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Original Article

Increased frequency of restless legs syndrome in chronic obstructive pulmonary disease patients

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Abstract

Background: Despite complaints of poor sleep being very common in people with chronic obstructive pulmonary disease (COPD), restless legs syndrome (RLS) symptoms have not been extensively investigated in these patients.

Objective: To assess the prevalence and severity of RLS in patients with COPD and to investigate the factors potentially associated with RLS.

Methods: A total of 87 patients with COPD and 110 controls, matched for age and sex, were evaluated regarding the presence and severity of RLS symptoms. A diagnosis of RLS was made according to the criteria of the International RLS Study Group (IRSLSSG), and severity was assessed by the IRLSSG severity scale. Excessive daytime somnolence was assessed using the Epworth sleepiness scale (ESS).

Results: RLS was significantly more frequent in COPD patients than in controls (36.8% vs. 11%; $p < 0.001$). Compared to controls, COPD patients with RLS showed higher disease severity (mean IRLSSG severity scale score: 20.5 ± 2.8 for COPD, and 18 ± 3.5 for controls; $p = 0.016$) and more pronounced daytime somnolence (mean ESS score: 11.8 ± 1.1 for COPD, and 8.6 ± 3.6 for controls; $p = 0.009$). Moreover, compared to those without RLS, COPD patients with RLS showed increased daytime sleepiness (mean ESS score: 11.8 ± 1.1 for COPD/RLS, and 7.3 ± 4 for COPD/non-RLS; $p < 0.001$) and longer disease duration (11.9 ± 7 years for COPD/RLS, and 8.7 ± 6.9 years for COPD/non-RLS; $p = 0.045$). Multivariate analysis showed that ESS score was the only factor significantly associated with RLS in COPD patients.

Conclusions: RLS is a frequent cause of disabling sleep disturbance in patients with COPD and should be specifically investigated in these patients.

Keywords: Chronic obstructive pulmonary disease; Restless legs syndrome; Epworth sleepiness scale; Daytime sleepiness; Sleep

1. Introduction

Restless legs syndrome (RLS) is a common sensorimotor sleep disorder which affects 5–15% of the general population [1,2]. The International Restless Legs Syndrome Study Group (IRLSSG) formulated four criteria defining RLS: (1) there is an urge to move the legs, usually accompanied by uncomfortable or unpleasant sensations in the legs; (2) the urge to move the legs begins or worsens during inactivity such as lying or sitting; (3) the urge to move is partially or totally relieved by movements; and (4) the urge to move is worse in the evening or at night [1]. RLS may have profound negative effects on sleep, and symptoms of insomnia or fatigue may frequently be the initially reported complaints.

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Epidemiologic studies suggest that RLS prevalence and disease severity increase with age [1,2], and the incidence is higher among women than among men [1,2]. RLS is considered an idiopathic disorder; however, it is frequently associated with iron deficiency anemia, pregnancy, end stage renal disease, neuropathies, rheumatoid arthritis and Parkinson's disease [1,2].

Chronic obstructive pulmonary disease (COPD) is a very common respiratory disease that afflicts millions of people worldwide, causing progressive and often irreversible airflow obstruction. Although sleep is commonly perturbed in these patients, they seldom disclose sleep-related symptoms [3]. Thus, sleep problems in these patients go unrecognized and significantly impact the quality of their lives [3]. Moreover, sleep-related complaints in these patients have usually been ascribed to disturbed gas exchange and hypoventilation [3,4].

We noticed that RLS seemed to be prevalent among COPD patients, even if no exhaustive study of this association has been published so far. One previous report described increased frequency of RLS symptoms in eight patients with chronic respiratory diseases [5] and another study reported a very high prevalence of RLS in patients receiving lung transplant [6].

We then decided to evaluate the prevalence and severity of RLS symptoms in a population of COPD patients and to investigate the factors potentially associated with RLS occurrence.

2. Methods

This study was approved by the institutional review board. Oral consent was obtained from all participants. A total of 87 consecutive patients with COPD were evaluated during their routine visit to our COPD Clinic between November 2006 and March 2007. The control group was composed of 110 healthy subjects, spouses or friends of the probands, matched for age and sex with the COPD group. All the subjects included in the study underwent a structured interview, including items related to the diagnosis of RLS (see below) conducted by one of the authors (D.L.C.) who was expert in sleep disorders. Clinical conditions that could mimic RLS symptoms (such as neuropathic pain syndromes, leg akathisia, nocturnal leg cramps, and propriospinal myoclonus) were excluded. We collected demographic data (age and sex), family history of RLS, associated diseases, drug or oxygen intake, sleep disorders and COPD duration. COPD disease severity was classified according to the Global Initiative for Obstructive Lung Disease (GOLD) staging system, which comprises four stages (from stage I or "mild" to stage IV or "very severe") based on Forced Expiratory Volume in 1 s (FEV_1) [7]. Daytime somnolence was evaluated using the Epworth sleepiness scale (ESS) [8]. Higher scores on the ESS implied a greater average propensity to fall asleep. Excessive daytime sleepiness (EDS) was defined by an ESS score $\geqslant 10$. Blood biochemical variables were taken from the patients' case notes and included hemogram, creatine, urea, iron, ferritin and transferrin. Basic demographic data of the COPD patients and controls are described in Table 1. The two groups were only significantly different on ESS score that was higher in COPD patients (mean ESS score 8.98 ± 3.89) than in controls (mean ESS score 5.58 ± 2.24; $p < 0.001$).

The presence or absence of RLS was assessed using the minimal criteria of the IRLSSG [1]. When RLS criteria were met the RLS severity scale was also applied [9]. The IRLSSG severity scale consists of 10 items assessing subjective severity of RLS-related complaints on a scale from 0 to 4, with a maximum score of 40. Moreover, a detailed description of RLS symptoms when they were present was recorded.

2.1. Statistics

Continuous variables were compared with the Student's *t*-test, and categorical variables were analyzed using the chi-squared test. Multivariate logistic regression was used to investigate the independent effect of each putative risk factor (age, sex, ESS score, COPD duration). Calculation of sensitivity and specificity at different cutoff points of ESS score were performed, using optimal cutoff values determined by receiver operating characteristics (ROC) curve analysis. The positive predictive value (PPV) and negative predictive value (NPV) were calculated for the optimal cutoff value in the ROC curve according to the Bayesian formula. Spearman correlation coefficients (ρ) were used to estimate the strength of the relationships between ESS score and the demographic or clinical variables of interest. SPSS 10.0 for Windows (Chicago, IL) was used for all statistical analyses. P values < 0.05 were considered to indicate statistical significance.

3. Results

Symptoms of RLS were more frequent in COPD patients (36.8%) than in controls (11.8%) (Table 1; $p < 0.001$). Main demographic and clinical features of the COPD patients and controls with RLS are shown in Table 2. Among the 32 COPD patients with RLS, 12.5% had a positive family history of RLS. A positive family history was also present in 15.4% of controls, and the difference was not significant ($p = 0.57$). Compared to controls, COPD patients with RLS showed higher disease severity (mean IRLSSG severity scale score: 20.5 ± 2.8 for COPD, and 18 ± 3.5 for controls; $p = 0.016$) and more pronounced daytime somnolence (mean ESS score: 11.8 ± 1.1 for COPD, and 8.6 ± 3.6 for controls; $p = 0.009$). Moreover, in the COPD group