

ORIGINAL ARTICLE

Restless legs syndrome in multiple sclerosis decreases health-related quality of life

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Abstract

BACKGROUND: Neuropsychiatric symptoms like dysesthesia, sleep disturbances and fatigue could be seen in patients suffering from both multiple sclerosis (MS) and restless leg syndrome (RLS). The aim of study was to investigate the prevalence and characteristics of RLS in MS patients.

METHODS: In a cross-sectional study, we used a questionnaire based on official diagnostic criteria for RLS. Data about MS, RLS, sleep and quality of life (QoL) were obtained. Data were statistically analysed.

RESULTS: From all 200 subjects, 26% (n=52) fulfilled all essential criteria for RLS. In RLS-positive group, sleep disturbances, fatigue/excessive daytime sleepiness (EDTS), and reduced QoL were more prevalent than in patients without RLS/WED ($p=0.03$, $p=0.04$, and $p=0.01$, respectively). Sleep disturbances positively correlated with intensity of RLS symptoms ($rs=0.421$). Reduced QoL was significantly correlated with sleep impairment ($rs=0.545$) and fatigue/EDTS ($rs=0.681$). Consumption of benzodiazepines was higher in RLS-positives ($p<0.001$).

CONCLUSION: RLS is prevalent in MS patients and has a negative impact on sleep leading to EDTS. It is possible that RLS/WED is underdiagnosed in MS patients, given the overlap in symptoms between these two conditions. Neurologists should actively search for RLS and treat the symptoms, as they are associated with lower QoL in MS patients.

Abbreviations:

Restless legs syndrome (RLS); Multiple sclerosis (MS); quality of life (QoL); excessive daytime sleepiness (EDTS); benzodiazepines (BZP); International restless legs syndrome study group (IRLSSG)

INTRODUCTION

Restless legs syndrome (RLS) is very common chronic neurological disorder with estimated prevalence of 7–9% in general population. According to the recent scientific data, combinations of genetic and environmental factors contribute to RLS onset. Any condition

leading to (i) iron deficiency, (ii) CNS hypodopaminergic state and/or (iii) spinal hyperexcitability could cause RLS symptoms in predisposed subjects. Primary features of this disorder are:

- an urge to move the legs,
- that worsens during rest or inactivity,

- is relieved by movement,
- is worse in the evening or night.

These symptoms have negative impact on sleep. Conclusively, affected patients suffer from fatigue and excessive daytime sleepiness (EDTS), lack of energy, problems with daily activities, and changes in behaviour, cognition and mood (1).

The aim of this cross-sectional study was to investigate the prevalence, characteristics and impact of RLS symptoms on quality of life (QoL) of the patients with MS.

PATIENTS AND METHODS

We examined random 200 patients recruited from a MS outpatient center within the Second Department of Neurology, Comenius University Bratislava, Slovakia. Inclusion criteria were minimum age of 18 years, and diagnosis of MS according to the revised 2010 McDonald criteria. Data were collected from September to December 2014. After signing informed consent, subjects completed a special questionnaire consisting of:

- demographic data,
- age of MS onset (in years), MS duration (in years),
- presence of sleep disturbances (yes or no), presence of fatigue/EDTS (yes or no), extent of decreased QoL due to sleep disturbances, fatigue and EDTS (none, mild, moderate, severe),
- diagnosis of depression, use of (g) antidepressants and (h) benzodiazepines (BZP).

Demographic data are shown in Table 1.

The main part of questionnaire consisted of 4 official diagnostic criteria according to the International RLS study group (IRLSSG). Subjects, who responded positively for all 4 questions, were assessed as positive for RLS. Experience neurologist excluded subjects with possible RLS mimics. Data on RLS symptoms onset, frequency, intensity and treatment followed. Rest of population was negative for RLS.

Data were statistically analysed using IBM® SPSS® Statistics version 21. We used descriptive statistical methods. Comparing nonparametric data between RLS+ and RLS- groups, we used Mann-Whitney U-test (with significance at $p < 0.05$). Spearman's rank correlation coefficient (Rho) was used to evaluate the association between the measured (nonparametric) parameters.

Tab. 1. Demographic data of MS patients.

n=200		Mean ± SD	Minimum	Maximum
Age	(y)	39.75 ± 9.72	20.00	62.00
MS onset	(y)	31.86 ± 9.15	14.00	61.00
MS duration	(y)	7.89 ± 5.26	0.25	28.00
Gender		males 26.5 %	females 73.5%	

RESULTS

From all 200 subjects, 26% (n=52) fulfilled all essential criteria for RLS (RLS+ subjects). More than 48% of RLS+ subjects (12.5% of all subjects, respectively; n=25) had clinically significant RLS, meaning symptoms of moderate to severe intensity at least twice per week (so called "RLS sufferers").

According to subjects' listed medications, only 16% of "RLS sufferers" (7.7% of all RLS+, n=4) were treated for RLS, (two with pramipexole, and two with pregabalin).

In the RLS+ group, sleep disturbances, fatigue/excessive daytime sleepiness (EDTS) and reduced quality of life (QoL) were significantly more prevalent than in patients without RLS ($p=0.03$, $p=0.04$, and $p=0.01$, respectively), as shown in Figure 1.

In RLS+ subjects, the intensity of RLS symptoms was positively correlated with sleep disturbances (Rho=0.421). This sleep impairment was positively correlated with reduced QoL (Rho=0.545). Also fatigue/EDTS correlated with decreased QoL (Rho=0.681). Patients with RLS used BZP more frequently ($p < 0.001$).

Patient with depression had significantly higher prevalence of sleep disturbances ($p=0.03$) and significantly decreased QoL ($p=0.01$). Sleep disturbances positively correlated with depression (rho=0.968).

DISCUSSION

In our study, the prevalence of RLS in MS patients was 26%. This finding is congruent with various epidemiological studies reporting the prevalence to be between

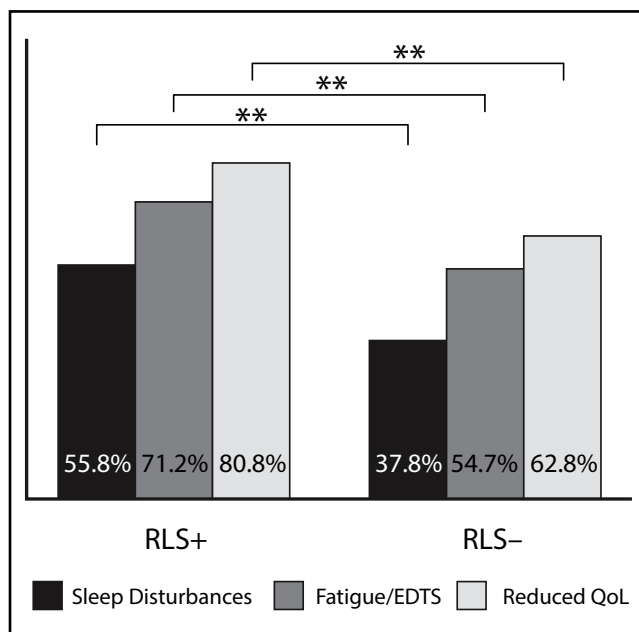


Fig. 1. Significantly higher prevalence of sleep disturbances, fatigue/excessive daytime sleepiness (EDTS) and reduced quality of life QoL ($p=0.03$, $p=0.04$, and $p=0.01$, respectively).

14.1% and 65.1% (Deriu *et al* 2009; Bruno *et al* 2015; Douay *et al* 2009; Auger *et al* 2005; Manconi *et al* 2007, 2008; Vávrová *et al* 2012). Brass *et al* (2014) found that 36.8% of patients with MS had symptoms of RLS; however only 12% the subjects in their study had previously been diagnosed with RLS. In our cohort, 4 out of 52 RLS+ subjects (less than 8%) were already taking RLS medication. This highlights the fact that RLS is underdiagnosed in MS patient more than in general population. One explanation could be the overlap between RLS and MS symptoms, as various dysesthesias, leg discomfort, and sleep disturbances are present in both conditions. Almost one quarter of RLS+ subjects were unable to describe their sensory symptoms; further complicating the diagnostic process.

Untreated subjects experiencing moderate or severe symptoms of RLS at least twice per week are considered as “RLS sufferers” and they represent approximately 2% of general population (Allen *et al* 2003). In our sample of MS patients, the prevalence of RLS sufferers was 12.5% (almost half of RLS+), which requires more attention among health-care providers.

More than 80% of RLS+ subjects in our study reported symptoms occurring either in the evening before sleep, or at night. They also suffered from sleep disturbances, which positively correlated with intensity of their symptoms. Patient previously diagnosed with depression had significantly higher prevalence of sleep disturbances. They were treated with BZP more frequently. This approach could have led to better sleep initiation, but could have been responsible for worsening of fatigue/EDTS. In addition, we confirmed that health-related QoL was also significantly lower in the RLS-positives.

Sleep impairment and fatigue/EDTS are common among MS patients in general, but are present to a significantly higher extent in RLS+ compared to RLS- subjects. Although these symptoms are not easy to treat, symptoms related to RLS may be successfully managed by medication. This is especially important, as our research has demonstrated health-related QoL was also significantly lower in the RLS+ group than the RLS- group.

MS presents with a wide range of neuropsychiatric symptoms including sleep disturbances, fatigue, and EDTS. All of these features lead to decreased QoL.

Management of these symptoms is often difficult, but in approximately one quarter of MS patient, these symptoms may be related to RLS, and thus successfully treated with appropriate medication. Clinicians aware of the overlap between these two conditions may prevent their patients from further QoL deterioration.

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