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Among multiple sclerosis and fatigue

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A B S T R A C T

Background: Fatigue is commonly reported in patients with multiple sclerosis (MS), however, its relations to patient's social and clinical characteristics are still investigated insufficiently.
Objective: To explore the peculiarities of association between social and clinical characteristics and fatigue in patients with relapsing-remitting multiple sclerosis (RRMS).
Methods: The study enrolled randomly selected volunteered RRMS patients. All of them were asked to complete or undergo the following: standard socio-demographic questionnaire, Fatigue Severity Scale (FSS), Medical Outcomes Study Sleep scale (MOSS), Numerical Rating Scale (NRS) for pain, Hospital Anxiety and Depression Scale (HADS) and the thirty-six item Short Form Health Survey (SF-36). Multiple linear regression model was used to assess the relationship between fatigue and socio-demographic and clinical characteristics of participants.
Results: The mean FSS score value was 5.3 ± 3.1. The total 68.6% of patients reported the prevalence of fatigue and 21.9% and 19.7% suffered from depression and anxiety respectively. Mean value of Physical and Mental component of health related quality of life (HRQOL) constituted 40.4 and 44.5 points accordingly. The study revealed the association between fatigue and higher disability, depression and lower physical component of HRQOL.
Conclusion: RRMS patients with higher physical disability and depression score, and lower physical QOL suffered from fatigue more frequently than the ones with lower physical disability and depression score and higher physical QOL.

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1. Introduction

Fatigue, depression and anxiety are all known to be common among MS, with estimates of prevalence varying, probably at least partly due to differences in study design and measurement instrument (Motl et al., 2009).

Anxiety is reported to affect 23.5–41% of MS patients, while 60–92% of MS patients are reported to complain of overpowering fatigue, with 30–55% rating it as their most disabling symptom (Wood et al., 2013).

Estimates of the prevalence of depression range from 10% to 41.8%. Depression is a significant risk factor for suicidal ideation and completed suicide, although anxiety has also been associated with suicidal intent and self-harm in MS. MS patients are nearly twice as likely to commit suicide as the general population (Feinstein et al., 2011).

More than 50% of MS patients report daily fatigue worsening during the day, which affects patient's quality of life (QOL). It is controversial whether fatigue is affected by disease status or duration, however, it is the first symptom of most patients in all-clinical types and age groups (Calabrese et al., 2010; Zwibel et al., 2011).

The aim of this study was to determine the overall effect of social and clinical aspects of fatigue in patients with RRMS in regard to depression, anxiety and HRQOL. To our knowledge, this is the first study in Lithuania that has examined fatigue aspect in RRMS patients.

2. Methods

2.1. Subjects

The research started in January 2013 and ended in February 2014. It was carried out at the Outpatients Clinic of the Hospital of Lithuanian University of Health Sciences Kauno klinikos after the local Ethics committee granted the approval. The study enrolled 137 patients with RRMS. All of them provided their written informed consent prior to enrolment.

Inclusion criteria for MS patients were: 1) RRMS diagnosis (McDonald et al., 2001), 2) Expanded Disability Status Scale (EDSS) score (Kurtzke et al., 1983) that ranges from 0 to 7.0, 3) no relapse

for at least 30 days prior to screening and during the study, and 4) no chronic steroid treatment for more than 30 days during the last 6 months.

Exclusion criteria were: 1) age under 18, 2) cognitive or psychiatric conditions that may not meet the requirements of the informed consent or study procedures, 3) presence of other significant issues or diagnosis (other than MS).

2.2. Measurement instruments

In order to assess the related aspects of the study, the following variables were chosen: demographic data (sex, age), MS clinical form (remitting-relapsing), disease duration, disease-modifying treatment (interferon beta, glatiramer acetate), neurological dysfunction defined by EDSS scores, fatigue, sleep problems evaluated according to the Medical Outcomes Study Sleep (MOSS) score, pain, depression and anxiety symptoms measured by Hospital Anxiety and Depression Scale (HADS), and mental and physical quality of life.

All patients had a full neurological examination. The neurological impairment and disability was assessed according to the EDSS scores. EDSS score 3 represented moderate disability, score 4 limited walking but without aid, score 6 walking with unilateral aid and score 7 meant a wheelchair user (Kurtzke et al., 1983).

The presence and severity of fatigue was assessed with the help of the Fatigue Severity Scale (FSS). It consists of nine items, which are rated on a seven-point scale with five equidistant anchor points for each: strongly disagree (1), rare (between 2 and 3), sometimes (4), frequently (between 5 and 6) and strongly agree (7). The higher the score (which was calculated by computing the average score for the nine items) the worse level of severity (Krupp et al., 1989). As recommended, the score value equal to 4 was used as a cut-off value for the presence of fatigue in the FFS.

Data about sleep condition was collected using the MOSS measure (Hays et al., 1992). Normative comparison populations for the MOSS measure included individuals with several chronic diseases (hypertension, diabetes, congestive heart failure, recent myocardial infarction, and depression) and individuals from the general population selected through random digit dialling, described elsewhere. Sleep scale was evaluated as recommended (Spritzer et al., 2003). Scores on the MOSS subscales range from 0 to 100, with the exception of sleep quantity. Higher score on the MOSS reflect more of the attribute indicated by the subscale name. A single indicator of mild, moderate, or severe sleep problems was calculated from item 12 of the MOSS measure based on recommendations of Manocchia et al. (2001).

The HADS is a self-assessed questionnaire consisting of 14 items, suitable for use in persons with medical conditions, if items corresponding to somatic symptoms are omitted, and recently validated for people with MS (Zigmond et al., 1983). Seven items are related to depression and 7 to anxiety. Patients provided their evaluation in a 4-point scale (from 0 = absent to 3 = definitely present/severe). For further analysis the cut-point of >10 to define prevalent anxiety or depression was used.

During the study participants rated their average pain intensity during the past week on a 0–10 numerical rating scale (NRS), from 0 = no pain to 10 = worst condition. NRSs are commonly used in pain research in persons with MS. Moreover, 0–10 NRSs have demonstrated their validity as measures of pain intensity in persons with MS through their significant and positive associations with measures of pain interference and pain-related disability. Evaluation of prevalence of pain in further analysis was dichotomous, that means either present ≥4, or absent <4 (Alschuler et al., 2012).

The thirty-six item Short Form Health Survey (SF-36) was designed to measure health-related quality of life (HRQOL) from the patient's point of view. It assesses 8 health concepts: (a) physical functioning; (b) role limitations because of physical health problems; (c) bodily pain; (d) general health perception; (e) vitality (energy/fatigue); (f) social functioning; (g) role limitations because of emotional problems; and (h) general mental health. These scales were further combined into 2 sections: a physical component summary score PCS (subscales a–d), which contains information about physical health status (PHS), and a mental component summary score MCS (subscales e–h), which informs about mental health status (MHS). All items scores were transformed into a values from 0 (poor health) to 100 (optimal health). For the general population, the mean score for each summary was equal to 50 and the standard deviation was equal to 10. Higher scores indicated better HRQOL (Ware et al., 1992).

2.3. Statistical analysis

Statistical analysis was completed using the program SPSS 15. Descriptive statistics were used to summarize data about subject's social and clinical characteristic. All the data was presented either as a mean value with 95% confidence interval (95% CI) or percentages. Taking into consideration that some scores did not fit a normal distribution, non-parametric tests were used. The analysis of correlation between the results of the tests was carried out using Spearman and Pearson correlation analysis and unpaired t-tests, as appropriate in MS subjects.

Multiple linear regression analysis was used to model the relationship of fatigue (fatigue as a dependent variable, present/absent = 0/1) with the two component summary scores for sleep problems, pain, depression, anxiety, and HRQOL, adjusting for gender, age, residence, education, marital status, professional activity, duration of the disease, EDSS and disease-modifying treatment of MS in RRMS patients (independent variables). A p value of <0.05 was taken as significant.

3. Results

The study recruited 137 (n = 137) MS patients of age varying from 18 to 74 years old (mean age 44.7 years; 95% CI = 41.2–49.4). There were 99 (72.3%) women (mean age 42.6 years, 95% CI = 40.8–49.7) and 38 (27.7%) men (mean age 45.2 years, 95% CI = 41.1–49.2). No significant difference in mean age between men and women was revealed. Fatigue was recognized for 68.6% of the subjects: 67.7% women and 71.1% men. Subjects with higher education (>12 years) were more likely to note the prevalence of fatigue compared to the less educated (≤12 years) RRMS patients (85.1 vs 52.9%, p < 0.001). Professionally inactive patients noted this feature more often than professionally active group (77.4 vs 42.8%, p < 0.001). Patients with higher EDSS score also pointed fatigue more often compared to the lower EDSS score group (77.8 vs 60.8%, p < 0.01). Subjects without disease-modifying therapy were more likely to suffer from fatigue than patients treated with interferon beta or glatiramer acetate (86.2 vs 63.9%, p < 0.01). The study showed that fatigue was significantly prevalent for the following subject groups: depressed patients compared to the not depressed ones (90.0 vs 62.6%, p < 0.001), patients with lower MCS compared to the higher one (74.7 vs 59.2%, p < 0.05), and patients with lower PCS compared to the patients who noted better physical QOL (83.7 vs 37.8%, p < 0.001).

The mean age of the subjects suffering from fatigue compared to the non-fatigued patients was 47.8 years (95% CI = 42.7–52.2) and 42.5 years (95% CI = 40.2–48.5) respectively. In addition it was statistically insignificant. However, evaluating the fatigued patients in comparison to the non-fatigued ones, the study discovered higher mean value of: disease duration (i.e. 15.1 years 95% CI = 12.3–16.1 vs 9.7 years, 95% CI = 6.6.–12.7; p < 0.001),