Original Article

Insomnia symptoms, objectively measured sleep, and disease severity in chronic obstructive pulmonary disease outpatients

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ABSTRACT

Background: Sleep disturbances are known to have a negative impact on a range of clinical outcomes in chronic obstructive pulmonary disease (COPD). We examined the associations of insomnia symptoms and objectively measured sleep parameters to a composite score for *b*ody mass index, airflow *o*bstruction, *d*yspnea, and *e*xercise capacity (BODE) index (a multidimensional index of COPD severity), arterial blood gases, nocturnal respiratory disturbances, periodic limb movements (PLM), psychologic distress, pain, age, and sex.
Methods: The sample comprised 73 COPD outpatients (mean age, 63.6 years; standard deviation {SD}, 7.5; range 47–85 years; 41.1% women). Insomnia symptoms were measured with the Bergen Insomnia Scale (BIS) and sleep efficiency (SE), slow-wave sleep (SWS), and total sleep time (TST) were assessed with clinical polysomnography (PSG).
Results: BODE index was positively associated with composite BIS score ($P = .040$). Patients with more severe COPD presented more complaints of nonrestorative sleep compared to patients with less severe COPD ($P = .010$). In multivariate analysis, the composite BIS score was independently associated with PLM ($P < .001$), nocturnal respiratory disturbances ($P = .001$), pain ($P = .031$), and psychologic distress ($P = .044$) but not with the BODE index. Objectively measured sleep variables were not associated with any of the health-related variables.
Conclusion: Insomnia symptoms in COPD patients result from a wide range of health-related factors. More severe COPD may be associated with a subjective experience of nonrestorative sleep but not with objectively measured sleep variables.

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1. Introduction

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality worldwide. The prevalence of COPD peaks in those over the age 65 years [1]. In recent years, the number of women with COPD has increased [2]. In addition to respiratory symptoms, COPD patients often report sleep impairment, and disturbed sleep has been found to be the third most common symptom in COPD after dyspnea and fatigue [3].

Patients with COPD report a higher prevalence of insomnia (33%) than the general population [4]. The prevalence of parasomnias and circadian rhythm sleep disorders in COPD patients currently is unknown [5], but there is some indication of a high frequency of restless legs syndrome (RLS) and periodic limb movement disorder in this patient group [6,7]. Patients with COPD often present with symptoms of obstructive sleep apnea (OSA), such as frequent snoring, apneas or hypopneas, and excessive daytime sleepiness [8], and 10–15% of patients may have comorbid OSA [9,10]. Despite the high prevalence of insomnia and other sleep disorders, sleep is an aspect that frequently is ignored in research protocols designed to assess the impact of COPD [11].

During sleep, there normally are reduced respiratory responses to chemical, mechanical, and cortical inputs; increased partial pressure of carbon dioxide; and reduced partial pressure of arterial

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blood oxygen. These changes do not have adverse effects in healthy individuals but may cause problems in patients with COPD [12]. In patients with severe COPD, sleep quality may be undermined by sleep fragmentation due to frequent arousals and repeated nocturnal hypoxemia [7,13].

Interestingly, results from previous research suggest that COPD severity is not strongly associated with subjective sleep complaints [8,14–16] or with impaired objectively assessed sleep variables [17]. In the studies mentioned above, COPD severity has been assessed with spirometry according to the existing diagnostic guidelines [18]. However, COPD produces structural and functional effects beyond its pulmonary components, and there currently is a consensus that airflow limitation by itself does not adequately describe the complexity of the disease [19].

In addition to the disease-related variables, insomnia and other sleep disturbances in COPD patients may be related to other health-related factors, such as obesity, other medical disorders, pharmacotherapy, psychologic distress, and pain; COPD patients also may be correlated to demographic characteristics (e.g., age, sex) [20,21]. Thus considering a range of potential mechanisms of sleep disturbances can lead to a better understanding of the relationship between COPD and disturbed sleep.

In our study, we assessed symptoms of insomnia and objective sleep variables in a sample of COPD outpatients. The composite score for *body* mass index, airflow *obstruction, dyspnea,* and *exercise* capacity (BODE) index was used to categorize disease severity. The BODE index is a composite marker of disease, which aims to determine the systemic nature of COPD, and has been found to better predict mortality and health-related quality of life than spirometry alone [22,23]. To the best of our knowledge, no previous study has examined the associations between the BODE index and sleep parameters in COPD. Against this background, the aims of our study were to: (1) examine the association between insomnia, objectively measured sleep variables (sleep efficiency [SE], slow-wave sleep [SWS], total sleep time [TST]), and the BODE index, as well as arterial blood gases as indices of respiratory status; (2) characterize the pattern of insomnia symptoms with regard to the BODE index score; and (3) investigate the independent associations between insomnia and objectively measured sleep variables with age, sex, sleep-related breathing disturbance, periodic limb movements (PLM), psychologic distress, and pain.

2. Materials and methods

2.1. Study sample

Patients with COPD were recruited for our study from an outpatient pulmonary clinic at the Haukeland University Hospital, Bergen, Norway. During a period of 18 months, COPD patients attending a pulmonary rehabilitation program and participants scheduled for follow-up visits in a longitudinal COPD study (the Bergen COPD cohort study) [24] were invited to participate in a sleep study. There were no other inclusion criteria besides COPD diagnosis. A written informed consent was obtained from all participants, and the patients were not compensated for participation. The study was approved by the Regional Committee for Medical Research Ethics in Western Norway and by the National Data Inspectorate.

2.2. Measures

2.2.1. BODE index

The BODE index integrates four factors relevant to the respiratory, perceptive, and systemic aspects of COPD, including body mass index, the degree of airflow obstruction, functional dyspnea,

and exercise capacity; the latter is assessed with a 6-min walking test (6MWD). Each component is graded and a composite score from 1 to 10 is obtained, with higher scores indicating greater severity. The index score reflects the impact of both pulmonary and extrapulmonary factors on the prognosis and survival in COPD.

Spirometry was performed with a Vitalograph S-model according to the American Thoracic Society criteria [25]. The Medical Research Council Dyspnea Scale was used for assessing the impact of dyspnea on physical functioning. Exercise tolerance was assessed with the shuttle walk test (SWT). For the purposes of calculating the BODE index score, the SWT results were converted into 6MWD scores by applying the conversion algorithm 6MWD = 195.2 + 0.82 (SWT) [26]. In addition, arterial blood gas analyses were performed the day after the second night of sleep registration on a Radiometer ABL 525 within 5 min of sampling.

2.2.2. Insomnia

Insomnia symptoms were assessed with the Bergen Insomnia Scale (BIS) [27]. The BIS has adequate psychometric properties and has been validated against subjective and polysomnographic data. It comprises six items based on the diagnostic criteria for insomnia in the *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition (text revision) [28] and covers the last month, which is in line with the time criterion for insomnia. Each item is rated on an 8-point scale, ranging from 0 to 7 (number of days per week experiencing symptoms). A total composite score is calculated, which ranges from 0 to 42. In a validation study, the mean BIS scores were 10.7 (standard deviation [SD], 9.7) in a representative community sample and 22.5 (SD, 9.9) in a patient sample that was recruited from a sleep clinic [27].

A dichotomous score for the presence or absence of insomnia also can be calculated [27] according to the definitions of insomnia by the American Psychiatric Association [28] and the clinical criteria suggested by Lacks and Morin [29]. Insomnia was operationalized by (1) reporting either sleep-onset latency, wake time after sleep onset, or early morning awakenings exceeding 30 min, or by (2) nonrestorative sleep for a minimum of three nights a week and reporting daytime sleepiness or dissatisfaction with sleep at least 3 days per week [29]. The internal consistency of the BIS as measured by the Cronbach α coefficient was .80 in the study sample, indicating a satisfactory reliability.

2.2.3. Objectively measured sleep

SE, SWS, and TST were registered with all night polysomnography (PSG). The participants underwent two nights of clinical PSG recordings. The recordings included a 4-channel electroencephalogram, electrooculogram, submental electromyogram, and electrocardiogram (Embla, ResMed, Norway). Additionally, an electromyogram of anterior tibialis, thoracic and abdominal motion, airflow using a nasal cannula/pressure transducer, and blood oxygen saturation using pulse oximetry were recorded. All participants met at the pulmonary clinic, in which ambulatory PSG equipment was hooked up by trained sleep laboratory technicians. Following the PSG hookup, the participants returned home and were instructed to follow their normal sleep routine. Data from the second night of PSG were used in the analyses to avoid first-night effects. A registered polysomnographic technologist scored all PSG recordings. Sleep stages, sleep-related breathing events, and PLM were scored according to the criteria of American Academy of Sleep Medicine [30].

2.2.4. Other health-related variables

Psychologic distress was assessed with the Hospital Anxiety and Depression Scale (HADS) [31], which is a self-administered questionnaire comprising 14-point Likert rating scale items, each scored from 0 to 3. Thus the total score ranges from 0 to 42. A total score of 15 or higher has been proposed for detecting clinically