2002). In terms of somatic functions, patients describe fatigue as a reduction in muscle strength, resulting in altered mobility, walking, and other activities requiring physical effort. In terms of psychosocial and cognitive functions, fatigue can manifest itself as cognitive decline, difficulty in acquiring, retaining, and retrieving new information, difficulty thinking and concentrating, and a reduction in motivation to perform activities. Fatigue related to MS patients is distinct from fatigue in the general population, and imposes significant limits on activities of daily living (Brañas et al., 2000; Rietberg Van Wegen, Kwakkel, 2010; Fedorová, Tamer, 2012).

Quantification of fatigue, and assessment of the impact on performance of activities of daily living in MS patients is difficult and complex due to the fact that fatigue is understood as a subjective symptom of multidimensional variability. Several measuring tools which can objectify this impact have been developed for this purpose in clinical practice. The following measuring instruments are used to assess different dimensions of MS-related fatigue: *Modified Fatigue Impact Scale* (MFIS), *Fatigue Impact Scale* (FIS), *Fatigue Severity Scale* (FSS), *Visual Analogue Scale* (VAS), *Fatigue Scale for Motor and Cognitive Function, MS-specific Fatigue Severity Scale* (MFSS) (Kos et al., 2003; Krupp, 2012).

Aim

The aim of the study was to determine the frequency of fatigue incidence, and its impact on the performance of activities of daily living in MS patients in their cognitive, physical and psychosocial functioning, by means of the *Modified Fatigue Impact Scale* (MFIS). The secondary objective was to identify differences in the incidence of fatigue, and its impact on the performance of activities of daily living in respondents who have been diagnosed with MS for up to five years, and those who have been diagnosed for longer than five years.

Methods

Design

The study follows a quantitative cross-sectional design.

Sample

The selection of respondents was based on inclusion and exclusion criteria. Patients were required to meet the following inclusion criteria: a diagnosis of MS for at least one year, age of over 18 years, without cognitive disorders, without episodes of the disease, and willingnes to cooperate. The exclusion criteria were: the presence of cognitive impairment and depression without treatment, or with less than three months' treatment, age under 18 years, and unwillingness to participate in a research study. Based on these criteria, doctors recommended the inclusion of patients in the sample. Respondents were directly approached during a regular examination in the dispensary. The initial number of respondents was 98; four questionnaires were removed due to insufficient survey data. The total research sample consisted of 94 respondents – 70 female and 24 male. The average age of respondents was 38.70 ± 20.11 years (min. 20 years; max. 69 years). The average duration of disease was 6.5 ± 4.7 years. 42 respondents had been diagnosed with the disease for five or less than five years, and 52 respondents had been diagnosed with the disease for more than five years. 61 respondents (64.89%) reported no associated disease. 33 respondents (35.11%) reported at least one associated disease, most frequently thyroid disease, and hypertension.

Data collection

Data were collected using the *Modified Fatigue Impact Scale* (MFIS) questionnaire (Ritvo et al. 1997), which was modified by a version of the *Fatigue Impact Scale* (FIS) questionnaire (Fisk et al., 1994). Ritvo et al. (1997) stress that the MFIS is a valid and reliable measuring instrument designed to determine the frequency of fatigue incidence in the preceding four weeks, and its impact on the physical, psychosocial and cognitive life of MS patients. Larson (2013) contends, however, that the validity and reliability of the MFIS is not sufficient, and further studies concerning the psychometric properties of the instrument are necessary. The questionnaire contains 21 items divided into three subscales (physical, psychosocial, cognitive), supplemented with demographic items. Participants rate on a 5-point Likert scale (0 = “never”, 1 = “rarely”, 2 = “sometimes”, 3 = “often”, 4 = “almost always”) their agreement with 21 statements. The cognitive subscale ranges from 0–40 points, the physical subscale ranges from 0–36 points, and the psychosocial subscale ranges from 0–8 points. The total score from the MFIS questionnaire ranges from 0–84, whereby a higher number indicates greater frequency of fatigue incidence, and its impact on the performance of activities of daily living. In the current study, Cronbach´s alpha was 0.941. Cronbach´s alpha in the cognitive subscale was 0.914, in the physical subscale, 0.937, and in the psychosocial subscale, 0.784. It took approximately 10–15 minutes to complete the questionnaire. Empirical data collection was carried out from January to April 2016 in the dispensary for demyelinating diseases of the Department of Neurology at the University Hospital, Martin.

The Vice President of the *National Multiple Sclerosis Society* and the co-author of the measuring instrument, Nicholas LaRocca, was contacted in order to obtain permission to use the MFIS. We were informed by Mr. Nicholas LaRocca that the tool is in the public domain, and specific authorization to use the measuring instrument is unnecessary.

The translation of the questionnaire into Slovak was accomplished by two authors independently. Any differences in translation were discussed with a third author, and a consensus-based questionnaire was developed.

Data analysis

All data were analyzed with the SPSS statistical package (version 16.0). Descriptive statistics of arithmetic mean (M) and standard deviation (SD) were used. The Mann-Whitney U test was used to test differences in mean. The level of statistical significance was set at 5% ($p < 0.05$) for the Mann-Whitney U test.

Results

The study results are given with reference to the total number of respondents, and also with regard to their division into two groups depending on the duration of the disease due to the fact that the clinical symptoms, including fatigue, intensify in the first 10 years after diagnosis (Basak, Unver, Demirkaya, 2015). In our study, we divided the respondents into two groups in order to determine whether there are differences in the frequency of fatigue incidence, and in its impact on the performance of daily activities over a shorter period (the first five years of disease duration). Therefore, group 1 consisted of patients diagnosed with the disease for up to five years, and group 2 consisted of patients diagnosed with the disease for more than five years. Table 1 shows the frequency of subjective fatigue incidence, and its impact on the performance of activities of daily living in MS patients in the whole sample, as well as in each groups of patients.

The results show that the physical subscale achieved a point score of 19.98 ± 8.71; the cognitive subscale achieved a point score of 14.86 ± 7.96; and the psychosocial subscale achieved a point score of 3.77 ± 2.19. In terms of subjective assessment for items of the MFIS, the item on the physical subscale “Trouble maintaining physical effort for long periods” (2.49 ± 1.24) achieved the highest point score (highest frequency of fatigue incidence / maximal rate of fatigue impact). The item on the cognitive subscale “Difficulty organizing thoughts when doing things at home or at work” (1.20 ± 1.00) achieved the lowest point score (lowest frequency of fatigue incidence / minimal rate of fatigue impact).

Table 1 Assessment of fatigue in MS patients according to the *Modified Fatigue Impact Scale* (MFIS)

Subscales / Items	**The entire sample of respondents n = 94 M ± SD**	**≤ 5 years n = 42 M ± SD**	**> 5 years n = 52 M ± SD**	**p**
Cognitive Subscale	14.86 ± 7.96	14.12 ± 8.03	15.46 ± 7.93	0.422
Decreased alertness	1.72 ± 0.92	1.79 ± 0.93	1.75 ± 0.93	0.803
Difficulty paying attention for long periods of time	1.64 ± 0.99	1.50 ± 1.04	1.75 ± 0.95	0.197
Inability to think clearly	1.21 ± 1.08	1.14 ± 1.05	1.27 ± 1.11	0.563
Forgetfulness	1.85 ± 1.05	1.88 ± 1.06	1.83 ± 1.04	0.883
Difficulty making decisions	1.32 ± 1.09	1.24 ± 1.10	1.38 ± 1.09	0.450
Low motivation to do anything that requires thinking	1.37 ± 0.97	1.26 ± 0.99	1.46 ± 0.96	0.250
Trouble finishing tasks that require thinking	1.44 ± 1.05	1.33 ± 1.14	1.52 ± 0.98	0.399
Difficulty organizing thoughts when doing things at home or at work	1.20 ± 1.00	1.14 ± 1.03	1.25 ± 0.99	0.634
Thinking slowing down	1.33 ± 1.11	1.21 ± 1.16	1.42 ± 1.07	0.274
Trouble concentrating	1.73 ± 1.03	1.62 ± 1.04	1.83 ± 1.02	0.283
Physical Subscale	19.98 ± 8.71	17.45 ± 8.93	22.02 ± 8.04	**0.019**
Being clumsy and uncoordinated	1.91 ± 1.14	1.57 ± 1.19	2.19 ± 1.03	**0.008**
Doing physical activities at own pace	2.21 ± 1.18	2.00 ± 1.17	2.38 ± 1.17	0.118
Low motivation to do anything that requires physical effort	2.15 ± 1.09	1.81 ± 1.15	2.42 ± 0.96	**0.010**
Trouble maintaining physical effort for long periods	2.49 ± 1.24	2.19 ± 1.31	2.73 ± 1.14	**0.037**
Muscles weakness	2.17 ± 1.28	1.90 ± 1.38	2.38 ± 1.17	0.080
Feeling physically uncomfortable	2.31 ± 1.06	2.10 ± 1.14	2.48 ± 0.96	0.104
Low ability to complete tasks that require physical effort	2.15 ± 1.25	1.79 ± 1.20	2.44 ± 1.23	**0.008**
Limitation of physical activities	2.18 ± 1.23	1.88 ± 1.25	2.42 ± 1.16	**0.040**
Need to rest more often or for longer periods	2.40 ± 1.19	2.21 ± 1.26	2.56 ± 1.11	0.195
Psychosocial Subscale	3.77 ± 2.19	3.05 ± 2.13	4.35 ± 2.09	**0.006**
Low motivation to participate in social activities	1.98 ± 1.21	1.74 ± 1.211	2.17 ± 1.18	0.085
Limitation in ability to do things away from home	1.79 ± 1.21	1.31 ± 1.115	2.17 ± 1.15	**0.000**
Total MFIS score	36.61 ± 15.88	34.62 ± 16.91	41.83 ± 14.36	0.075

SD – standard deviation; M – arithmetic mean. The higher the score, the greater the frequency of fatigue incidence and its impact on the activities of daily living; level of statistical significance p < 0.05.

Discussion

The frequency of fatigue in MS patients affects several areas of their lives, with a predominance of impacts on physical functioning, as the results of several studies using the above-mentioned measuring instruments have demonstrated (Kos et al., 2003; Rietberg Van Wegen, Kwakkel, 2010; Fazli, Shayesteh-Azar, 2013). This was also confirmed by the results of our study. The worst rated item on the physical subscale (the highest frequency of the problem / maximal rate of fatigue impact) was "Trouble maintaining physical effort for long periods", confirming the fatigue characteristics of MS. Symptomatology of the disease can result in the onset of fatigue, and, conversely, fatigue incidence may worsen particular symptoms of multiple sclerosis, in relation to the deterioration of functional capacity. Pathophysiological mechanisms of the disease responsible for disability and degeneration of axonal transport result in the onset of subjectively perceived symptoms, such as, increased fatigability, muscle weakness, clumsiness, and movement coordination problems. Deficient muscle strength in MS patients may result in limited ability to engage in physical exercise of sufficient intensity and duration (White, Dressendorfer, 2004).

The frequency of fatigue incidence and its impact on the performance of activities of daily living is also affected by the duration of MS, which is a variable significant factor in this context (Kim et al., 2010). In our research study we have identified the impact of disease duration on assessment of the impact of fatigue in each subscale of the MFIS tool. Statistically significant differences were confirmed between the two groups (respondents diagnosed with MS for up to five years, and respondents diagnosed with MS for more than five years) on the physical and psychosocial subscales. Chronification of MS disease causes experience of fatigue in the greater number of patients during much of the day, which results in impaired physical, psychosocial, and cognitive functioning (Lerdal, Celius, Moum, 2003; Fazli, Shayesteh-Azar 2013; Razazian et al., 2014; Fiest et al., 2016). Another aspect of fatigue is the reduction in motivation to perform activities, together with a loss of interest in activities that require physical activity and effort (Fernández-Muñoz et al., 2015; Kaas, Tóthová, 2015). One reason for patients' disinclination to perform such activities is the variability (fluctuation) of the symptom, as fatigue impedes patients in their completion of activities.

Patients may be able to perform activities requiring physical effort independently, and without difficulty earlier in the day, but might require help to do so, or may not be able to accomplish the same activities at all, in the afternoon (Northrop, Frankel, 2010).

In our clinical study we used the MFIS – one of the measuring instruments used to quantify fatigue in neurological clinical practice abroad – in the process of diagnosis and management of this symptom. Despite the benefits described above, such targeting instruments are not yet used in Slovak clinical practice. Objectification of fatigue, which is a very burdensome symptom for MS patients, can contribute to a better understanding of the variability of these symptoms over the course of the disease. It can also be a good starting point for the planning of individual daily regimes in order to eliminate the negative impact of fatigue on various aspects of life in this group of patients (Krupp, 2016). A diagnostic process using standardized tools aimed at the management of the clinical symptoms of MS, including fatigue, may be the basis for selection of appropriate interventions that are part of clinical guidelines, not only for healthcare professionals, but also for the patients themselves, and their carers.

Limitations of the Study

Due to our sample size, the results cannot be extrapolated. In our research study, we used only one measuring instrument, while several foreign research studies for assessing fatigue in a similar, or even smaller, number of respondents have used multiple tools simultaneously (cf. Kos et al., 2003; Forwell et al., 2008; Rietberg Van Wegen, Kwakkel, 2010).

As reported above, Larson (2013) draws attention to the limits of the validity, reliability and interpretations of the total score. For further research, as well as clinical application of the MFIS, it would be advisable to complete a comprehensive linguistic validation of the tool in Slovak. In light of the given facts, additional research studies focusing on the psychometric properties of the instrument are necessary. Our present study can provide a useful basis for such additional research.

Conclusion

As fatigue negatively affects activities of daily living, fatigue and its management in MS patients requires due attention from healthcare professionals. Its objective quantification is possible by use of a variety of measuring instruments. Among the most commonly used scales in MS patients is the Modified Impact Scale (MFIS), which was also used in this study. The scores in the MFIS show that fatigue affects the performance of activities of daily living in our respondents via impairments predominantly in physical functioning. When the two groups of respondents with differing duration of disease were compared, we found statistically significant differences for those with disease duration of five years or more in the physical and psychosocial subscale. The results also show that the incidence and impact of fatigue on each of the assessed functions tends to increase with disease duration. Further research studies could be aimed at testing the MFIS in the context of Slovak clinical practice, with a focus on the predictive value of the tool.

Ethical aspects and conflict of interest

The research study was approved by the ethics committee of University Hospital, Martin. Respondents were informed about the study objectives, method of data collection, anonymity, and voluntary nature of their participation in the study. The authors of the article are not aware of any conflicts of interest.

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Author contribution

Concept and design (MM, SB, AO, JČ), data collection (MM, SB), analysis and interpretation of data (MM, SB, AO, JČ), drafting of the manuscript (MM, AO, JČ), critical revision of the manuscript (MM, AO, JČ), final completion of the article (MM, AO, JČ).

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