Original Article

Study of Nocturnal Oxygen Desaturation in Chronic Obstructive Pulmonary Disease Patients

Naveen Kuzhikkattil, Kamal Nayan Shringi, Babulal Bansiwal, Anil Saxena, Suman Khangarot, Shinu A. Wahab

Department of Respiratory Medicine, Government Medical College, Kota, Rajasthan, India

Abstract

Background: Abnormal sleep architecture with decreased rapid eye movement sleep and arousals during the periods of nocturnal oxygen desaturation (NOD) are seen in patients with chronic obstructive pulmonary disease (COPD) with significant consequences. This study was done to evaluate the prevalence of NOD and other sleep-related disorders in COPD patients. **Patients and Methods:** This prospective cross-sectional study was conducted in the sleep laboratory of our tertiary center over 1 year. Fifty COPD patients were enrolled in this study. They were classified into mild COPD and moderate COPD, according to the Global Initiative for Obstructive Lung Disease (GOLD) classification. Complete history, physical examination, and relevant laboratory investigations were taken. All patients were subjected to overnight polysomnography. **Results:** Eight patients had mild COPD, whereas 42 patients had moderate COPD. Mean sleep efficiency was decreased with an average of 71.08% with a significant difference between mild and moderate COPD cases. Minimal SpO_2, average SpO_2, SpO_2 <90%, and duration of SpO_2 <90% in the study group showed mean values of 80.77%, 94.33%, 3.93%, and 12.09 min, respectively, with a mean respiratory disturbance index (RDI) of 2.45. NOD was seen in 18% (9 patients) and overlap syndrome was seen in 12% (6 patients) in our study. Forced expiratory volume in 1 s and SpO_2 were found to have statistically significant difference ($P < 0.05$) between patients with respect to NOD. It correlated well with body mass index (BMI) and neck circumference with RDI and also overlap syndrome. **Conclusions:** NOD is related to the degree of respiratory dysfunction and can coexist with overlap syndrome. Occurrence of overlap syndrome can be predicted with the help of BMI and RDI.

Keywords: Chronic obstructive pulmonary diseases, nocturnal oxygen desaturation, overlap syndrome, respiratory disturbance index

Introduction

Sleep is a naturally occurring recurrent event in the body characterized by altered consciousness along with the inhibition of sensory activity along with voluntary muscles and unresponsiveness with disengagement from the environment. The body alternates between two highly distinct modes of sleep known as nonrapid eye movement (NREM) and rapid eye movement (REM) sleep. Onset occurs with NREM sleep, which is divided into four stages based on electroencephalographic (EEG) recordings. Apart from REMs, REM sleep is characterized by muscle atonia and EEG activity similar to wakefulness.[1]

Different organ systems of the body undergo physiological alterations during sleep. In NREM sleep, periodic breathing is seen in Stages 1 and 2 and then becomes regular in Stages 3 and 4. In REM sleep, the pattern of respiration is often irregular with periods of central apnea. Minute ventilation also decreases during sleep owing to a decrease in tidal volume. Hypoxemia and hypercapnia are also seen along with a decrease in the ventilatory response to the same which is more pronounced in REM sleep. These state-dependent physiologic changes which do not have significant clinical changes in normal subjects have deleterious effects in patients with underlying pulmonary disease as in chronic obstructive pulmonary disease (COPD).

COPD is a major health problem where cigarette smoking is common and is the fourth leading cause of death worldwide.[2] The death rate has been increasing in recent decades in contrast with the falling death rates from heart and cerebrovascular disease. During sleep, increase in ventilation is minimal in patients with COPD, as the hypercapnic chemosensitivity

Access this article online

Quick Response Code:

Website: www.ijrconline.org

DOI: 10.4103/ijrc.ijrc_6_19

Address for correspondence: Dr. Naveen Kuzhikkattil, Room No. 225, PG Hostel 2, New Medical College Hospital, Rangbari Road, Kota - 324 005, Rajasthan, India.
E-mail: naveengopikrishnan22@gmail.com

How to cite this article: Kuzhikkattil N, Shringi KN, Bansiwal B, Saxena A, Khangarot S, Wahab SA. Study of nocturnal oxygen desaturation in chronic obstructive pulmonary disease patients. Indian J Respir Care 2019;8:87-91.

Received: 26-02-2019 **Revised:** 15-05-2019 **Accepted:** 31-05-2019

for a given rise in CO_2 is reduced.[3] Atonia occurs in the respiratory muscles during sleep, which causes a decrease in functional residual capacity, leading to a ventilation-perfusion mismatch. Due to cough suppression, mucus plugging and hypersecretion occur affecting nocturnal gas exchange. The concurrence of obstructive sleep apnea (OSA) with COPD known as overlap syndrome can also occur. Nocturnal oxygen desaturation (NOD) can occur in COPD patients during sleep most markedly during REM sleep.[4]

The study was done to find the prevalence of NOD and other sleep disturbances in patients with COPD at a tertiary care hospital.

Patients and Methods

This was a prospective, cross-sectional study carried out in the sleep laboratory of the Department of Respiratory Medicine, New Medical College Hospital, Kota, over 1 year from August 2017 to July 2018. Fifty COPD patients were enrolled in the study and were classified into mild COPD and moderate COPD, according to the GOLD spirometric classification of the severity of airflow limitation in COPD. Informed consent was obtained from all the participants. Detailed history, physical examination, and all relevant laboratory investigations were obtained as per protocol. The complete procedure of polysomnography was explained to each patient and subjected to overnight polysomnography. The machine used for polysomnography is Embletta MPR, and the software used is RemLogic™ 3.4 (Embla Systems, division of Natus Medical Incorporated, Kanata, Canada). It is a Level II device with seven channels including EEG, electrooculogram, chin electromyogram, electrocardiogram, oximetry, airflow, and respiratory effort channels.

Patients aged >40 years, diagnosed to have mild and moderate COPD patients based on GOLD Spirometric classification on the basis of forced expiratory volume in 1 s (FEV_1), and without repeated exacerbations in the past 4 months were included in the study. Those patients with a history of psychiatric illnesses, those with regular use of hypnotics, those who underwent upper airway surgery for snoring, or with other lung diseases were excluded from the study. Sleep efficiency was defined as the total sleep time divided by the total time in bed during recording (Normal value - more than 85%). Respiratory disturbance index was defined as the average number of respiratory disturbances (obstructive apnea, hypopnea and respiratory effort related arousals) per hour of sleep.

NOD was defined as mean nocturnal oxygen saturation (SaO_2) <90%, SaO_2 <90% for >30% of recording time or SaO_2 <90% for at least 5 min with a nadir SaO_2 ≤85%.

Statistical analysis

For comparison of means between mild COPD and moderate COPD; NOD and nNOD (no nocturnal desaturation); overlap and without overlap, the Student's *t*-test and analysis of variance were applied. Fisher's exact test and correlation analysis were performed between the variables. All the above-mentioned tests were applied using IBM SPSS Statistics 20 Windows (SPSS Inc., Chicago, Illinois, USA).

Table 1: Comparison of sleep efficiency

Severity of COPD	Mean age (years)	Mean sleep efficiency
Mild	53.21	76.1000
Moderate	59.59	69.5565

COPD: Chronic obstructive pulmonary disease

Results

The age distribution of patients is given in Table 1. There were 46 males and 4 females. Comparison of sleep efficiency is given in Table 2. Figure 1 shows comparison of mean sleep efficiency in mild and moderate COPD. As per the GOLD spirometric classification, eight patients had mild COPD, while 42 patients had moderate COPD. Sleep efficiency was found to be decreased in these patients with a mean sleep efficiency of 71.08%. A significant difference was seen between mild and moderate COPD cases.

Mean values of minimal SpO_2, average SpO_2, SpO_2 <90%, and SpO_2 <90% for the duration of the study were 80.77%, 94.33%, 3.93%, and 12.09 min, respectively. Mean respiratory disturbance index (RDI) of the study population was 2.45. There was no significant difference in RDI between mild and moderate COPD groups. A significant difference ($P < 0.05$) is found in sleep efficiency between mild COPD and moderate COPD patients. Nine (18%) patients had NOD among whom, 2 had mild COPD, whereas 7 had moderate COPD. In this study, 6 (12%) patients had overlap syndrome. Among these, 2 had mild COPD and 4 had moderate COPD.

Table 3 shows comparison of mean FEV_1 and other sleep parameters in those with and without NOD. On analysis of the two subgroups, several parameters such as FEV_1 and SpO_2 were found to have statistically significant difference ($P < 0.05$) between patients who have NOD and those who did not have NOD. SpO_2 parameters were found to have statistically significant difference ($P < 0.05$) between patients with overlap syndrome and those with COPD alone.

Sleep parameters, body mass index (BMI), and neck circumference (NC) in those with and without overlap syndrome are shown in Table 4. Association between overlap syndrome and NOD is given in Table 5. Correlation between BMI and RDI is depicted in Figure 2 and between RDI and NC in Figure 3.

A significant difference was found between sleep parameters in patients with overlap syndrome and those without overlap. On correlation analysis, a significant positive correlation was found between BMI and NC with RDI in COPD patients ($r = 0.812$ and 0.756, respectively, with $P < 0.0001$). Thus, BMI and NC might predict the occurrence of OSA in COPD patients. Those with overlap syndrome were found to have NOD more than patients with COPD alone.

Table 2: Group characteristics

Serial number	Age group	Mild COPD	Moderate COPD	Overlap syndrome present	Overlap syndrome absent	NOD present	NOD absent
1	41-50	3	2	1	4	1	4
2	51-60	4	23	2	25	5	22
3	61-70	1	15	2	14	2	14
4	71-80	0	2	1	1	1	1
Total		8	42	6	44	9	41
Prevalence				Prevalence of overlap=12%		Prevalence of NOD=18%	

NOD: Nocturnal oxygen desaturation, COPD: Chronic obstructive pulmonary disease

Table 3: Comparison of mean forced expiratory volume in 1 s and other sleep parameters in those with and without nocturnal oxygen desaturation

Desaturation	Mean SpO_2 average	Mean $FEV_{1\%}$	Mean SpO_2 minimum
NOD absent	94.8694	74.4857	81.8576
NOD present	91.9273	66.2545	75.9091
P		<0.05	

NOD: Nocturnal oxygen desaturation, FEV1: Forced expiratory volume in 1 s, SpO2: Oxygen saturation

Discussion

Majority of the study cohort comprised individuals above 50 years of age with a mean age of 58.10 years which is in concordance with the prevalence rates of the disease in different parts of the world. Most of the subjects were in the age group of 51–60 years. On subgroup analysis, the mean age of mild COPD patients was 53.21 years and moderate COPD patients had a mean age of 59.59 years. This indicates the relation of the duration of smoking with the severity of the disease. In this study, there were 46 males and 4 females. This uneven distribution was due to multiple factors like the pattern of flow of patients in the study period and refusal of the female patients to consent for sleep study.

The mean BMI of the study cohort was 18.54 kg/m^2. This suggests the poor nutritional status of the patients, which might be due to the chronicity of the disease and sociodemographic profile of the patients. The cases with overlap syndrome had a mean BMI of 23.18, whereas those without overlap syndrome were undernourished with a mean BMI of 17.82. The findings are similar to previous studies which found a positive correlation between BMI and RDI. Bixler *et al*.[5] found a similar positive correlation between BMI and RDI. Decreased exercise capacity can contribute to obesity, which, in turn, can trigger lower airway inflammation through various cytokines as well as oxidative stress.

NC showed a similar trend with higher NC in those with overlap syndrome. Mean NC in our study was 34.32 cm. Mean NC of those with overlap syndrome was 38.67 cm, whereas those with COPD alone had a mean NC of 33.64 cm. Soler *et al*.[6] in their study found a mean NC of 38.4 cm with no significant difference between those with overlap syndrome and those without overlap syndrome which is different from our result which revealed a statistically significant difference. Patients with severe COPD are on chronic oral or inhaled steroids which contribute to

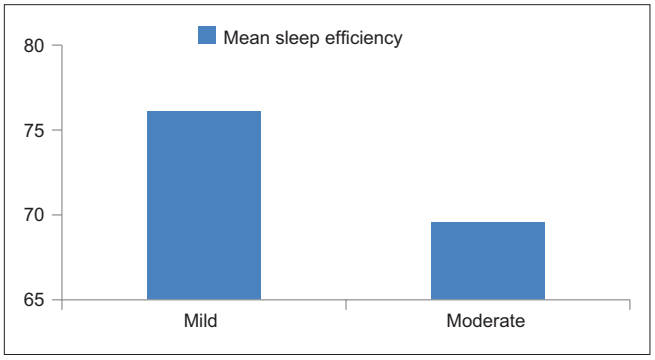

Figure 1: Comparison of mean sleep efficiency in mild and moderate chronic obstructive pulmonary disease

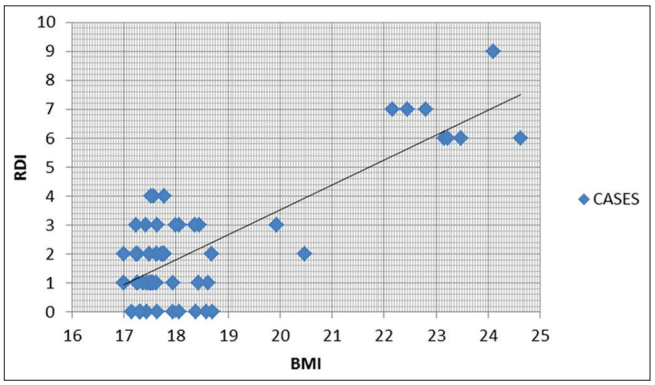

Figure 2: Scatter diagram showing correlation between body mass index and respiratory disturbance index

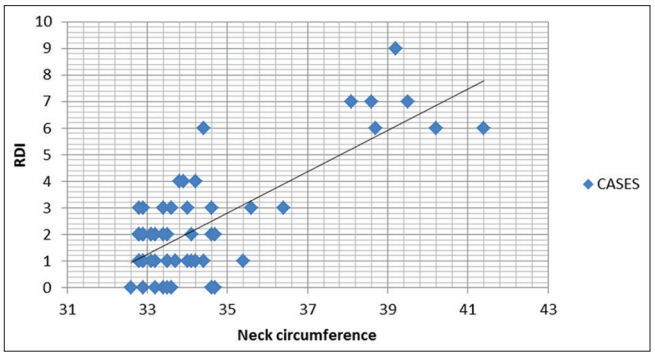

Figure 3: Scatter diagram showing correlation between respiratory disturbance index and neck circumference

Table 4: Sleep parameters, body mass index and neck circumference in those with and without overlap syndrome

Overlap	Mean SpO_2 average (%)	Mean duration of SpO_2<90% (min)	Mean SpO_2 minimum (%)	Mean±SD	
				BMI	NC
Absent	94.9077	5.7846	81.66	17.811±0.662	33.638±0.818
Present	90.5750	53.1000	74.98	23.181±0.819	38.673±2.045

BMI: Body mass index, SD: Standard deviation, SpO2: Oxygen saturation, NC: Neck circumference

Table 5: Association between overlap syndrome and nocturnal oxygen desaturation

Total=50	Overlap syndrome		Fisher's exact test (*P*)
	Present	Absent	
NOD			
Present	4	5	0.0068
Absent	2	39	

NOD: Nocturnal oxygen desaturation

central obesity and fat deposition in neck increasing the risk of OSA. COPD complicated by cor pulmonale may lead to edema in the pharyngeal soft tissues leading to OSA.

Radwan *et al*.[7] studied sleep-disordered breathing in obese subjects with and without COPD. They find no statistically significant difference in RDI, mean nocturnal saturation, and BMI between the two groups. Our findings suggest that it is BMI and NC that contributes to increased RDI in COPD patients.

The mean value of FEV_1 was 73.30% of the predicted, and the mean FEV_1/FVC was 58.14% of the predicted. In the present study, FEV_1 was found to have a positive correlation with NOD and a weak negative correlation with RDI. COPD is also associated with generalized muscle weakness leading to higher upper airway collapsibility. In a study by Papachatzakis *et al*.[8] to find the comorbidities in overlap syndrome, the mean FEV_1 was 62% of the predicted in patients with overlap syndrome and 91% of the predicted in those without overlap syndrome. The present study did not show a statistically significant difference between these two groups with respect to FEV_1 parameter, although a weak negative correlation was seen with RDI.

The average SpO_2 during polysomnography in our study was 94.33%. The minimum mean SpO_2 was 80.77% with a mean duration of 12.09 min under 90%. The average SpO_2 in patients with NOD was 91.93% and those without NOD were 94.87%. The average SpO_2 was 94.91% in those with overlap syndrome and 90.58% in those without overlap syndrome. The mean minimum SpO_2 was 75% in those with overlap syndrome and 81.66% in those without overlap syndrome. Mean duration spent under 90% was 5.8 min in those without overlap syndrome and 53.1 min in those with overlap syndrome. Papachatzakis *et al*.[8] in their study found that the mean average SpO_2 in those with overlap syndrome was 91.15% and the mean minimum SpO_2 was 80.08%. The mean duration of time spent under 90% in their study was 37.74 min. Steveling *et al*.[9] in their study found that those with apnea-hypopnea index >10 had a mean average nocturnal SpO_2 of 91% and the mean duration spent under 90% was 147 min.

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 NOD in COPD and the factors that can predict the occurrence of NOD in these patients. Several mechanisms proposed to explain NOD 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 the presence of coexisting OSA.

In our study, nine patients had NOD (18%). Six patients had OSA (12%) with a mean RDI of 2.45. Soler *et al*.[6] in their study of OSA in moderate and severe COPD patients found out the prevalence to be 65.9%. Studies by Bednarek *et al*.[10] and others have reported OSA to be present in about 9.2% of patients with COPD.

Lewis *et al*.[11] observed the prevalence of NOD to be <5% in his study to identify isolated NOD in COPD. In this study, the prevalence of NOD without sleep apnea was found to be 6.67%. INOX trial reported the prevalence of NOD in severe COPD to be around 40%.

FEV_1 and other sleep parameters were found to be significantly different between patients with NOD and those without NOD. Lacasse *et al*.[12] found similar difference between patients with NOD and those without NOD with respect to these parameters in his study.

Conclusions

This study concluded that sleep quality is poor in patients with COPD. FEV_1 is also significantly lower in patients with NOD. This fact demonstrates that respiratory function impairment is directly related to nocturnal hypoxemia. COPD patients with NOD should be screened for OSA. Finally, BMI and NC can be predictive of the occurrence of OSA in COPD patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Carskadon MA, Rechtschaffen A. Monitoring and staging human sleep. Princ Pract Sleep Med 2000;3:1197-215.

2. Gerald LB, Bailey WC. Global initiative for obstructive lung disease. J Cardiopulm Rehabil Prev 2002;22:234-44.
3. McNicholas WT. Impact of sleep in COPD. Chest 2000;117:48S-53S.
4. Mulloy E, McNicholas WT. Ventilation and gas exchange during sleep and exercise in severe COPD. Chest 1996;109:387-94.
5. Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Rein J, Vela-Bueno A, *et al.* Prevalence of sleep-disordered breathing in women: Effects of gender. Am J Respir Crit Care Med 2001;163:608-13.
6. Soler X, Gaio E, Powell FL, Ramsdell JW, Loredo JS, Malhotra A, *et al.* High prevalence of obstructive sleep apnea in patients with moderate to severe chronic obstructive pulmonary disease. Ann Am Thorac Soc 2015;12:1219-25.
7. Radwan L, Maszczyk Z, Koziorowski A, Koziej M, Cieslicki J, Sliwinski P, *et al.* Control of breathing in obstructive sleep apnoea and in patients with the overlap syndrome. Eur Respir J 1995;8:542-5.
8. Papachatzakis I, Velentza L, Zarogoulidis P, Kallianos A, Trakada G. Comorbidities in coexisting chronic obstructive pulmonary disease and obstructive sleep apnea – Overlap syndrome. Eur Rev Med Pharmacol Sci 2018;22:4325-31.
9. Steveling EH, Clarenbach CF, Miedinger D, Enz C, Dürr S, Maier S, *et al.* Predictors of the overlap syndrome and its association with comorbidities in patients with chronic obstructive pulmonary disease. Respiration 2014;88:451-7.
10. Bednarek M, Plywaczewski R, Jonczak L, Zielinski J. There is no relationship between chronic obstructive pulmonary disease and obstructive sleep apnea syndrome: A population study. Respiration 2005;72:142-9.
11. Lewis CA, Fergusson W, Eaton T, Zeng I, Kolbe J. Isolated nocturnal desaturation in COPD: Prevalence and impact on quality of life and sleep. Thorax 2009;64:133-8.
12. Lacasse Y, Sériès F, Vujovic-Zotovic N, Goldstein R, Bourbeau J, Lecours R, *et al.* Evaluating nocturnal oxygen desaturation in COPD – Revised. Respir Med 2011;105:1331-7.