Original article

Correlation between putative indicators of primary restless legs syndrome severity

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Abstract

Background and purpose: Several methods of assessing disease severity in restless legs syndrome (RLS) have been suggested. The purpose of this study was to examine the relationship between the suggested immobilization test (SIT), the International RLS Study Group rating scale (IRLS), sleep efficiency, and periodic leg movements of sleep index (PLMI).

Patients and methods: Forty primary RLS patients with periodic leg movements of sleep were included in this prospective study. Study procedures were all performed during the same night, beginning with IRLS administration and following with SIT and polysomnography (PSG) evaluations, in that order. SIT was composed of two parameters: SIT mean discomfort score (SIT-MDS) and SIT periodic leg movements of wakefulness index (SIT-PLMW). PSG target measures were PLMI and sleep efficiency. Pearson's correlation was used for analysis at a $P < 0.01$ significance level.

Results: PSG-PLMI correlated with IRLS ($r = 0.462$; $P = 0.003$) and with SIT-PLMW ($r = 0.681$; $P = 0.0004$). A correlation was also found between IRLS and SIT-MDS ($r = 0.447$; $P = 0.004$), even though SIT-PLMW and IRLS did not correlate with each other ($P = 0.286$). A negative correlation was found between PSG-PLMI and sleep efficiency ($r = -0.435$; $P = 0.005$). Neither SIT nor IRLS correlated with sleep efficiency. Only SIT discomfort scores from the second half of SIT correlated with SIT-PLMW ($r = 0.457$, $P = 0.004$), and they had a stronger correlation with IRLS ($P = 0.003$).

Conclusions: This study attempted a much needed comprehensive evaluation of the relationship between various RLS severity indicators. Our findings support a strong role of motor dysfunction on sleep quality in RLS, as well as the potential use of SIT-PLMW as a sensitive indicator of RLS severity.

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Keywords: Restless legs syndrome; Periodic limb movement disorder; Periodic movement disorder; Sleep; Suggested immobilization test

1. Introduction

Restless legs syndrome (RLS) is a sleep-related movement disorder originally described in the 17th century and singled out as a clinical syndrome by Ekbom [1]. In 1995, four essential diagnostic criteria were first established by the International Restless Legs Syndrome Study Group (IRLSSG) [2]. In a recent workshop sponsored by the National Institutes of Health (NIH) [3], the essential diagnostic criteria were revised as follows: (1) an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs; (2) the urge to move or unpleasant sensations that begin or become worse during periods of rest or inactivity such as lying or sitting; (3) the urge to move or unpleasant sensations that are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues; and (4) the urge to move or unpleasant sensations that are worse in the evening or night than during the day or that only occur in the even-

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ing or night. Several methods of assessing the severity of this highly prevalent neurological disorder have been suggested, each one having its own strengths and limitations.

RLS frequently disturbs the quality of sleep, as indicated by objective measures such as sleep latency and sleep efficiency [3,4]. Sleep quality is also assessed by the most frequently used measure of RLS severity, the International RLS Study Group rating scale (IRLS) [5]. This is a purely subjective, self-administered, 10-question instrument, which has been extensively used for clinical and research purposes. Its reliability and validation have been established in multiple centers worldwide [5,6]. Patients answer the questions according to their symptoms and the impact of these symptoms on their lives. Responses are rated on a five-point scale from 0 to 4.

Lugaresi et al. [7] reported that RLS patients often have periodic leg movements of sleep (PLMS). Also seen alone or in association with several other sleep disorders, PLMS are present in the vast majority of RLS patients, 82.2% when recording during one night of polysomnography (PSG) and 87.8% when recording during two consecutive nights of PSG [8]. According to standard criteria, first described by Coleman et al. [9], and revised by the American Sleep Disorders Association [10], PLMS are scored if they occur in series of four consecutive movements lasting 0.5–5 s and separated by 4- to 90-s intervals. A periodic leg movements index (PLMI, described as number of PLMS per hour of sleep) greater than 5 is considered pathologic. High cost and technical complexities, together with less than ideal sensitivity and specificity, preclude the use of PLMI index as a practical indicator of RLS severity.

Introduced by Montplaisir [11] as an objective tool for RLS diagnosis, the suggested immobilization test (SIT) was first used to determine the therapeutic effect of L-dopa in patients with RLS [12]. During this test, the patient sits motionless on a bed with legs outstretched and eyes open while leg movements are monitored by surface electromyogram (EMG) recordings [11]. A score of discomfort is given by the patient every 5 min. The number of periodic leg movements during SIT (periodic leg movements in wakefulness, SIT-PLMW) and the discomfort scores are measured. Michaud et al. [13] reported higher discomfort scores and greater PLMW in RLS patients than in normal controls. When comparing SIT scores with PSG results

from patients with RLS and various other sleep disorders, the same group also found that SIT significantly adds to the diagnostic accuracy of RLS [14]. However, there are several limitations of SIT. SIT results depend on the subjective report of discomfort and the amount of effort applied by patients to keep their legs still. Movements during SIT could progress from voluntary to involuntary. Thus, SIT-PLMW could also be influenced by individual variations of the movements and by technical aspects [15].

The main purpose of this study is to describe the relationship between these various methods in the assessment of the severity of RLS. We did not consider a priori any of these methods to be the measurement of reference for RLS severity.

2. Methods

2.1. Subjects

Forty patients with primary RLS, diagnosed according to IRLSSG diagnostic criteria [2], participated in this study, which was performed in two centers: the National Institutes of Health in Bethesda, MD, USA, and the Erciyes University Medical Faculty, in Turkey. All patients signed written informed consent forms in accordance with Institutional Review Board (IRB) guidelines. They were non-randomly selected by the order in which they came to clinic. All clinical examinations and study procedures were performed by the same physicians in both centers.

Inclusion criteria were as follows: aged between 18 and 80 years, body mass index (BMI) between 19 and 34, PLMI greater than 5, and normal clinical and paraclinical (blood chemistry and routine hematology) examinations. Patients were excluded from study participation on the basis of their unwillingness or inability to stop their usual RLS medications for 7 days prior to the study, evidence of known causes of secondary RLS, clinical and/or biochemical evidence of iron deficiency, and clinical or PSG evidence of a dissomnia or parasomnia other than primary RLS (including subjects with apnea–hypopnea index greater than 5 per hour).

Patient demographics are summarized in Table 1. All RLS-related medications were stopped at least 7 days or 5 half-lives (whichever longer) before the study. Eleven of the patients were newly diagnosed and were not receiving any medication for RLS.

Table 1
Patient demographics

Patients	Number (new diagnosed + under treatment)	Age (years) (mean±SD)	RLS duration (years) (mean±SD)
Male	28 (7 + 21)	54.6±6.2	4.2±4.8
Female	12 (4 + 8)	58.1±9.3	5.4±4.5
Total	40 (11 + 29)	56.7±5.9	4.9±4.1