Abstract

Purpose: The aim of this survey was to gather data about the incidence of various sleep disorders, particularly sleep apnea, in subjects with IPF who participated in a regional patient-oriented seminar on this condition. We hypothesized that the frequency of Obstructive Sleep Apnea (OSA) and psychiatric sleep disorders would be disproportionately high in the IPF population.

Methods: The project was a one-time survey administered to stable patients with IPF and their family members from the South eastern USA who participated in the “Living with IPF” public seminar at the Emory University campus. The survey used a validated questionnaire, i.e., Sleep Disorders Questionnaire (SDQ), to detect presence of Sleep Apnea (SA) and selected sleep disorders - Restless Legs Syndrome (RLS), Psychiatric Sleep Disorders (PSY) and narcolepsy (NAR). The questionnaire was administered to all participants (with and without IPF), in a confidential manner. The findings were used to determine if there were differences in the incidence of SA and other sleep disorders between individuals with IPF and those without the disease.

Results: A total of 52 people agreed to participate in the study. One subject was excluded due to unclear IPF status. The median SDQ raw scores in IPF patients for SA, RLS, PSY and NAR were 28.7, 27.1, 26.2 and 26.5, respectively; overall, they were not statistically different in IPF patients versus control subjects. However, as validated in other studies, patients with history of OSA had significantly higher SDQ-SA scores.

Conclusions: The present study aimed to investigate cross-sectionally the incidence of self-reported sleep conditions in patients with IPF versus healthy family member controls. Overall, we did not find a disproportionately higher incidence of sleep disorders in the IPF population. This may be explained by inherent methodological limitations and the small sample size.

Keywords: Idiopathic pulmonary fibrosis; Obstructive sleep apnea; Restless legs syndrome; Narcolepsy; Psychiatric sleep disorders

Introduction

Obstructive Sleep Apnea (OSA) associated with excessive daytime sleepiness, or OSA syndrome, is estimated to occur in 1 of 20 adults or about 5% of the general population in the United States [1]. An epidemiological review by Young et al. estimates that about 1 in 5 adults have at least mild OSA and 1 in 15 adults have at least moderate OSA [2]. OSA is becoming increasingly prevalent. Nevertheless, mainly due to lack of awareness by the public and healthcare professionals, the vast majority remain undiagnosed and untreated. Data from the Wisconsin Sleep Cohort study estimated that 93% of women and 82% of men with moderate-to-severe sleep apnea were undiagnosed [3]. A follow-up publication from the Wisconsin Cohort Study five years later indicated that the prevalence of OSA in people aged 30-60 years was 9-24% for men and 4-9% for women [2].

Idiopathic Pulmonary Fibrosis (IPF) is a progressive fibrosing lung disease of unknown etiology that affects an estimated 160,000 Americans, and accounts for over 15,000 deaths a year [4]. The median survival from the time of diagnosis is 2 to 3 years [5]. To date, most of the pharmacologic agents evaluated in clinical trials in IPF have failed to demonstrate improvement in clinically meaningful outcomes (e.g. symptoms, functional status or survival) [6]. The absence of any effective treatment for IPF suggests that the recognition and treatment of comorbid sleep conditions in IPF patients should become a priority in their management [7,8].

The aim of this survey was to gather data about the incidence of restless legs syndrome, psychiatric sleep disorders, narcolepsy and OSA in subjects with IPF, who participated in a regional patient-oriented seminar on this condition. Recently published studies report an increased incidence of OSA in patients with IPF [7,9,10]. Prior studies have demonstrated interdependence between upper airway size in OSA and lung volumes. Snorers with OSA were found to have a more dramatic fall in measured pharyngeal cross-sectional area as lung volume decreased [11,12]. In spite of overall lack of effectiveness in IPF, until recent years Gluco Cortico Steroids (GCS) were often used in treatment regimens for IPF. The well known corticosteroid-related central fat deposition in the neck region may be a reason for the deterioration of underlying OSA during the course of IPF.

To the best of our knowledge, there are no published English

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studies investigating the frequency of insomnia, narcolepsy and restless legs syndrome in patients with IPF. The main goal of the present study was to investigate cross-sectionally the frequency of common sleep disorders in patients with IPF. We hypothesized that the frequency of sleep apnea and psychiatric sleep disorders is disproportionately increased in the IPF population.

Methodology

Aims

This survey was designed to serve as a pilot investigation on the types and incidence of comorbid sleep disorders, particularly sleep apnea, in subjects with IPF participating in a regional patient-oriented awareness day. Unaffected participants (family members attending the event) were also surveyed and analyzed as controls. This project was a one-time survey of participants in the “Living with IPF” seminar, using a validated questionnaire to detect the presence of sleep apnea and selected sleep disorders. The questionnaire was administered to all participants with and without IPF in a confidential manner. The findings are used to determine if there are differences in the incidence of sleep apnea and other sleep disorders between individuals with IPF and those without the disease.

Study population and study site

The survey was administered to stable patients with IPF from the South eastern USA who participated in the “Living with IPF” public seminar on November 12, 2005 at the Emory University campus. Unaffected participants were also surveyed and represented the control group. The “Living with IPF” public seminars typically had up to 50 subjects with IPF in addition to family members, leading to about 200 participants in total. Institutional Review Board (IRB) at Emory University approved the protocol prior to the survey. The diagnosis of IPF was generally made according to the standard of clinical care at that time, i.e., in approximately 60% of the patients by lung biopsy and in 40% by correlating the clinical and tomographic features of their presenting condition.

Survey instrument - Sleep disorders questionnaire (SDQ)

The SDQ was designed and validated by Sleep Lab Software Ltd., (Ann Arbor, MI). SDQ is a 175-item questionnaire which ascertains the risk of having or developing a sleep disorder. The SDQ was derived from Sleep Questionnaire and Assessment of Wakefulness (SQAW), used since the 1970s at Stanford University. Four sleep domains are assessed: Sleep Apnea (SA), narcolepsy (NAR), Psychiatric Sleep Disorders (PSY), and Restless Legs Syndrome (RLS). For each category, total score ranges from 0 to 60. In validative cohorts, SA and NAR scales proved to be the most discriminating and to have the highest sensitivity, specificity, positive and negative predictive values compared to PSY and RLS scales. Typically, the survey takes 60–90 minutes to complete, though individuals with a high school reading level may finish as quickly as 25 minutes [13].

The questionnaire was offered to all participants along with a demographic sheet with queries about age, gender, height, weight, history of OSA, other sleep problems, Positive Airway Pressure (PAP) use, oxygen use, lung problems, heart problems and smoking status. The sheet clearly states that no identifying information is present and destroyed the envelopes. The questionnaires were then given to the investigators for analysis.

Analysis

Each question of the SDQ was rated by the subject nominally as “never,” “rarely,” “sometimes,” “usually,” or “always.” The responses are converted to an ordinal scale of 1 to 5, respectively. Higher numerical scores reflect greater clinical severity of symptom. The sum of individual responses previously validated to predict the presence of each of the four categories of sleep disorders - sleep apnea, narcolepsy, psychiatric sleep disorder, and restless leg syndrome, generate a raw score for each category. The raw scores of subjects with IPF were compared to individuals without the disease in each category using nonparametric methods (Wilcoxon test). The Chi-square test (with Fisher correction, where needed) was used to test for differences between the control group and subjects with IPF, among the four categories of sleep disorders. JMP 9.0 (SAS Inc., Cary, NC) was used for the statistical analysis.

Results

A total of 52 people agreed to participate in the study. One subject was excluded due to unclear IPF status. The participant characteristics for IPF patients (n = 27) and control subjects (n = 24) are shown in table 1. The subjects in the IPF group were generally older than the control group. The age distribution of the cohort is shown in Figure 1 (median age of 62). As expected, more males were present in the IPF group. The Body Mass Index (BMI) was slightly lower in the control group, although not statistically significant (p = 0.24).

The median raw scores for sleep apnea, restless legs syndrome, psychiatric sleep disorders and narcolepsy were not statistically different in the IPF patients vs control subjects. The median score and 25th–75th interquartile ranges are shown in table 2. Of note, the median raw scores did not differ between males and females of the IPF and the control groups (data not shown). Patients with history of sleep apnea had on average a higher SDQ-SA score, which was statistically

| Demographic Variable | IPF Median (25th, 75th percentiles)* | Control Median (25th, 75th percentiles)* |
|----------------------|------------------------------------|----------------------------------------|
| Age                  | 65 (59, 71)                        | 56 (48.5, 64)                          |
| Gender (M/F)         | 16/11                              | 6/18                                   |
| BMI**                | 28.1 (24.5, 1.8)                   | 26.9 (22.3, 29)                        |
| Smoking status 0/27  |                                    | 3/24                                   |

*Non-normally distributed data shown as median (25th, 75th percentiles).
**BMI, Body Mass Index

Table 1: Demographic data.
significant and shown in Figure 2. The SA-SDQ has a total of 12 items, out of which only one item [Q139: ‘I have a problem with my nose blocking up when I am trying to sleep (allergies, infections)’] reached statistical significance (p=0.04). The RLS-SDQ has a total of 9 items, out of which one item [Q45: ‘I feel that I have insomnia’) reached statistical significance (p=0.05). The PSY-SDQ has a total of 9 items, out of which one item [Q101: ‘Someone in my family has been hospitalized for a psychiatric illness or nervous breakdown’) showed statistical significance (p=0.002). The NAR-SDQ has a total of 15 items, out of which one item [Q67: ‘I get sudden muscular weakness when laughing, angry or in situations of strong emotions’) showed statistical significance (p=0.03).

Discussion

It is increasingly recognized that OSA has significant attributable morbidity (and, possibly, mortality). Well recognized complications associated with OSA include systemic hypertension, pulmonary arterial hypertension, insulin resistance, metabolic syndrome and potentially atherosclerosis, mediated by sleep fragmentation, intermittent hypoxemia or oxidative stress mechanisms [14,15]. While and potentially atherosclerosis, mediated by sleep fragmentation, arterial hypertension, insulin resistance, metabolic syndrome fat deposition in the neck region may be a reason for the deterioration architecture, etc. [16,17]. Also, the well known corticosteroid-related insomnia, frequent nocturnal awakenings and alterations in sleep stage effects on sleep quality, causing sleep-onset and sleep-maintenance efficacy in this condition. Corticosteroids have well known negative treatment regimens for IPF population, despite the apparent lack of

In summary, using SDQ and a sample of patients with IPF and family member controls, we found that there was no increase in the incidence of sleep apnea, restless legs syndrome, psychiatric sleep disorders or narcolepsy in IPF. Concordant with prior studies, in our survey, patients with history of Obstructive Sleep Apnea (OSA) had higher SDQ-SA scores. Nevertheless, larger studies are needed to thoroughly evaluate the incidence of restless legs syndrome, psychiatric sleep disorders and narcolepsy in patients with IPF.

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