

A Comparison of Nocturnal Hypoxia Markers in Apnea Patients with Chronic Obstructive Pulmonary Disease and without it: A Cross-sectional Study

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Received: 10 Sep. 2016 Accepted: 10 Dec. 2016

Abstract

Background and Objective: The main causes of nocturnal hypoxemia are pulmonary diseases or sleep related breathing disorders. In overlap syndrome, the co-existence of chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA), blood oxygen alteration, and hypercapnia may be more severe. We aimed to study hypoxemia markers in OSA patients with or without COPD.

Materials and Methods: This cross-sectional study evaluated clinical data and polysomnographic findings of 210 patients with apnea hypopnea index (AHI) > 5 among whom 35 patients had COPD.

Results: A total of 210 patients with mean age of 57 years were enrolled in this study. 140 patients (66.7%) had severe OSA (AHI ≥ 30). At wake stage, the mean oxygen saturation (SpO₂) was 89.7 ± 5.1 mmHg for those with severe apnea, 91.0 ± 5.7 mmHg for non-severe apnea patients (AHI < 30), 82.7 ± 10.1 mmHg for COPD patients with severe apneas, and 89.3 ± 7.5 mmHg for COPD patients with non-severe OSA (P < 0.0001). Mean pressure of carbon dioxide was 52.9 ± 7.6 mmHg for COPD patients with severe apneas, and 50.2 ± 10.1 mmHg among those with not-severe OSA (P < 0.0001). In average, blood SpO₂ dropped to 68.0 ± 12.6 mmHg in severe OSA group, to 57.0 ± 13.6 mmHg in COPD patients with severe OSA (P < 0.0001).

Conclusion: Hypoxemia is significantly prominent in overlap syndrome. The presence of diurnal hypoxemia and hypercapnia may predict nocturnal hypoxemia in these patients.

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Keywords: Nocturnal hypoxia; Chronic obstructive pulmonary disease; Sleep-disordered breathing; Polysomnography

Citation: Rezaeitalab F, Asadpour H, Ahmadi-Mousavi M, Safa M, Panahi A, Adimi-Naghan P. A Comparison of Nocturnal Hypoxia Markers in Apnea Patients with Chronic Obstructive Pulmonary Disease and without it: A Cross-sectional Study. *J Sleep Sci* 2016; 1(4): 143-7.

Introduction

Failure of ventilation because of pulmonary diseases may result in nocturnal hypoxemia and hypercapnia. Blood gas disturbances during sleep may also be present in sleep disordered breathing without pulmonary disorders (1, 2).

Breathing stimulation during sleep is decreased compared with wake state. Ventilation and oxygenation during sleep rely mostly on chemical stimuli. As normal sleep reaches to deeper levels of sleep (N2 and N3), respiratory response to hypoxemia and hypercapnia decreases (3-5). Therefore, the threshold of blood pressure of carbon dioxide (PCO₂), which stimulates ventilation, elevates from 40 mmHg in wake to 45 mmHg in sleep. Thus, alveolar ventilation decreases slightly and blood oxygen saturation (SpO₂) drops for 3-4 percent (6). In rapid eye movement (REM)

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stage, because of muscle atonia (except for diaphragm) and irregular respiration, alveolar ventilation is even more disturbed. While normal individuals do not experience major alteration in PCO_2 and PO_2 , at the presence of pulmonary diseases nocturnal blood gases change to some degrees.

Nocturnal hypoxemia is commonly seen with chronic obstructive pulmonary disease (COPD). In a study, 27-70% of such patients suffered from nocturnal hypoxemia especially in REM stage, while diurnal study of Partial pressure of oxygen (PaO_2) was normal (7). In summary, obstructive sleep apnea (OSA) may be commonly accompanied by pulmonary diseases, thus management strategies which cover both, such as non-invasive ventilation (NIV) and oxygen therapy during night, are pivotal. To the best of our knowledge, there is no study on evaluation of nocturnal hypoxemia when COPD coexists with OSA. In this study, we tried to determine hypoxemia markers and PaCO_2 during sleep and wake in OSA patients with or without COPD, and their association to major polysomnographic elements such as apnea hypopnea index (AHI).

Materials and Methods

A total of 307 adults (above 18 years of age) referred to Masih Daneshvari Hospital for polysomnography during 2014-2015 entered this cross-sectional study. Consent form was obtained from all the study participants. To normalize the data and enhance the accuracy of analysis, only patients underwent the test with Philips Respironic Alice 5 appliance were enrolled. Individuals without clear medical record, spirometry, and arterial blood gas (ABG) were excluded from the study. All files were analyzed by the new PSG software of Philips Respironics company for Alice hardware and related data including the lowest level of PaO_2 during sleep, the percent of sleep time with $\text{SpO}_2 < 90\%$, and AHI were measured. To avoid the pulse oxymetry artifacts, $\text{SpO}_2 < 50\%$ was considered as 50. Demographic parameters, spirometric data, and ABG were collected from their medical records. Arterial SpO_2 and partial PCO_2 were recorded for each patient before the polysomnography test when the patient was still awake. The average level of the lowest SpO_2 was calculated.

Then, data were entered into the software SPSS statistics (version 23; SPSS Inc., Chicago, IL, USA). The patients then were divided into two groups according to AHI: severe sleep apnea

($\text{AHI} \geq 30$), and non-severe apnea ($\text{AHI} < 30$) group. COPD was diagnosed based on clinical records, spirometry test with forced expiratory volume 1/forced vital capacity $< 70\%$, and lung computed tomography scan. At this stage, patients with cystic fibrosis, opium addiction, and obesity hypoventilation syndrome [defined by body mass index (BMI) > 30 , diurnal $\text{PaCO}_2 > 45$ mmHg, and the absence of other cardiopulmonary conditions] were removed from the study. Ultimately, clinical and polysomnographic data of 210 patients were analyzed. In this manner, the above factors were evaluated and compared between the severe and non-severe sleep apnea, and between the COPD group (overlap syndrome) and non-COPD group (OSA alone). Statistical analysis was performed using ANOVA test for this purpose. The value of $P < 0.05$ was considered statistically significant.

Definitions

Nocturnal hypoxemia: International Classification of Sleep Disorders, the third revise (ICSD-3) defines nocturnal oxygen desaturation (NOD) as $\text{PaO}_2 < 88\%$ in adults and 90% in children lasting for at least 5 minutes without hypoventilation (8).

COPD: A type of obstructive pulmonary disease characterized by chronic abnormal airflow. 50% of these individuals suffer from sleep disturbances such as difficulty in maintaining the continuity of sleep due to respiratory failure (9). More than half of these patients, whose diurnal SaO_2 are above 90% , spend 30% of their sleep time with $\text{SaO}_2 < 90\%$ (10).

OSA: A pathologic condition during sleep characterized by increased upper airway resistance and absence or decreased respiratory flow. Using polysomnographic findings, OSA is classified to mild (respiratory events represented by $\text{AHI} > 5$) (11), moderate (AHI between 16 and 29) and severe ($\text{AHI} \geq 30$) (12-16).

Overlap syndrome: This term was applied by Flenley (17) for co-existence of OSA and COPD. However, this term does not determine which condition is more severe and which treatment is more appropriate when one of two conditions is more prominent (18-21). The important point is that this coincidence increases the risk of NOD and also diurnal hypoxemia and hypercapnia (22). Furthermore, there are studies which have shown the increased risk of cardiovascular events and mortality rate due to overlap syndrome in comparison with each condition alone (23).

Results

A total of 97 (46.2%) males and 113 females (53.8%) aged from 54 to 89 years with a mean age of 57 years were enrolled in this study. All of them had OSA (AHI > 5). 25 patients (12%) suffered also from COPD, and the remaining 185 did not have COPD. Based on AHI, 140 (66.7%) patients were labeled as severe OSA (AHI \geq 30), whereas the others (33.3%) were in non-severe OSA group. As we excluded patients with obesity hypoventilation syndrome, BMI was not taken into consideration.

The mean SpO₂ at the beginning of polysomnography (wake phase) for severe OSA group was 89.7 ± 5.1 mmHg, and it was 91.0 ± 5.7 mmHg for non-severe group. For COPD patients with severe apneas, this figure was 82.7 ± 10.1 mmHg, and for COPD patients with non-severe apneas, it was 89.3 ± 7.5 mmHg ($P < 0.0001$).

The mean CO₂ before the test was 46.3 ± 7.1 mmHg for those with severe apnea, and 45 ± 7 mmHg for the others. The mean CO₂ was 52.9 ± 7.6 mmHg for COPD patients with severe apneas, and 50.2 ± 7.1 mmHg with not-severe OSA ($P < 0.0001$).

The average percentage of sleep time spent with SpO₂ < 90% was 56.2 ± 40.2 in severe OSA group, 25.9 ± 36.0 in non-severe group, 75.0 ± 34.7 in COPD patients with severe apneas, and 42.3 ± 38.9 in COPD patients with mild to moderate apneas ($P < 0.0001$).

The average minimum SpO₂ was 68 ± 12 mmHg in severe OSA group, and 77.0 ± 11.6 mmHg in non-severe group, 57.0 ± 13.6 mmHg in COPD patients with severe OSA, and 71.9 ± 17.8 mmHg in such patients with mild to moderate OSA ($P < 0.0001$).

Table 1 demonstrates the above data.

Discussion

The mean SpO₂ at wake phase is considerably low in coexistence of COPD and severe sleep apnea (82.7 ± 10.1 mmHg). Furthermore, the average minimum SpO₂ in severe OSA with COPD group was 16.2% lower than severe OSA group without COPD. Characteristically, the average percentage of sleep time spent with SpO₂ < 90% also increased with COPD superimposed on severe sleep apnea. Thus, wake hypoxemia and hypercapnia may predict nocturnal blood gas disturbances.

Pulmonary disease and sleep-disordered breathing may result in more blood oxygen desaturation than normal sleep condition. Accordingly, and because of its consequences, in the last version of ICSD, nocturnal hypoxemia is defined as a separate sleep disorder (24-26).

Tidal volume decreases slightly during normal sleep, even up to 15% in REM sleep (27). Tidal volume in COPD sufferers decreases to 16% in non REM sleep and to 32% in REM sleep and this is another cause for nocturnal hypoxemia in such patients (28-30). Lacasse et al. (31) found that 38% of their COPD patients who had mean diurnal SpO₂ of 65 mmHg spent 30% of their night with SpO₂ less than 90%. Thus, diurnal hypoxemia and PCO₂ may predict somehow nocturnal hypoxemia (10, 22).

Flenley's study (17) showed that coexistence of OSA and COPD results in significant hypoxemia during sleep and similar to the current study, it was correlated with AHI. Also in such patients, dyspnea and diurnal symptoms such as tiredness are more prominent (22, 32).

Table 1. Comparison of the nocturnal hypoxia markers in OSA and overlap syndrome

Hypoxia-related markers	AHI	COPD - Mean \pm SD (mmHg)	COPD + Mean \pm SD (mmHg)	P-value
SPO ₂ at base of the study	< 30	91.5 ± 5.7	89.3 ± 7.5	< 0.0001
	\geq 30	89.7 ± 5.1	82.7 ± 10.1	
PCO ₂ at base of the study	< 30	45.0 ± 4.0	50.2 ± 7.1	< 0.0001
	\geq 30	46.3 ± 7.1	52.9 ± 7.6	
Time spent with SpO ₂ < 90%	< 30	$25.9\% \pm 36.0$	$42.3\% \pm 38.9$	< 0.0001
	\geq 30	$56.2\% \pm 40.22$	$75.0\% \pm 34.7$	
Minimum SpO ₂ at average	< 30	77.0 ± 11.6	71.9 ± 17.8	< 0.0001
	\geq 30	68.0 ± 12.0	57.0 ± 13.6	

AHI: Apnea hypopnea index; SpO₂: Oxygen saturation; COPD-: Patients without chronic obstructive pulmonary disease; COPD+: Patients with Chronic obstructive pulmonary disease; SD: Standard deviation

Nocturnal hypoxemia due to pulmonary diseases usually last for several minutes or more, however, when hypoxemia occurs following sleep apnea, it is shorter and recurs frequently. The patients may be asymptomatic or suffer from sleep insufficiency, nocturnal dyspnea, and excessive daytime sleepiness. Polycythemia is found frequently. Hypoxemia may result in serious consequences such as pulmonary artery hypertension (33), systemic hypertension (34, 35), atherosclerosis, and ischemic heart disease (36-38), cardiac arrhythmia (39), congestive heart failure (40), stroke (41), diabetes mellitus (24), and activated inflammatory mediators due to sleep fragmentation (18, 42, 43).

Respiratory distress is enhanced during sleep in COPD patients. As PCO_2 rises, their disease worsens. In this stage, respiratory effort is more than patient's ability. Consequently, decreased diaphragm force, edema, and increased positive end expiratory pressure result in low tidal volume decompensated respiration. Appropriate NIV can reduce muscle exhaustion and let compensated oxygenation restore while it is monitored during full PSG.

It seems that variables such as mean apnea-hypopnea duration (AHD), and preferred apnea or hypopnea play important role in hypoxemia. Because of the software technical limitations, we were not able to determine AHD. In addition, the fragmented sleep due to respiratory disturbances did not allow the individual to enter REM sleep appropriately. Therefore, further investigation needs to determine the disturbances of blood oxygen in different stages of sleep.

The other issue in our sleep lab was low barometric pressure (655 mmHg), so SpO_2 was lower than that of sea level.

Conclusion

The average percentage of sleep time spent with $SpO_2 < 90\%$ and the mean PCO_2 increase significantly in COPD patients when complicated by severe OSA. Wake hypoxemia and hypercapnia may be a clue in making a diagnosis of pulmonary disease responsible for worsening the condition of OSA and can guide sleep clinics to draw a plan for appropriate treatment during sleep. In fact, nocturnal hypoxemia must be corrected to improve diurnal hypoxemia and hypercapnia. To achieve this goal, cardiopulmonary reassessment is essential and the patients should

be encouraged to have a plan for weight loss, opium reduction, and smoke quitting. Moreover, conducting standard sleep study (polysomnography) is recommended; concurrently NIV and oxygen therapy should be applied.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

Authors would like to thank all the patients participated in this study.

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