Original Research Article

Sleep Profile and Symptoms of Sleep Disorders in Patients of Chronic Obstructive Pulmonary Disease (COPD)

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Abstract: There has been an interest in the nature of sleep and dreams throughout recorded history. Hippocrates in his texts refers to disordered sleep and dreams. The monograph, The Philosophy of Sleep was written by the Scottish physician, Robert MacNish in 1830, in which he regarded sleep as the intermediate state between wakefulness and death, exemplifying the passive nature of sleep. The development of the EEG in 1929 by the German Psychiatrist, Hans Berger allowed the examination of brain activity during sleep. A series of investigation in the 1930's established the characteristics of an EEG during sleep with the features of high amplitude slow waves and spindles and during wakefulness alpha rhythm and lower amplitude background rhythms. Sleep disorders are common in patients of COPD. Less rapid eye movement (REM) sleep and arousals during period of desaturation are often noted in patients with COPD. Hypoxemia during sleep in patients with COPD has significant cardiovascular, neurophysiological and hematological consequences. Cardiac dysarrhythmias, polychythemia, pulmonary and systemic hypertension, corpulmonale are known to occur with increase precedence culminating into nocturnal death.
Keywords: Chronic Obstructive Pulmonary Diseases (COPD), REM sleep, Nocturnal Oxygen Desaturation (NOD)

INTRODUCTION

Modern definition of sleep defines sleep as a ''reversible behavioral state of perceptual disengagement from, and unresponsiveness to, the environment''. On the basis of a constellation of physiological parameters sleep can be divided into two broadly defined states, rapid eye movement (REM) sleep and non rapid eye movement (NREM) sleep. NREM sleep is further subdivided into four stages, which are relatively based on EEG recordings, representing the continuum of deepening sleep. REM sleep, by contrast is defined by EEG activation, muscle atonia, and episodic bursts of rapid eye movements [1].

The physiology of different organ systems of the body is altered during sleep. During sleep there are definite alterations in the respiratory functions in the normal human beings. Hypoventilation, periodic breathing and erratic shallow breathing with resultant hypoxemia are observed in different stages of sleep, the ventilatory changes being within physiological limits [2-4]. These respiratory alterations become more pronounced and pathological when the lungs are diseased and lung functions are altered as in Chronic Obstructive Pulmonary Disease (COPD). COPD is a common disease worldwide. It is currently the fourth leading cause of death in the world and is projected to be the third leading cause of death by 2020 [5]. Hypercapnic chemosensitivity is also reduced such that, for a given change in CO_2, the increase in ventilation is minimal in people with COPD during sleep [6]. Patients with COPD can experience profound desaturation instances during rapid eye movement (REM) sleep in part related to atonia in the skeletal muscles including the accessory muscles of respiration. Second, cough is typically suppressed during sleep such that people with COPD can develop mucus plugging and hypersecretion, affecting nocturnal gas exchange. Lack of cough overnight often leads to productive cough in the morning, which can be disabling. Third, obstructive sleep apnea is a common disorder which can occur in COPD patients, the concurrence of these two conditions is known as overlap syndrome which is associated with a poor prognosis [7].

Patients with COPD also become more hypoxemic during sleep then when awake and the hypoxemia during sleep is even greater than that encountered during exercise [8]. Hypoventilation is the major cause of hypoxemia during REM sleep in patients with COPD and there may be additional contributions from ventilation-perfusion mismatches and reductions in functional residual capacity [9].

Nocturnal oxygen desaturation (NOD) is a significant sleep abnormality associated with COPD. NOD occurs most markedly during rapid eye movement (REM) sleep, when florid hypoxemia may occur [10].Obstructive sleep apnea (OSA) is a form of sleep-disordered breathing (SDB) clinically recognized 4 decades ago[3] and defined by total or partial intermittent collapse of the upper airway resulting in nocturnal hypoxemia and arousals from sleep [11]. The presence of both OSA and COPD was termed the "overlap" syndrome by Flenley [12].

MATERIAL AND METHODS

The present study was prospectively carried out in the well equipped sleep laboratory of Department of TB and Chest Diseases, Government Medical College, Amritsar, with an aim to evaluate the sleep profile and symptoms of sleep disorders in patients with COPD. This study had been conducted after taking approval from the ethical committee.

Study Design: The present study was a cross sectional study

Size: A total of 60 consecutive COPD patients were enrolled into the study and were classified into Mild COPD and Moderate COPD, according to GOLD spirometric classification of severity of airflow limitation in COPD.

Table-1: Classification of Severity of Airflow Limitation in COPD (Based on Post-Bronchodilator FEV$_1$)

Table-1In patients with FEV$_1$/FVC <0.70		
Gold 1	Mild	FEV$_1$ ≥80% predicted
Gold 2	Moderate	50% ≤ FEV$_1$<80% predicted
Gold 3	Severe	30% ≤ FEV$_1$<50% predicted
Gold 4	Very Severe	FEV$_1$<30% predicted

Selection criteria for patients included in the study were as follows:-

Inclusion Criteria
- Diagnosis of COPD stage 1 and 2 for more than 12 months based on GOLD Spirometric Classification of Severity of Airflow Limitation in COPD.
- Age > 40 years.
- Stable condition, defined as a stable disease without repeated exacerbations from the previous 4 months.
- Willingness to participate.

Exclusion criteria are as follows
- Patient with lung disease other than COPD.
- Those with history of upper airway surgery for snoring.
- Patients with known psychiatric conditions.
- Patients using hypnotics on regular basis.

Consent
All the patients enrolled in this study had given informed consent to participate in the study.

METHOD

A total number of 60 consecutive COPD patients were enrolled into the study. Detailed history, physical examination, full night polysomnography and all relevant laboratory investigations were done as per protocol. These patients were further classified into Mild and Moderate COPD according to GOLD spirometric classification of severity of airflow limitation in COPD. The complete procedure of polysomnography was explained to each patient and an informed consent was taken from each patient. These patients were subjected to a full night sleep study (overnight polysomnography). The machine used for polysomnography is SomnomedicsSOMNOscreenplus^{TM} and the software used is DOMINO VERSION 2.6.0.

Leads used and the procedure followed for the placement of electrodes is as follows:

Reference and Ground electrodes- the patients were connected to Reference (REF) electrode first. This is done using 10/20 system of placing the electrodes. Ground (GND) electrode is placed at centre at the middle of the forehead.
EOG (Electrooculogram) Electrodes -

EOG l : It is placed 1 cm laterally and above outer canthus of left eye.
EOG r : It is placed 1 cm laterally and below outer canthus of right eye.
EEG (Electroencephalogram) electrodes - all the leads are placed according to 10/20 system of placing electrodes.
C3 : It is placed on top left of the forehead.
C4 : It is placed on top right of the forehead.
Occipital leads (O1 and O2); Central leads (C3 and C4) are also placed as per 10/20 system.
A1 : It is placed over left mastoid process.
A2 : It is placed over right mastoid process.

EMG (Electromyogram) electrodes- Two electrodes were placed on the bottom of the chin 1 cm apart.

ECG (Electrocardiogram) electrodes - Two electrodes were placed for ECG signal. One on the left 4^{th}intercoastal in midclavicular line and the other is placed in right 2^{nd}intercoastal space in midclavicular line.

PLM (Periodic Limb Movement) sensors- One electrode on each side was placed on Musculus Tibialis Anterior (centred between the knee and the ankle) of each leg.

Airflow Sensor - It was placed between nostrils and upper lip so that two elements of the sensor have to be fitted directly below the nostrils and one element has to be fitted in front of the patient's mouth.

Microphone - It is placed on the lateral aspect of the neck between medial to pulsations of carotid artery.

External Effort Belts - Thoracic belt was attached around patient's chest and abdominal belt was attached around patient's abdomen.

SpO_2 sensor- A finger clip sensor which measures oxygen saturation was attached to patient's finger.

Activity sensor - It is attached on the extensor aspect of wrist of the non dominant hand.

After ensuring that all the electrodes were rightly attached, the study was started. The study was closely watched throughout and any displacement of the electrodes was immediately corrected. The study was stopped the next morning after the patient woke up voluntarily.

Sleep staging and sleep disordered breathing was evaluated in accordance to American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events, Version 2.0.

Nocturnal Oxygen Desaturation:
Atleast three different definitions are being used to define NOD
- Mean nocturnal oxygen saturation (SaO_2) < 90%.
- SaO_2< 90% for more than 30 % of recording time.
- SaO_2< 90% for atleast 5 minutes with a nadir SaO_2 ≤ 85%.

STATISTICAL ANALYSIS
For comparison of means between Mild COPD and Moderate COPD; NOD and nNOD, the student t-test and analysis of variance (ANOVA) were applied. The various correlation analysis and ROC curve were also done. All the above mentioned tests were applied using SPSS 17 software.

RESULTS AND DISCUSSION
The present study was conducted in the well equipped Sleep Laboratory Department of TB and Respiratory Diseases, Government Medical College, Amritsar. A total of 60 patients of COPD with the diagnosis established by Spirometry were enrolled into the study. These patients are classified into two groups – mild and moderate COPD, based on GOLD guidelines. All of these patients underwent an overnight sleep study in the sleep lab. The observations were analyzed and the results are presented in the following tables.

Table-2: Characteristics of The Study Cohort

Age in Yrs	No. of Patients
40-50	8
51-60	27
61-70	23
71-80	2
Mean±S.D.	58.67±6.86

Majority of the study cohort comprised of individuals above 50 years of age with a mean age of 58.67 years. Most of the subjects were in the age group of 51-60 years. On subgroup analysis mean age of Mild COPD patients is 52.9 years and moderate COPD patients have a mean age of 60.4 years

Study cohort had 58 males and 2 females who underwent overnight polysomnography. The mean Body Mass Index (BMI) of the study cohort was 18.42

kg/m^2 and mean Neck Circumference (NC) was 33.03 cm. Most of the patients enrolled in the study were heavy smokers, with mean pack years of 28.55.

All the patients underwent spirometric analysis, based on which they were classified as either Mild COPD or Moderate COPD, as per GOLD spirometric classification of severity of airflow limitation in COPD. Table 4 depicts the values of two spirometric parameters viz FEV$_1$ (% predicted) and FEV$_1$/FVC. The mean value of FEV$_1$ was 67.17 while the mean value of FEV$_1$/FVC was 56.14.

Table-3: Nocturnal Oxygen Desaturation (NOD) (n=60)

Sr. No.	Nocturnal oxygen desaturation (NOD) (n=60)	No. of Patients
1	Present	11 (18.33%)
2	Absent	49 (81.67%)

Total number of patients who had nocturnal oxygen desaturation (NOD) was 11, constituting 18.33% of the study cohort.

Table-4: Overlap Syndrome (n=60)

	OVERLAP SYNDROME (n=60)	NO. OF PATIENTS (%AGE)
1	Present	8 (13.33%)
2	Absent	52 (86.67%)

A total of 8 COPD patients have concomitant obstructive sleep apnea (OSA). So the prevalence of overlap syndrome in the study cohort was 13.33%.

Personal details and characterstics of study population:
COPD is the disease of the elderly population, the mean age group of the study cohort in the present study is 58.67, which is in concordance with the prevalence rates of the disease in different parts of the world. Subgroup analysis of COPD patients revealed significant difference in age of patients, with patients of mild COPD having mean age of 52.86 years while moderate COPD patients have mean age of 60.43 years. This indicates the relation of duration of smoking with the severity of the disease.

Most of the patients enrolled into our study are males (M: F=58:2). This uneven distribution might be due to multiple factors- the pattern of flow of patients in the study period, refusal of the female patients to consent for the sleep study etc

The mean BMI and neck circumference of the study cohort are 18.42 and 33.02 respectively. This suggests the poor nutritional status of the patients, which might be due the chronicity of the disease and sociodemographic profile of the patients. Earlier studies had enrolled obese subjects which it is a confounding factor for obstructive sleep apnea [13]. Radwan *et al.* [14] studied sleep disordered breathing in obese subjects with and without COPD. They find no statistically significant difference in AHI, mean nocturnal saturation and BMI between the two groups. Our findings suggest that it is BMI and neck circumference (NC) that contributes to increased RDI in COPD patients.

Patients of COPD become more hypoxic during sleep to a significant extent. There had been a great deal of efforts to recognize the factors responsible for nocturnal oxygen desaturaton (NOD) in COPD and the factors that can predict the occurrence of NOD in these patients. Several mechanisms have been proposed to explain NOD which include hypoventilation, ventilation perfusion mismatch, impact of oxyhemoglobin dissociation curve (hypoxemic patients at baseline are more likely to drop their SaO$_2$ with hypoventilation during sleep) and presence of coexisting obstructive sleep apnea (OSA). Various studies have shown correlation between FEV$_1$, FEV$_1$/FVC and daytime SpO$_2$/awake SpO$_2$ with the occurrence of NOD in COPD patients [15-18].

In our study 11 patients have nocturnal oxygen desaturation (NOD). Thus prevalence of nocturnal oxygen desaturation (NOD) in our study came out to be 18.33%.In our study 8 patients are having obstructive sleep apnea, so the prevalence of overlap syndrome in the study population has come out to be 13.33%.

It can be finally concluded that sleep efficiency is decreased in patients of COPD which indicates a poor sleep quality. FEV$_1$ is also found to be significantly higher in nocturnal oxygen desaturation (NOD) subjects. This fact demonstrates that the more the respiratory functions is impaired, the more likely these subjects will be nighttime hypoxemic. Awake SpO$_2$ is an important parameter for prediction of nocturnal oxygen desaturation (NOD) in COPD patients.

SUMMARY AND CONCLUSION
The present study was conducted in the Sleep Laboratory of Dept. of Tuberculosis and Respiratory Diseases, Govt. Medical College, Amritsar. A total of 60 consecutive COPD patients were enrolled into the study after taking informed consent from them. Following observations were made in the study.

There was an overall male preponderance in the study with 96.66% being males and 3.34% females.

As per GOLD spirometric classification of severity of airflow limitation in COPD, these patients are classified. 14 patients came out to be of Mild COPD while 46 patients were of Moderate COPD.

These patients then underwent overnight polysomnography. The machine used for polysomnography is Somnomedics SOMNO screenplus^{TM} and the software used is DOMINO VERSION 2.6.0.

Sleep efficiency was found to be decreased in these patients with a mean sleep efficiency of 71.8%.

Mean values of minimal SpO_2(%age), Average SpO_2 (%age), $SpO_2<90\%$ (%age) and $SpO_2<90\%$ in duration were 80.27,93.18,4.22 and 12.23 respectively.

Mean RDI (respiratory disturbance index) of the study population was 2.29.

Significant difference (p<0.05) is found in sleep efficiency between Mild COPD and Moderate COPD patients.

11 (18.33%) patients had nocturnal oxygen desaturation (NOD) among which 2 were Mild COPD patients and 9 were Moderate COPD patients.

On analysis of the two subgroups, several parameters likeFEV_1 and SpO_2 parameters were found to have statistically significant difference (p<0.05) between patients who have NOD and those who do not have NOD.

COPD with obstructive sleep apnea (RDI>5) is known as Overlap Syndrome. In this study, 8 (13.33%) patients had overlap syndrome. Among these 3 had Mild COPD and 8 had Moderate COPD.

On Correlation analysis a significant positive correlation is found between BMI and neck circumference with RDI in COPD patients. Thus BMI and neck circumference might predict the occurrence of OSA in COPD patients.

On ROC analysis of SpO_2 with respect to NOD the cut off value for $SpO_2$was found to be 94% for which the sensitivity, specificity and AUC values are 72.7, 77.6 and 0,817 respectively. This shows that patients of COPD having daytime SpO_2 below 94% are likely to have to nocturnal oxygen desaturation (NOD).

To conclude, sleep efficiency is reduced in patients of Mild and Moderate COPD.

The prevalence of Nocturnal oxygen desaturation (NOD) in the study is found to be 18.33%.

FEV_1 and SpO_2 parameters differ significantly between patients who have NOD and those who do not have NOD.

The prevalence of obstructive sleep apnea in COPD is found to be 13.33%.

BMI and Neck circumference are found to be significant factors that contribute to increase RDI in COPD patients and thus might predict the occurrence of OSA in these patients.

Daytime SpO_2 is an important parameter in predicting the occurrence of nocturnal oxygen desaturation (NOD) in COPD patients.

The limitation of this particular study is that it lacks a large sample size. Hence, it needs to be supported by a larger cohort, in order to have more consistent results.

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