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RESTLESS LEGS SYNDROME IN MULTIPLE SCLEROSIS PATIENTS – PATIENT EXPERIENCE AT LIPIK SPECIAL HOSPITAL FOR MEDICAL REHABILITATION

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SUMMARY – The study included 60 patients with multiple sclerosis (MS) hospitalized at our institution from September 1 to December 31, 2014. The aim of the study was to assess the prevalence of restless legs syndrome (RLS) in MS patients and RLS relationship with patient age, sex, degree of disability, form of MS, time elapsed from MS diagnosis and use of antidepressants. The diagnosis of RLS was made according to the criteria set by the International Restless Legs Syndrome Study Group. Of the 60 patients, 24 (40%) met the criteria for the existence of RLS. In the group of patients with RLS, there was a significantly higher proportion of women and those that were taking antidepressants. There were no statistically significant between-group differences according to age, duration of illness, degree of disability and clinical course of MS. In the study, 37.5% of patients that met the criteria for RLS diagnosis had not informed the neurologists about their difficulties. The high prevalence of RLS and the fact that a large proportion of patients did not inform the neurologists about their difficulties related to RLS point to the need of an active approach to diagnosis and treatment.

Key words: *Multiple sclerosis – epidemiology; Restless legs syndrome – diagnosis; Hospitals, special; Croatia*

Introduction

Restless legs syndrome (RLS) is a common movement disorder with prevalence in the general population between 4% and 29%[1]. The syndrome is characterized by an urge to move the legs, usually accompanied or caused by unpleasant sensations in the legs that begin or worsen during a period of rest or inactivity. The symptoms are partially or totally relieved by movement and occur or worsen in the evening or night. The RLS diagnosis is established according to the International Restless Legs Syndrome Study Group (IRLSSG) criteria[2]. RLS can be idiopathic or due to secondary causes. Secondary RLS is associated with various pathological conditions such as iron deficiency, peripheral neuropathy, Parkinson's disease, essential tremor, renal failure, spinocerebellar ataxias, myelopathies, and myasthenia gravis[3-9]. Although the pathophysiology remains unclear, brain iron deficiency and dysfunctions of the dopaminergic system seem to play an important role[10].

Available research suggests the RLS prevalence in multiple sclerosis (MS) patients to be higher as compared with the general population[11-14]. Although the true reason for this is not known, cervical cord damage was found to be associated with a higher prevalence of RLS in MS patients[15]. The prevalence of idiopathic

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RLS in Croatia is 9.5%[16]. In this study, we investigated RLS prevalence in MS patients.

Patients and Methods

This study analyzed the RLS prevalence in patients with MS that underwent inpatient rehabilitation at the Lipik Special Hospital for Medical Rehabilitation from September 1 to December 31, 2014. In addition, current antidepressant medication was also analyzed. The study included patients older than 18 and diagnosed with MS according to the revised McDonald criteria[17].

Exclusion criteria were serious cognitive damage, recent infectious illness, or other acute complication in the previous 3 months. Based on the exclusion criteria, four patients were not enrolled in the study. The following data were collected on each patient: age, gender, MS course, time elapsed from MS diagnosis, presence of RLS, use of antidepressants, and whether they informed the attending neurologist about their feeling of leg restlessness.

The RLS diagnosis was established using the IRLSSG criteria[2]. The level of incapacity was determined in each patient based on the Expanded Disability Status Scale (EDSS) score[18], whereas assessment of the cognitive status was performed using the Mini Mental Status[19]. The study was approved by the Hospital Ethics Committee, and a written consent for participation was obtained from the patients.

Statistical analysis was done using the SOFA Stats. Comparison of variables was performed using the Student's t-test and Pearson's correlation test.

Results

The study included 60 subjects, 37 (61.7%) women and 23 (38.3%) men, mean age 49.5 (range, 29-71) years. The mean time elapsed from MS diagnosis was 12.2 years (range, 6 months to 32 years). The mean EDSS was 4.9 (range of 1.5-9). Seventeen (28.3%) patients were taking antidepressant medication. Thirty (50%) patients had the relapsing-remitting (RRMS) and the remaining 30 (50%) patients had the secondary progressive (SPMS) course of the disease.

Twenty-four (40%) study patients fulfilled the clinical criteria for the presence of RLS. Characteristics of MS patients with and without RLS are summarized in Table 1. There was no significant difference between the groups with and without RLS according to age (p=0.255), while the prevalence of RLS was significantly higher in women (p=0.011).

Table 1. Characteristics of patients with and without restless legs syndrome

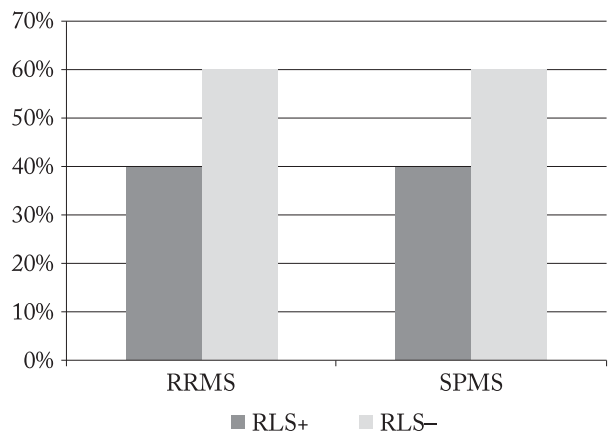
Characteristic	RLS +	RLS -
n/%	24/40	36/60
Age (yrs) $\bar{X}$/SD	52.4/7.59	48.0/12.37
Female (n/%)	19/79	18/50
Male (n/%)	5/21	18/50
EDSS $\bar{X}$/SD	5.0/1.86	4.8/1.93
Antidepressant use (n/%)	10/42	7/19
Time elapsed from MS diagnosis (yrs) $\bar{X}$/SD	13.0/7.23	11.7/8.88

RLS = restless legs syndrome; MS = multiple sclerosis

There were no significant differences between the RLS positive and RLS negative groups in the global values of EDSS (p=0.735) and the time elapsed from MS diagnosis (p=0.564).

Antidepressant intake was significantly higher in the RLS positive group (p=0.043).

The distribution of RLS prevalence was equal in the two MS clinical courses present in our patients (p=1.000) (Fig. 1). Nine (37.5%) of the 24 RLS positive patients did not inform the attending neurologist about their feeling of leg restlessness.



RRMS = relapsing-remitting multiple sclerosis;
SPMS = secondary progressive multiple sclerosis

Fig. 1. Distribution of the prevalence of restless legs syndrome (RLS) in 2 clinical courses of multiple sclerosis.

Discussion

In our study, RLS prevalence in MS patients was 40%. The estimated RLS prevalence in MS patients varies widely. A meta-analysis that included 24 studies, conducted in 2012[11], showed that RLS prevalence in MS patients ranged from 12.1% to 57.5%. In the studies published after the aforementioned meta-analysis, the estimated RLS prevalence in patients with MS varied from 14.5% to 65.1 %[12-14]. The variation of RLS prevalence in general population is due to differences in demographic factors, health status and study populations[1]. Heterogeneity is also present in the studies that investigated RLS prevalence in patients with MS, which could explain differences in the estimated prevalence among the studies[11]. Pooled analysis performed in the meta-analysis by Schürsk and Bussfeld[11] indicates that MS is associated with a fourfold increase in the odds for RLS compared with people without MS. This is in concordance with our survey, since the estimated prevalence of the idiopathic form of RLS in Croatia is 9.5%[16].

In the present study, there was no age difference between the groups with and without RLS. The same findings have been reported from most of other studies[13,20-22].

The higher prevalence of RLS syndrome in women in our study may have reflected the higher proportion of women with RLS in the general population[1]. Manconi *et al*. also found a higher prevalence of women in the RLS positive group[5], although no gender differences were recorded in other studies[13,20-22]. The time elapsed from MS diagnosis did not differ between the RLS positive and RLS negative groups, which is also consistent with other studies[13,14,20-22]. There was no association between the EDSS score and presence of RLS either; however, we did find positive association between the use of antidepressants and the prevalence of RLS. A higher use of antidepressants in the RLS positive group was recorded in the study by Manconi *et al*.[5], but no such difference was found in the study by Shaygannejad *et al*.[14]. Considering that some antidepressants have the potential of causing RLS[23,24], while others do not[23,25], a different medication regimen could explain, at least partly, the above mentioned differences among the studies.

Our subjects were suffering from RRMS and SPMS, whereas the primary progressive (PPMS) course was not present. We found no significant difference in the prevalence of RLS in any clinical course. Comparable results have been reported by Miri *et al*.[13] and Morieira *et al*.[21], whereas other studies demonstrated an increased prevalence of RLS in patients with RRMS[20] and PPMS[20,22]. Nine (37.5%) of the 24 patients with RLS did not inform the neurologist about their leg restlessness.

Conclusion

In this study, RLS was present in 40% of MS patients. The presence of RLS was associated with female gender and use of antidepressants. More than one-third of patients with RLS did not inform the neurologist about their feeling restlessness in the legs. In a chronic debilitating disease such as MS, long-term preservation of the quality of life in terms of health should be considered as a critical marker of therapeutic success[26]. Due to the high prevalence of RLS in MS patients, there is the need to search actively for RLS symptoms.

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Sažetak

SINDROM NEMIRNIH NOGU KOD OBOLJELIH OD MULTIPLE SKLEROZE – ISKUSTVA BOLESNIKA LIJEČENIH U SPECIJALNOJ BOLNICI ZA MEDICINSKU REHABILITACIJU U LIPIKU

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U studiji je obuhvaćeno 60 oboljelih od multiple skleroze (MS). Svi su bili hospitalizirani u našoj ustanovi od 1. rujna 2014. do 31. prosinca 2014. Cilj rada je bio istražiti učestalost sindroma nemirnih nogu (RLS) i odrediti međusobnu povezanost RLS-a s dobi ispitanika, spolom, stupnjem onesposobljenosti, oblikom MS, vremenom proteklim od postavljanja dijagnoze MS i uzimanjem antidepresiva. Dijagnoza RLS-a postavljena je sukladno kriterijima Međunarodne studijske grupe za sindrom nemirnih nogu (IRLSSG). Od ukupno 60 ispitanika njih 24 (40%) ispunilo je kriterije za postojanje RLS-a. U skupini ispitanika s RLS utvrđena je statistički značajno veća zastupljenost žena i onih koji uzimaju antidepresive. Nije nađena statistički značajna razlika između skupina u odnosu na životnu dob, trajanje bolesti, stupanj onesposobljenosti i klinički tijek MS. Od 24 bolesnika koji su ispunili kriterije za dijagnozu RLS-a njih 37,5% nije obavijestilo neurologa o prisutnim smetnjama. Visoka učestalost RLS-a i činjenica da velik udio oboljelih ne iznosi nadležnom neurologu smetnje iz okvira RLS-a zahtijevaju aktivan pristup u dijagnostici i liječenju.

Ključne riječi: *Multipla skleroza – epidemiologija; Sindrom nemirnih nogu – dijagnostika; Bolnice, specijalne; Hrvatska*