

Predictors of Nocturnal Oxygen Desaturation in Normoxemic Patients with Moderate to Very Severe Chronic Obstructive Pulmonary Disease

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ABSTRACT

Introduction: COPD is associated with complications such as reduced oxygen saturation and hypoventilation during sleep and is underdiagnosed among normoxemic patients. To identify the daytime parameters to predict nocturnal oxygen desaturation in normoxemic patients with moderate to very severe chronic obstructive pulmonary disease. To correlate the presence of nocturnal oxygen desaturation with pulmonary hypertension.

Material and methods: A cross-sectional study was performed at ACS medical college Chennai for 14 months from May 2017 to June 2018. The study population included 103 participants. Data on variables such as 6-minute walk test, spirometry, nocturnal oximetry, partial pressures of O₂ and CO₂ were assessed.

Results: A total of 103 patients were included in the analysis with 93.2% males and 3.9% current smokers and 87.4% ex-smokers. 52.4% had a normal chest X-ray. Around 45.6% had hyperinflated lungs. In the 6 minutes-walk-test, 32% participants had desaturation. 50.5% had positive C-reactive protein levels indicating the presence of systemic inflammation. Right atrial/right ventricular dilatation was noted among 34% participants. Nocturnal desaturation with 3 to 4 episodes/hour was present among 39% participants. Univariate analysis results show that post FEV₁, partial pressure of oxygen and carbon dioxide, presence of desaturation and RA/RV dilatation on echocardiography were all statistically significant predictors of nocturnal oxygen desaturation in normoxemic patients with moderate to very severe Chronic Obstructive Lung Disease.

Conclusion: Screening the COPD patients for these daytime predictors will enable in identifying the patients who have nocturnal desaturation. This in turn will aid in early initiation of home oxygen therapy.

Keywords: COPD, Nocturnal Desaturation, Normoxemic, Pulmonary Disease, Lung Disease

INTRODUCTION

Chronic obstructive pulmonary disease is characterized by complications such as reduced oxygen saturation, abnormalities in breathing rhythm which occur during sleep.^{1,2} Even among healthy individuals, there is a transient reduction in the alveolar ventilation during sleep. This phase is characterized by an increase in pCO₂. During REM sleep, the pulmonary arterial pressure rises. Among those with COPD, there is hypoxia, hypercapnia, both of which contribute to reduction in sleep quality. The physiological changes resulting in oxygen desaturation occurring among

individuals, together with the pathological features in COPD result in increased oxygen desaturation and increased pulmonary arterial pressures during sleep.³

Among the COPD patients who have severe hypoxia, long term oxygen therapy used for treatment corrects for nocturnal desaturation. However, among the normoxemic patients, this nocturnal desaturation occurring during sleep remains underdiagnosed. Untreated nocturnal hypoxia and hypercapnia among patients with COPD may lead to pulmonary arterial hypertension, cor-pulmonale and respiratory failure.⁴ In addition, the risk of mortality at night is higher among those with significant nocturnal desaturation.⁵

Due to these complications, diagnosis and treatment of nocturnal desaturation is crucial in the management of COPD. For the diagnosis, polysomnography remains the gold standard. But polysomnography is not feasible in all patients due to the increased requirement of equipment, time needed for performing and not able to be implemented on an outpatient basis.⁶ Due to these pitfalls, multiple predictors of nocturnal desaturation among normoxemic COPD patients are being studied.^{7,8} If a significant association is found between these predictors and nocturnal desaturation, it will aid in identifying those at increased risk and thereby initiate early treatment. This will be a cost-effective mode of management in developing countries like India. This study seeks to assess the same. The current study was done to identify the daytime parameters and to predict nocturnal oxygen desaturation in normoxemic patients with moderate to very severe chronic obstructive pulmonary disease and to correlate the presence of nocturnal oxygen desaturation with pulmonary hypertension

MATERIAL AND METHODS

This was a prospective cross-sectional study in normoxemic

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patients with moderate to very severe COPD attending the outpatient department of Pulmonary Medicine in ACS medical college Chennai. Data was collected over a period of 14 months from May 2017 to June 2018. The study population comprised of all patients who attended the Pulmonary Medicine OPD in PIMS with symptoms of COPD. The grade of COPD was ascertained after spirometry using the criteria put forth by the Global initiative for Chronic Obstructive Lung Disease (GOLD).⁹ Those with moderate to severe COPD having normoxemia at daytime ($SpO_2 >90\%$) were included in the study. Those who had hypoxia during the day, those who had co-morbidities such as cardiovascular disease, obstructive sleep apnea and those with acute exacerbation of COPD were excluded from the study. MIR Spiro bank II was used for Spirometry, 6 min walk test, and nocturnal oximetry.

The research protocol was approved by institutional human Ethics committee ACS Medical college and hospital and was in accordance to the Declaration of Helsinki. Informed written consent was obtained from all the study participants, after explaining the risks and benefits involved in the study, voluntary nature of participation. The confidentiality of the data was maintained throughout the study period and while reporting the results.

Sample size and Sampling method

A total of 364 patients with COPD were screened, of which 142 were eligible for participation in this study. Among them, 22 did not consent for participation in the study and the remaining 120 underwent nocturnal oximetry and detailed evaluation. 103 patients were finally included for analysis.

Operational definitions

Normoxemia – a daytime PaO_2 greater than 55 mmHg in patient breathing room air and is not in acute exacerbation and is on optimal medical treatment.

Nocturnal oxygen desaturation – a desaturation of minimum of 4% from baseline during the period of time spent in bed

Data on the following variables were collected from the study participants:

Daytime- Detailed clinical history including years of COPD, smoking index, pack years, Epworth sleepiness score. Detailed clinical examination with BMI, Chest X-Ray, Spirometry, 6 Min Walk Test, Echocardiography, ABG, Haemoglobin, Haematocrit and C - reactive protein
Night time:

Nocturnal oximetry – measurement of oxygen saturation was done at night from 11:00pm to 07:00am in the hospital using MIR Spiro bank II with a transcutaneous finger probe while patient is breathing environmental air.

The following variables were analysed for statistical significance in prediction of nocturnal oxygen desaturation: Years of COPD, Smoking status including pack years, smoking index and current smoking status of the patient, baseline saturation, BMI, Presence of hyperinflation on Chest X-ray, FEV1 pre and post bronchodilator, post bronchodilator

FEV1/FVC, stage of COPD, 6 minute walk test and presence of desaturation, haemoglobin, haematocrit, CRP, Partial pressures of oxygen and carbon dioxide, presence of RA/RV dilatation and pulmonary artery pressures.

STATISTICAL ANALYSIS

The patients have been grouped into desaturates and non-desaturates, the daytime parameters have been estimated and mean and standard deviation estimated. Patients who were found to have desaturation were pooled and analysed using Chi square test and Mann Whitney test. The predictors have been expressed with significance taken as a P value of less than 0.05. The statistical analysis was done using SPSS software.

RESULTS

A total of 103 patients were finally included in the analysis. 39 patients were found to have significant desaturation; desaturation was described as a fall of minimum of 4% from baseline saturation. The presence of desaturation was correlated with the various daytime parameters that were assessed. Among the study participants, 93.2% were males and 6.8% were females. The other baseline characteristics of the study participants is summarized in table 1.

Among the study participants, 3.9% were current smokers, 87.4% were ex-smokers and only 8.7% were never-smokers. The average smoking index among the study participants was 393.51 with 19.68 pack years. With regards to the chest X-ray findings, a little more than half (52.4%) had a normal chest X-ray. Around 45.6% had hyperinflated lungs and 2 patients had left destroyed lung. In the 6 minutes-walk-test, 32% of the study population had desaturation. The presence of desaturation during 6-minute walk test indicates a poor exercise tolerance and has been associated with poor prognosis in patients with COPD. With regards to the laboratory parameters, 50.5% of the study participants had positive C-reactive protein levels indicating the presence of systemic inflammation. Right atrial/right ventricular dilatation was noted among 34% of the study participants

Variables	Number	Mean	Standard deviation
Age (yrs.)	103	64.77	9.8
Duration of COPD (yrs.)	103	3.67	2.3
Smoking Index	94	393.51	246.97
Pack Years	94	19.68	12.34
Baseline SPO2%	103	95.65	1.77
BMI kg/m ²	103	22.128	3.72
FEV1 (Pre)%	103	40.17	13.51
FEV1 (Post)%	103	43.68	14.33
FEV1/FVC	103	51.664	10.05
Distance (6MWT) meters	103	258.70	100.515
Haemoglobin g/dl	103	13.35	1.88
Haematocrit%	103	39.817	5.75
PaO_2 mmHg	103	68.13	9.47
$PaCO_2$ mmHg	103	45.85	9.67
PAP mmHg	32	37.63	10.49

Table-1: Baseline characteristics of the study participants

Variable	Desaturation (Mean± SD)		p value
	DE saturators (n=39)	Non-DE saturators (n=64)	
Duration of COPD (yrs.)	3.82±1.98	3.58±2.51	0.58
Baseline SpO ₂ %	95.26±1.98	95.89±1.60	0.09
BMI (kg/m ²)	21.55±3.51	22.50±3.82	0.191
FEV1-Pre (%)	37.15±13.68	42.02±13.18	0.08
FEV1-Post (%)	40.00±14.48	45.92±13.88	0.044*
FEV1/FVC	49.32±11.52	53.08±8.83	0.085
6MWT distance (m)	238.03±82.72	271.30±108.64	0.083
Haemoglobin (g/dl)	13.42±1.97	13.30±1.84	0.753
Haematocrit (%)	40.02±6.05	39.69±5.61	0.785
PaO ₂ (mmHg)	63.95±8.07	70.67±9.42	<0.001*
PaCO ₂ (mmHg)	51.56±9.87	42.38±7.77	<0.001*

* indicates statistical significance

Table-2: Factors associated with nocturnal oxygen desaturation

Factors associated with desaturation	Desaturation		p value
	DE saturators (%)	Non-DE saturators (%)	
Smoking status			
Current smoker	2 (5.1%)	2 (3.1%)	0.525
Ex-smoker	32 (82.1%)	58 (90.6%)	
Never smoker	5 (12.8%)	4 (6.3%)	
Desaturation in 6MWT			
Present	19 (48.7%)	14 (21.9%)	0.008*
Absent	20 (51.3%)	50 (78.1%)	
RA/RV dilatation			
Present	22 (56.4%)	13 (20.3%)	<0.001*
Absent	17 (43.6%)	51 (79.7%)	

Table-3: Factors associated with desaturation

NOD	Number	Mean	Standard Deviation	P Value
DE saturators	24	38.50	10.95	0.388
Non-DE saturators	8	35.00	9.10	

Units: kg/m²: kilogram per meter square; m: Meter; g/dl: gram per deciliter; mmHg: millimetre of mercury

Table-4: Pulmonary arterial pressure and nocturnal Oxygen desaturation

with concomitant features of cor pulmonale. Nocturnal desaturation with 3 to 4 episodes/hour was present among 39% of the study participants. The groups statistics based on nocturnal oxygen desaturation can be seen in Table 2.

Based on table 2, it is seen that, post bronchodilator FEV1 has a statistically significant correlation with the presence of nocturnal oxygen desaturation. Partial pressure of oxygen and carbon dioxide were also found to be statistically significant markers for predicting the presence of nocturnal oxygen desaturation. Pulmonary hypertension was not a statistically significant predictor of nocturnal oxygen desaturation according to our study

Univariate analysis was performed to test the factors associated with nocturnal oxygen desaturation in normoxemic patients with moderate to very severe Chronic Obstructive Pulmonary Disease. The results are presented in Table 3.

The results of this study show that Post FEV 1, Partial pressure of oxygen and carbon dioxide, Presence of desaturation during 6-minute walk test and RA/RV dilatation on echocardiography were all statistically significant predictors of nocturnal oxygen desaturation in normoxemic

patients with moderate to very severe Chronic Obstructive Lung Disease. The cut off value for post bronchodilator FEV 1 was found to be in the region of 40% (Mean value). The partial pressure of oxygen and carbon dioxide both had a mean value of 63.95mmHg and 51.56mmHg respectively.

The presence of nocturnal hypoxemia has been postulated as the etiopathological factor resulting in the development of pulmonary hypertension in COPD patients. But in our study, we were unable to find a positive correlation between the presence of NOD and Pulmonary hypertension.

DISCUSSION

In the current study, the mean age was 64.77 years which was similar to the study by Little et al⁷ where the mean age was 67.2 years. The average age is lesser than the 70 years in the study by Lacasse et al¹⁰ but higher than the study by Thomas et al⁸ where the mean age is 54.88 years.

In the present study, 37.86% had significant nocturnal desaturation which is similar to the study by Lacasse et al¹⁰ where 38% were nocturnal desaturates. The present estimate is lesser compared to the study by Thomas et al⁸, where

46.6% were desaturates. But the estimate in the current study was higher than that of by Vos et al¹¹, where 30.03% were significant desaturates.

The current study assessed the FEV1 both before and after administering bronchodilators. The GOLD staging assesses only FEV1. Post bronchodilator FEV1 has been found to be associated with nocturnal desaturation in the present study, which is in accordance with the study by De Angelis et al.¹² It is inferred that, patients who do not have significant improvement in FEV1 after bronchodilators are more prone to nocturnal desaturation.

This study found a significant association PaO₂ and PCO₂ with nocturnal desaturation, which is accordance with the study by Fletcher et al¹³ and Thomas et al.⁸ Similarly Little et al⁷, De Angelis et al¹² and Lacasse et al¹⁰ found a significant association between PaO₂ and nocturnal desaturation. This study is in accordance with McKeon et al¹⁴ where day time PaCO₂ was a significant predictor of nocturnal desaturation in COPD patients.

In the present study, there was a significant association between right atrial dilatation and nocturnal desaturation. This is concordance with the study by Minai et al¹⁵ where the authors indicate that there is a significant correlation between right ventricular dysfunction and nocturnal desaturation. The right ventricular dilatation has been postulated to be the result of pulmonary arterial hypertension.

Desaturation present in 6-minute walk test has been found to be a significant predictor of nocturnal desaturation. This is in concordance with the studies by Garcia-Talavera et al¹⁶ and Moreira et al¹⁷ where 6 minute walk test is found to be an important indicator of nocturnal desaturation and prognosis in COPD. Similar to other studies.^{13,14} there was no significant association in the present study between haemoglobin and nocturnal desaturation.

In the present study, there was no significant correlation between pulmonary arterial pressure and nocturnal desaturation. This is in concordance with the study Chaouat et al¹⁸ where pulmonary hypertension was not associated with nocturnal desaturation in COPD. This may also be explained by the fact that pulmonary hypertension was diagnosed by Echocardiography which has limited value in diagnosing pulmonary hypertension.

CONCLUSION

In conclusion, it is inferred that 37.86% of the normoxemic patients had significant nocturnal desaturation. The significant predictors of nocturnal desaturation are post bronchodilator FEV1, PaO₂, PaCO₂, 6-minute walk test and right atrial/right ventricular dilatation. Hence, screening the COPD patients for these predictors at the outpatient department will enable in identifying those at increased risk of nocturnal desaturation. Furthermore, this will alleviate the need for performance of all-night polysomnography and hence will be cost effective and less time consuming. Early identification will aid in early initiation of treatment such as home oxygen therapy and reduction of complications. The gold standard for diagnosing pulmonary arterial

hypertension is right heart catheterization. This study used echocardiography which hence may be a limiting factor. The use of transcutaneous finger probe for nocturnal oximetry might be another potential limitation of the study.

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