ORIGINAL ARTICLE

Sleep Disordered Breathing in Chronic Obstructive Pulmonary Disease

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ABSTRACT

We prospectively studied sleep disordered breathing in 50 consecutive patients (39 males) with chronic obstructive pulmonary disease (COPD) with chronic respiratory failure (CRF) (n=33) and without CRF (n=17) by performing polysomnography. Patients with CRF had a lower mean nocturnal oxygen saturation (SaO_2 %) (88.6 ± 6.7 *vs.* 96.3 ± 0.8; p=0.0001) and a lower *minimal* nocturnal SaO_2 (73.6±12.0 *vs.* 84.3 ± 7.3; p=0.002) compared to those without CRF, suggesting that patients with CRF tend to have more severe drops in nocturnal SaO_2. Patients with CRF also had a lower FEV_1 (% predicted) (p=0.01) and PEFR (% predicted) (p=0.031) compared to those without CRF suggesting an indirect relation to the oxygen saturation. Other pulmonary functions were comparable between both the groups. Among patients with and without CRF, the total sleep time (minutes); the rapid eye movement (REM) stage (% of total sleep time); the non-rapid eye movement (NREM) stage (% of total sleep time) were comparable (p=NS). Only three of the 50 patients with COPD had a significant (>5) apnea-hypopnea index (AHI) (total no. of apneas + total no. of hypopneas/ total sleep time [(hours) = AHI] and these three patients had a mean BMI = 27.7 which was higher than the mean BMI of the whole group (21.1). The AHI was comparable in patients with and without respiratory failure. Multiple regression analysis revealed a positive correlation between AHI and the neck circumference (r=0.41; p=0.005) and BMI (r=0.31; p=NS). There was a small but statistically insignificant negative correlation between AHI and neck length (r= -0.28; p=NS). We conclude that, BMI *per se* contributes to the AHI and nocturnal desaturation in patients with COPD.

Key words : *Sleep disordered breathing, Chronic obstructive pulmonary disease, Chronic respiratory failure.*

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INTRODUCTION

Sleep apnea is defined as cessation of nasobuccal airflow for 10 seconds or more during sleep associated with a drop in arterial oxygen saturation of at least 4% from the baseline. Though the first literary description of apnea was given by Charles Dickens[1], the modern medical history of the syndrome began when polygraphic technique was used by Burwell *et al*[2]. to study sleep disordered breathing in a patient who had the so-called "Pickwickian syndrome".

Obstructive sleep apnea (OSA) constitutes an important component of sleep disordered

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breathing because of the availability of the effective therapeutic modalities. Some of the studies reported earlier have shown a high prevalence of increased apnea-hypopnea index (AHI) in patients with chronic obstructive pulmonary disease (COPD), which was explained on the basis of high individual prevalence of both of these disorders[3]. The co-existence of AHI and COPD has been termed "overlap syndrome[4]. Very often the overlap syndrome is associated with obesity which is an independent risk factor for sleep disordered breathing[4]. Thus, the prevalence of sleep disordered breathing in non-obese patients with COPD remains to be assessed. Furthermore, there are few reports on sleep disordered breathing in COPD patients with chronic respiratory failure. The present study was designed to evaluate the prevalence of sleep disordered breathing in COPD patients with and without respiratory failure.

MATERIAL AND METHODS

Fifty consecutive patients with COPD selected from the Medicine ward, Medical Out-patient Department, and the Chest Clinic of the All India Institute of Medical Sciences (AIIMS) Hospital, New Delhi between March 1998 and February 2000 were studied. Out of these, 39 were males. Chronic bronchitis was diagnosed as per the British Medical Research Council criteria[5]. Emphysema was diagnosed as per the radiological criteria of Laws and Heard[6]. Patients with associated renal, hepatic or cardiovascular disease, pregnancy, unconscious patients and those who were unwilling to participate in the study were excluded. Informed consent was obtained from all the patients.

A detailed history was recorded and a thorough physical examination was done. Detailed otorhinolaryngological evaluation was done in 32 patients by a specialist otorhino-laryngologist who was not aware of the findings of the sleep study.

Anthropometry

Weight and height were measured to the nearest 500 g and one cm, respectively and the body mass index (BMI) was calculated based on the formula [BMI = weight (kg) / height^2 (m^2)]. Neck circumference (cm) was measured at the level of cricothyroid membrane. Neck length (cm) was measured from occipital tubercle to the vertebra prominens.

Pulmonary Functions

Pulmonary functions were evaluated in all the patients. The lung volumes and their subdivisions were measured using a constant volume variable body pressure body plethy-smograph [P.K. Morgan Chatham, Kent, U.K.]. Airway resistance and thoracic gas volume were estimated with the patient panting inside the box at a frequency of one Hz. The patients were instructed to withhold the morning dose of inhaled bronchodilators on the day of pulmo-nary function testing.

Imaging Studies

In all patients chest radiograph (postero-anterior view) was taken. Lateral cephalometry was performed in 34 patients with specific emphasis on soft tissue and bony landmarks to look for abnormalitis of craniofacial and upper airway anatomy. Posterior airway space was measured by a line drawn from point B (supramentale) through Go (gonion). This line intersects the base of the tongue and posterior pharyngeal wall. The linear measurement between the base of the tongue and the posterior pharyngeal wall was taken as the measure of posterior airway space.

Arterial Blood Gas Analysis

In all the patients, arterial blood gas (ABG) analysis was done using ABL3 arterial blood gas analyser (Radiometer, Copenhagen). Based on the ABG analysis, patients were categorised as having type-I respiratory failure if they manifested arterial hypoxemia (PaO_2< 60 mm Hg) with normal carbon dioxide tension. If they manifested arterial hypoxemia (PaO_2< 60 mm Hg) with hypercarbia ($PaCO_2$>50 mm Hg), they were categorised as type-II respiratory failure.

Polysomnography

Patients reported to the Sleep Laboratory of the Department of Medicine at 8 : 00 p.m. on the day of their appointment. They were hooked to Alice 3 infant and adult computerised polysomnography machine (Healthdyne Technologies, USA) by standard gold cups after cleansing the area of attachment by spirit followed by Omniprep®. The patient was requested to sleep at around 21:00 hrs. The recording of sleep study was started after ensuring that the impedance of electrodes was set to zero. The parameters monitored included electroencephalogram (EEG), electrooculogram (EOG), electgrocardiogram (ECG), chin and leg electromyogram (EMG), nasal airflow, tracheal breath sounds, thoracic wall movements, abdominal movements, transcutaneous oxygen saturation, body position and continuous positive airway pressure (CPAP) measurement where required. The sleep data recorded by the computer were manually scored for sleep stages, apneas, and hypopneas. AHI was calculated based on the following formula :

$$AHI = \frac{\textit{Total no. of apneas + total no. of hypopneas}}{\textit{Total sleep time (in hours)}}$$

AHI>5 was considered significant.

Statistical Analysis

Anthropometric parameters, pulmonary functions and polysomnographic findings in COPD patients with and without respiratory failure were compared using Student's 't' test; p value < 0.05 was considered to be significant. Regression analysis was used to study the relation between the AHI and anthropometric variables, pulmonary functions and polysomnographic parameters. Statistical analysis was performed using statistical software package STATA (version 6).

RESULTS

The mean age was 54.2 years (range 35 to 78 years; 39 males). Of these, 33 patients had respiratory failure (mean age 54.4 years; SD 10.4; range 35-78). Out of these, 15 had type-I and the remaining 18, type-II respiratory failure. Their anthropometric variables, pulmonary functions and arterial blood gas analysis findings are presented in table 1. Polysomnographic findings in patients with and without respiratory failure are presented in table 2.

Mean BMI was in the normal range in both the groups. Patients with respiratory failure had a lower mean nocturnal oxygen saturation (SaO_2, %) (p=0.0001) and a lower *minimal* nocturnal SaO_2 (p=0.002) compared with those without respiratory failure (Table 2). While there was no statistically significant difference in the mean nocturnal and daytime baseline SaO_2 values in patients without respiratory failure, the mean nocturnal SaO_2 was lower as compared to the day time SaO_2 in patients with respiratory failure. Most of the study patients had cardiac arrhythmias associated with a drop in saturation and included classical bradycardia associated with obstructive sleep apnea and tachyarrhythmias.

Sub-group analysis did not reveal any significant difference in the results in patients with type-I and type-II respiratory failure. Therefore, patients with type-I and type-II respiratory failure were considered together as a single group of "respiratory failure". Thus, patients with respiratory failure also had a lower forced expiratory volume in first second (FEV_1) (p=0.01) and peak expiratory flow rate (PEFR) (p=0.034) as compared to those without respiratory failure (Table 1). Other pulmonary functions were comparable between the two groups. Among the patients with and without respiratory failure, the total sleep time (minutes), the rapid eye movement (REM) stage (% of total sleep time), and the non-rapid eye movement (NREM) stage (% of total sleep time) were camparable (p=NS) (Table 2). Only three of the 50 patients with COPD had a significant (>5) AHI and these three patients had a mean BMI = 27.7 which was higher than the mean BMI of the whole group (21.1 kg/m^2). The mean AHI was comparable in patients with and without respiratory failure. Regression analysis revealed a positive correlation between AHI and the neck

Table 1. *Anthropometric variables, pulmonary functions and arterial blood gases in patients with chronic obstructive pulmonary disease with (n=33) and without respiratory failure (n=17)*

Variable	Without respiratory failure (n=17) Mean ± SD	With respiratory failure (n=33)‡ Mean ± SD	p value
Age (years)	53.5 ± 8.2	54.4 ± 10.3	0.81
BMI (kg/m^2)	22.2 ±5.5	20.6 ± 4.8	0.27
Neck circumference (cm)	35.1 ± 3.1	35.8 ± 4.1	0.5
Neck length (cm)	11.2 ± 1.1	10.4 ±1.7	0.08
Posterior airway space (cm)*	1.6 ± 0.5	1.6 ± 0.6	0.93
FEV_1†	49.8 ± 19.4	34.8 ± 13.6	0.002
FEV_1, FVC (%)	82.6 ± 40.5	66.9 ± 17.7	0.061
PEFR†	44.7 ± 28.9	31.4 ± 14.5	0.03
TLC†	80.5 ± 27.6	70.7 ± 25.7	0.23
		Type I respiratory failure (n=15)	Type II respiratory failure (n=18)
pH	7.39 ± 0.01	7.4 ± 0.01	7.39 ± 0.01
$PaCO_2$ (mm Hg)	43.4 ± 2.6	43.2 ± 2.8	54.6 ± 4.1
PaO_2 (mm Hg)	75.2 ± 5.6	56.6 ± 2.5	67.3 ± 3.6
HCO_3 (meq/L)	28.5 ± 1.9	31.0 ± 2.0	34.8 ± 3.3

* = Tested in 13 of the 17 patients without and 21 of the 33 patients with respiratory failure.
† = Variables expressesd as % predicted; ‡=Patients were receiving oxygen through face mask (FiO_2=0.4) . n=number of subjects, SD = standard deviation, BMI = body-mass index, FEV_1=forced expiratory volume in the first second, PEFR = peak expiratory flow rate, FEV_1/FVC = ratio of the forced expiratory volume in one second to forced vital capacity, TLC = total lung capacity.

Table 2. *Polysomonographic findings in patients with chronic obstructive pulmonary disease with (n=33) and without chronic respiratory failure (n=17)*

Variable	Without respiratory failure (n=17) Mean ± SD	With respiratory failure (n=33) Mean ± SD	p value
Total sleep time (min)	490.6 ± 92.7	468.5 ± 63.5	0.35
Rapid eye movement stage	14.4 ± 13.3	11.8 ± 9.8	0.20
Non-rapid eye movement stage*	60.2 ± 16.1	66.0 ± 12.0	0.71
Day time oxygen saturation	95.3 ± 1.3	91.4 ± 2.3	0.001
Nocturnal oxygen saturation (%)	96.3 ± 0.8	88.6 ± 6.7	0.0001
Minimum nocturnal oxygen saturation (%)	84.3 ± 7.3	73.6 ± 12.0	0.0028
Episodes of desaturation	20.9 ± 21.3	29.3 ± 23.7	0.27
Apnea-hypopnea index	1.1 ± 1.6	1.8 ± 2.3	0.33

*Expressed as % of total sleep time.

circumference (r=0.41; p=0.005) but not between AHI and BMI (r=0.31; p=NS) or between AHI and neck length (r= -0.28; p=NS). Further, there was no statistically significant correlation between any of the pulmonary function parameters and polysomnographic findings.

DISCUSSION

Earlier studies have reported a high prevalence of obstructive sleep apnea and other related breathing disorders in patients with COPD[4,7]. These studies had a selection bias and included patients from sleep clinics. These patients had excessive daytime somnolence as one of the chief complaints. Moreover, these patients were obese and obesity itself is a risk factor for sleep disordered breathing. Our patients did not have complaints of excessive daytime somnolence and their mean BMI was in the normal range. We observed that only three of our patients had significant AHI (mean = 8.8 per hour). These three patients had a mean BMI of 27.8 kg/m^2 and a mean neck circumference of 41.7 cm. Otherwise, the total sleep time, the REM stage; the NREM stage and AHI were comparable in patients with and without respiratory failure. Radwan *et al* studied sleep disordered breathing in obese patients with and without COPD. They did not find any statistically significant difference in AHI, mean nocturnal saturation and BMI between the two groups. However, COPD patients who were obese had a lower ventilatory and PaO_2 responses for CO_2[8]. Our observations also suggest that it is the BMI *per se* that contributes to AHI and nocturnal desaturation.

We also observed that episodes of desaturation (nocturnal SaO_2 drop of 4% or more), were more frequent in our patients than can be explained by apneas and hypopneas. The mechanism leading to drop in saturation without apnea or hypopneas is poorly understood with a few studies providing a measure of minute ventilation during sleep. In one study, the mean minute ventilation of patients with nocturnal desaturation decreased by 21% during NREM stage and 39% during REM stage irrespective of the underlying lung disease[9]. This was primarily due to a reduction in tidal volume with only minor changes in respiratory rate. This may be explained by upper airway resistance syndrome that may be present in these patients which may not manifest with frank apnea or hypopnea but may simply lead to desaturation. Jackowski *et al*[10] studied sleep apnoea syndrome in 220 non-selected patients with obstructive airways disease. Of these, 48 subjects had frequent episodes of nocturnal desaturation. When these patients were subjected to polysomnography, only 13 patients (26%) had significant AHI and the rest of the 35 patients had only episodes of desaturation without apnea or hypopnea, which were thought to be due to upper airway resistance syndrome. In the present study, the episodes of desaturation were comparable between patients with and without respiratory failure.

We also observed that patients with respiratory failure had a lower mean nocturnal SaO_2 and a lower *minimal* nocturnal SaO_2 as compared to those without respiratory failure suggesting that the patients with respiratory failure tend to have more severe drops in nocturnal SaO_2. The nocturnal worsening of SaO_2 has been linked to severe derangement of lung mechanics[11-13]. Little *et al*[13] studied daytime arterial blood gas analysis and nocturnal SaO_2 among other parameters in 33 patients with stable COPD. They found that the patients who experienced severe nocturnal desaturation had significantly lower mean PaO_2 and SaO_2 values as compared to those who did not have desaturation and there was a positive correlation between the mean nocturnal and the daytime saturation. They also observed nocturnal desaturation in all patients who had daytime saturation less than 93% but in no patient with daytime saturation exceeding 95%. Some of the studies point out that diurnal change in PaO_2 is a reasonably good predictor of nocturnal SaO_2 levels[11,12].

Patients with respiratory failure also had a lower FEV_1 (% predicted) and PEFR (% predicted) compared to those without respiratory failure suggesting an indirect relation to the SaO_2. Appelberg *et al*[14] reported that FEV_1/FVC was slightly, but significantly lower in subjects who had nocturnal apneas and desaturation as compared to those who did not have these. In our study, there was no significant correlation between any of the pulmonary function test parameters and the

parameters related to sleep disordered breathing such as AHI, apnea, hypopnea and episodes of desaturation.

Most of our patients had cardiac arrhythmias associated with a drop in saturation. These included the classical bradycardia associated with obstructive sleep apnea and also tachyarrhythmias. The cause of these may be the ventricular ectopics that are known to occur during hypoxemic episodes. Many studies have reported the association of nocturnal arrhythmias with hypoxemic episodes in COPD patients[15,16]. These arrhythmic episodes are reported to have been treated effectively by non-invasive methods of ventilation[17].

The positive correlation between the neck circumference and the AHI observed in the present study suggests that thicker the neck, higher would be the AHI. This association has been reported by many earlier studies[18-20]. Rivlin *et al*[21] found a significant correlation between AHI and pharyngeal cross-sectional area ($r=0.87$, $p<0.01$). It was also reported that patients with the so-called idiopathic obstructive sleep apnea syndrome might have an anatomic predisposition to the development of upper airway occlusion, which may not be detectable on clinical examination[18]. In a recent study, it was concluded that in the absence of sleep apnea-hypopnea (SAH), sleep heart health study (SHHS) participants with COPD did not have clinically severe sleep perturbations, and that there was a threshold at FEV_1/FVC <65% for a 2-to 3-fold risk for sleep-related oxyhemoglobin desaturation (SOD) in community-dwelling SHHS adults with COPD without SAH[22]. Furthermore, in a large community population, COPD was not associated with an increased prevalence of SAH. SAH confers greater risk for desaturation during sleep than COPD[23]. In our study, none of the 32 patients who underwent an ororhinolaryngological examination had any clinically detectable abnormality. We conclude that, BMI *per se* contributes to the AHI and nocturnal desaturation in patients with COPD.

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