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Study of assessment of improvement in sleep apnea with continuous positive airway pressure trial in patients of obstructive airway diseases with obstructive sleep apnea

Mahavir S. Bagrecha[1], Sachinkumar S. Dole[1*], Chetan B. Chaudhari[2] and Kundan N. Mehta[1]

[1]Department of Respiratory Medicine, Dr. D.Y. Patil Medical College, Hospital & Research Centre, Sant Tukaram Nagar, Pimpri Colony, Pune-411018, Maharashtra, India and [2]Department of Pulmonary Medicine, Dr. Ulhas Patil Medical College & Hospital, Bhusawal Road, Jalgaon-425309, Maharashtra, India

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Abstract: *Background & Objectives:* Sleep disordered breathing, mainly obstructive sleep apnea (OSA) and obstructive airway diseases (OADs) are among the most common pulmonary diseases. Patients with both disorders, has more severe nocturnal hypoxia than either disease alone. This study is an attempt to explore risk factors and effect of positive airway pressure therapy on severity of sleep apnea in these (overlap syndrome) patients. *Methods:* This prospective, observational study was conducted in sleep laboratory of the department of pulmonary medicine over a period of 18 months. Patients with obstructive airway diseases diagnosed by spirometry; later on underwent polysomnography to confirm diagnosis of OSA. These patients were subjected to one full night attended nasal continuous positive airway pressure (auto-CPAP) therapy to determine its effect on OSA severity. *Results:* Hundred patients of obstructive airway diseases were included in the study after written and informed consent. These patients underwent polysomnography for presence of OSA. Age more than 45 years, male sex, obesity, smoking, nasal polyps were the risk factors associated with development of OSA in patients with COPD and bronchial asthma. 26 patients were diagnosed as having OSA. Total 19 patients in whom positive airway pressure therapy (CPAP) was indicated, were given one full night attended auto-CPAP. Before CPAP application, mean apnea-hypopnea index (AHI) was 33.12 and after application of auto-CPAP, it decreased upto 5.95. *Conclusions:* Polysomnography should be done in patients of overlap syndrome to diagnose OSA. Auto-CPAP therapy was found to be well tolerated amongst these patients and it improves OSA by decreasing the AHI.

Keywords: Overlap Syndrome, Polysomnography, Positive Airway Pressure, Sleep Disorders.

Abbreviations: AHI: Apnea - Hypopnea index; BMI: Body Mass Index; COPD: Chronic obstructive pulmonary disease; CPAP: Continuous positive airway pressure; ENT: Ear Nose and Throat; FEV1: Forced expiratory volume in first second; FVC: Forced vital capacity; OSA: Obstructive sleep apnea; PSG: Polysomnography; MS: Microsoft; RDI: Respiratory Disturbance Index; OSAS: Obstructive sleep apnea syndrome.

Introduction

Sleep disordered breathing (mainly OSA) and obstructive airway diseases are common pulmonary diseases, so a great number of patients have both disorders. This "overlap syndrome" causes more severe nocturnal hypoxia than either disease alone [1].

Specifically patients with COPD and OSA have a substantially greater risk of morbidity and mortality compared to either condition alone. There is still lack of clarity with regards to disease definition, prognosis, and optimal treatment. Noninvasive ventilation may be helpful in these patients. In patients with COPD, as the depth of sleep increases, there is a reduction in minute ventilation with an increase in upper airway resistance with up to 20% patients of severe COPD exhibiting coexistent OSA [2]. The severity of airway

obstruction, as evidenced by FEV1/FVC ratio, was directly proportional to severity of OSA [3-4]. There is high prevalence of OSA symptoms reported in patients with asthma. These symptoms are predicted by severity of asthma and in patients with difficult to control asthma, polysomnography reveals high frequency of OSA [5].

In obstructive lung diseases, alteration in sleep architecture with overall poor quality of sleep has been observed. Various studies shows that the severity of sleep apnea as measured with polysomnography (apnea-hypopnea index) increases with increasing obesity as measured with BMI and weight loss has been shown to reduce the severity of obstructive sleep apnea [6-8].

This study was undertaken to evaluate the correlation between obstructive lung diseases and OSA, with the help of spirometry and polysomnography. We explored risk factors in patients of overlap syndrome and effect of CPAP therapy on OSA severity in these patients.

Material and Methods

This prospective, observational study was conducted in sleep laboratory of the Department of Pulmonary Medicine of a tertiary care centre over a period of 18 months. Ethical clearance was obtained before conducting the study. Patients after clinical examination and spirometry with post bronchodilator reversibility were categorized into bronchial asthma and COPD.

Inclusion criteria:

a) Patients of obstructive airway diseases (COPD and bronchial asthma) with symptoms obstructive sleep apnea.
b) Those with age >18 yrs.
c) Patients giving informed consent.

Exclusion criteria:

a) Patients with other chronic lung diseases.
b) Patients admitted with acute respiratory failure, altered sensorium, left ventricular failure.
c) Acute exacerbation of COPD/bronchial asthma, acute myocardial infarction.
d) Uncooperative patients.

Patients after fulfilling above inclusion & exclusion criteria were recruited into the study. Comprehensive sleep history was obtained in all patients which include an evaluation for snoring, witnessed apneas, gasping/choking episodes, excessive sleepiness not explained by other factors, nocturia, morning headaches, sleep fragmentation/sleep maintenance insomnia, and decreased concentration and memory. In all patients baseline spirometry with post bronchodialator reversibility was done as per American Thoracic Society guidelines [9].

The best of three consecutive measurements were taken. Patients were further categorized into asthma {FEV1/FVC < 70% and FEV1 < 80% predicted with good bronchodilator reversibility i.e. as improvement FEV1 by 12% and 200ml.) and COPD {FEV1/FVC < 70% and FEV1 < 80% predicted with poor bronchodilator reversibility i.e. as improvement FEV1by < 12% and 200ml.) Subsequently polysomnography was done of these patients to find out presence of OSA.

Polysomnography (PSG): PSG was performed with EMBLA 7000 Polysomnography machine having multiple channels [10]. Patient underwent polysomnography in the evening at 8:00 pm after taking informed consent and explaining the procedure in native language. This test was completed in 6-8 hrs and patient was discharged at 7.00 AM. Significant findings in the form of any breathing irregularity including apnea, hypopnea and apnea-hypopnea index (AHI), were noted and entered in the proforma.

The diagnosis of OSA is confirmed if the number of obstructive events (apneas, hypopneas + respiratory event related arousals) on PSG is greater than 15 events/hr or greater than 5/ hour in a patient who reports any of the following: unintentional sleep episodes during wakefulness; daytime sleepiness; unrefreshing sleep; fatigue; insomnia; waking up breath holding, gasping, or choking; or the bed partner describing loud snoring, breathing interruptions, or both during the patient's sleep [11]. The apnea-hypopnea index (AHI-the number of apneas plus hypopneas per hour of sleep) is the

standard metric used to quantitate the severity of obstructive sleep apnea. OSA severity is defined as per AHI into mild (5-15), moderate (15 -30) and severe (>30).

Application of auto-CPAP therapy: One full night attended nasal continuous positive airway pressure (auto-CPAP) therapy using auto-CPAP machine (Devilbiss machine) was given to the patients with AHI > 15. Post procedure AHI was recorded and it was compared with previous AHI results.

Statistical analysis: Data of all the patients including spirometry and polysomnography findings was meticulously collected and entered in case record forms and in the MS EXCEL spreadsheet. The results were expressed in terms of mean, percentages and absolute values. The statistical analyses were performed using SPSS 10 Software.

Results

Total 100 patients of OADs (COPD, bronchial asthma) were included in the study after fulfilling inclusion& exclusion criteria over a period of 18 months. Spirometry with post bronchodilator FEV1 reversibility was done in all these patients and were further categorized into asthma and COPD. Among 100 patients 68 were of COPD and 32 were of bronchial asthma which included 70 males and 30 females with male to female ratio of 2.3:1. 67 patients out of 100 were smokers. Body mass index was normal in 55 patients [BMI 18.5-24.99], while 18 patients were overweight [BMI 25-29.99] and 27 were obese [BMI >30]. In the present study mean age of the patients with COPD was 54.57 (± 9.37) years and that of bronchial asthma patients was 37.61 (± 9.11) years.

In patients of COPD, breathlessness was the most common symptom (82 %), followed by cough (61%), chest tightness (46%) and wheeze (27%). While in patients of bronchial asthma, breathlessness was the most common symptom (87%), followed by wheeze (84%), cough (78%) and chest tightness (42%). Most common symptom of OSA observed in study population was snoring (63%), while other symptoms observed were excessive daytime sleepiness (31%), nocturnal awakening (29%) and memory loss (2%). After doing overnight polysomnography, 17(25%) patients of COPD and nine (29 %) patients of asthma were diagnosed as having obstructive sleep apnea.

Among 26 patients of OSA 20 patients (77%) were in the age group of more than 45 years suggesting that OSA is more prevalent in middle and elderly patients. Among patients with obstructive sleep apnea 20 patients (77%) were males and 06 patients (23%) were females. Out of 26 patients of OSA, 16 (61.54%) were smokers of which 14 patients had COPD and two patients had bronchial asthma. Of all patients diagnosed with OSA, 19 were obese (73.08%), six overweight and only one patient (3.85%) had normal BMI. Among 26 patients, 20 (76.92%) were males and six (23.08%) were females. Sixteen (61.54%) patients were smokers of which 14 patients had COPD and two had bronchial asthma.

It was observed that obesity was risk factor for the development of obstructive sleep apnea in the study population. Other risk factors observed to be associated with OSA includes: middle to elderly age (>45 years), male sex, obesity, smoking, and ear nose throat (ENT) pathologies (nasal polyps) (Table no-1).

Table-1: Risk factors observed in patients of overlap syndrome

Risk factors	COPD with OSA (n=17)	Asthma with OSA (n=9)	Total
Age >45 years	16	04	20 (77%)
Male sex	13	07	20 (77%)
Obesity	12	07	19 (73%)
Smoking	14	02	16 (62%)
Nasal polyp	00	01	01 (4%)

All 26 patients of obstructive airway diseases (COPD & asthma) with diagnosis of OSA by polysomnography was categorized according to the mild, moderate and severe OSA with the help of AHI (Table no-2).

Table-2: Severity of OSA in terms of AHI in overlap syndrome patients				
OSA Grade	**AHI**	**COPD + OSA**	**Asthma + OSA**	**No of patients**
Mild	5-15	05	02	07 (27%)
Moderate	15-30	10	04	14 (53%)
Severe	>30	02	03	05 (20%)
Total		17(65%)	9 (35%)	26(100%)

After application of auto-CPAP in 14 patients of moderate AHI and five patients of severe apneas, there was significant reduction in AHI as described below (Table no-3). 19 patients, in whom positive airway pressure therapy was indicated, were given one full night attended auto-CPAP. Before CPAP application, mean AHI was 33.12 (±21.52), and after application of auto-CPAP mean AHI decreased to 5.95 (±4.53).

Table-3: Effect of auto-CPAP on severity of OSA using AHI					
AHI	**Before CPAP (No of patients)**	**After auto-CPAP AHI (No of patients)**			
		<5	**5-15**	**16-30**	**>30**
Moderate (16-30)	14	10	04	00	00
Severe (>30)	05	02	01	02	00
Total	19	12	05	02	00

Discussion

Obstructive sleep apnea (OSA) is a common condition characterized by repetitive obstruction of the upper airway during sleep with resultant episodic hypoxia and arousal. There is continuous spectrum of severity of sleep-related upper airway dysfunction ranging from simple snoring and upper airway resistance syndrome through mild to severe obstructive hypopnea and apnea [12-13]. The prevalence of OSA increases with age, especially in persons older than 60 years. OSA is also more prevalent among persons who are obese. Both an aging population and a growing rate of obesity contribute to the increasing rate of OSA [14-15].

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is one of the most important medical conditions identified in the last 50 years. It is a major cause of morbidity, a significant cause of mortality throughout the world and the most common medical cause of daytime sleepiness. In India the prevalence of obstructive sleep apnea is reported to be 7.5% in male and 4.5% in female [6]. Thus, sleep apnea is exceedingly common and is a significant public health issue especially in middle age group that will continue to become more common in parallel with its increasingly prevalent risk factors [16]. The signs, symptoms and consequences of OSA are a direct result of the derangements that occur due to repetitive collapse of the upper airway: sleep fragmentation, hypoxemia, hypercapnia, marked swings in intrathoracic pressure, and increased sympathetic activity.

Clinically, OSA is defined by the occurrence of daytime sleepiness, loud snoring, witnessed breathing interruptions, or awakenings due to gasping or choking in the presence of at least five obstructive respiratory events (apneas, hypopneas or respiratory effort related arousals) per hour of sleep. The presence of 15 or more obstructive respiratory events per hour of sleep in the absence of sleep related symptoms is also sufficient for the diagnosis of OSA due to the greater association of this severity of obstruction with important consequences such as increased cardiovascular disease risk [11].

Total 100 patients admitted in a tertiary care hospital were studied over a period of 18 months. Observations and results were compared with other similar studies done in India and across the world. Prevalence of

overlap syndrome that is association of obstructive airway diseases (COPD and bronchial asthma) patients having OSA is also on rise and we intended to study it along with the risk factors responsible in the present study population. Polysomnography was used to study the presence of obstructive sleep apnea and to study the sleep pattern in the study population. Mean age for patients of OSA was 53.46 years (SD ±12.53), and among total 26 patients diagnosed as having OSA, 20 patients (76.92%) were in the age group of more than 45 years suggesting that OSA is more prevalent in middle and elderly patients of the study population. These findings correlate with other studies [17-18].

Out of 26 patients with obstructive sleep apnea, 20 patients (76.92%) were male and six patients (23.08%) were female. Male to female ratio 3.33: 1. This suggests male predominance in the present study. Amongst patients with OSA, snoring was seen in 20 (76.92%), excessive daytime sleepiness in 16 (61.54%), nocturnal awakening in 12 (46.15%) and memory loss in two and personality change in one (3.85%) patients. This implies that snoring and excessive day time sleepiness are major manifestations of OSA. In the present study it was observed that age >45 years, male sex, obesity, smoking, nasal polyps were the risk factors associated with development of OSA in patients with COPD and bronchial asthma. Similar risk factors were observed for the development of obstructive sleep apnea in general population [19].

Treatment of OSA constitutes a) General measures that includes avoidance of alcohol, sedatives, and hypnotics, weight loss and b) Specific measures which consists of Position therapy, Positive airway pressure (CPAP, Auto-CPAP), oral appliances**.** Continuous positive airway pressure (CPAP) therapy remains the first line of treatment in patients with OSA. It reverses upper airway obstruction during sleep and reduces many of the consequences of OSA which leads to improvement in quality of life, improvement in metabolic derangements that occurs in OSA patients as well as prolongs the life with good compliance of therapy [19].

CPAP has the advantage of being noninvasive and has been shown to reduce the number of apneic and hypoxic episodes during sleep. It also reduces daytime sleepiness and improves neuropsychiatric function in patients with OSA [20, 21]. Autotitrating CPAP or auto-CPAP adjusts CPAP throughout the night by detecting of airway flow, snoring, apneas, inspiratory flow limitation and airway vibration (snoring). In COPD and Obstructive Sleep Apnea (Overlap Syndrome) group, data suggest a more severe course of sleep-disordered breathing in subjects with coexisting COPD. This common combination of OSA and COPD has important implications for diagnosis, treatment, and outcome. Treatment currently consists of continuous positive airway pressure, and oxygen as needed. In conclusion sleep apnea whenever present with COPD associated with severe degree of hypoxemia and hypercapnia, these patients present with more severe nocturnal desaturation than the individual disease [22].

CPAP has been shown to acutely improve overnight oxygenation in patients with overlap syndrome. In fact, CPAP with supplemental oxygen for correction of upper airway obstructive episodes and hypoxemia during sleep is the treatment of choice for these patients [3].

Asthma and Obstructive Sleep Apnea: Patients with asthma appear to have an increased risk for OSA. Large epidemiologic studies demonstrate that asthma patients more frequently report snoring. Conversely, OSA could worsen asthma. Treatment for OSA improves asthma symptoms, use of rescue bronchodilator, peak expiratory flow rates, and disease-specific quality of life. In short, OSA and asthma may have a bidirectional relationship in which each can exacerbate the other.

There is a significant association between fragmented sleep and increased airway collapsibility and upper airway resistance indicating that fragmented sleep may lead to early upper airway closure. Study done by Shahida Bashir suggested that nocturnal asthma can lead to sleep disruption, daytime fatigue and hypersomnolence and there is increased sleep latency, reduced sleep efficiency and reduction in slow wave sleep and treatment with CPAP improves asthma

control [23]. In patients with both OSA and asthma, the impaired responses to hypoxia and increased prevalence and decreased perception of bronchoconstriction may lead to a vicious cycle of worsening asthma and sleep deprivation and potentially increased morbidity and mortality. OSAS is an independent risk factor for asthma exacerbations and that OSAS symptoms are more common in asthmatic patients than in the general population [24].

In present study 12 (10 moderate AHI and 2 severe AHI patients) of 19 had optimal titration [An optimal titration reduces AHI to <5 events per hour of sleep and does so for a 15-minute or longer interval and is not continually interrupted by arousals or awakening] and rest seven had adequate titration (AHI of ≤ 10). In some patients, normal values are not achieved, an adequate titration is one that reduces AHI by 75% or more was considered in them. This level of AHI reduction is often difficult to achieve using of auto-CPAP [25].

In study done by Sharma S. et al, twenty patients with moderately severe OSA [AHI > 15/hour] were enrolled in a randomized, controlled, prospective clinical trial and initial diagnostic sleep study was performed, followed by randomization to a manually adjusted CPAP titration on one night and self titrating CPAP on the other night .The AHI decreased from 50.8 +/- 28.8/hour to 3.8 +/- 3.1/hour ($p < 0.005$) during manually adjusted and 6.1 +/- 5.3/hour ($p < 0.005$) during self-titrating CPAP. Based on a single-night laboratory study, they concluded that self-titrating CPAP was well tolerated and improved OSA and sleep architecture comparable to manually adjusted CPAP [25].

In study of F. Sagheer et al., 37 men had OSA, COPD, auto titrating CPAP device study and in lab overnight CPAP titration polysomnogram. Of these, 14 patients (37%) had optimal CPAP titration determined, pre CPAP treatment RDI was 56 ±34.2 and the post CPAP treatment RDI was 5 ±3.36 events/hr, this study suggests that CPAP pressure determined by auto titrating devices are reasonably accurate when compared to in lab CPAP titration pressures in obstructive sleep apnea patients coexisting with COPD [26]. In study done by A. Stammnitz et al. concluded that automatic continuous positive airway pressure devices produce a significant reduction in apnea/ hypopnea index [27].

CPAP therapy is usually indicated in patients with moderate to severe OSA. In our study, 19 patients in whom positive airway pressure therapy was indicated, were given one full night attended auto-CPAP. There was considerable decrease in AHI after auto-CPAP application. A. Stammnitz et al [27] and Teschler H. et al [28] also observed significant reduction in apnea/ hypopnea index using auto-CPAP. In study done by Alkhalil M et al, the data suggest that OSAS is an independent risk factor for asthma exacerbations. CPAP has been shown in prospective clinical studies to have a positive impact on asthma outcome in patients with concomitant OSAS.

Probable mechanism includes mechanical and neuro-mechanical effects, gastro-esophageal acid reflux suppression, local and systemic anti-inflammatory effects (including suppression of increased serum levels of inflammatory cytokines, chemokines, and vascular endothelial growth factor), cardiac function improvements, leptin level suppression, weight reduction, and sleep restoration.

They concluded that asthma and OSAS are increasingly troublesome public health issues. Mounting evidence implicates OSAS as a risk factor for asthma exacerbations, thereby linking these two major epidemics and CPAP, the first line of therapy for OSAS, might modify airway smooth muscle function and asthma control in patients with both disorders. Despite the ever-increasing population of patients with both disorders, large, prospective, randomized controlled studies are necessary to more fully evaluate CPAP and asthma outcomes [29].

Our study has few limitations, first being an observational study conclusions were merely results of observations. Confounding parameters of OSA were not dealt within depth as it was beyond the scope of the study and sleep parameters like stages of sleep were not compared with age matched population. Secondly due to resource limited setup we could not go into the details of risk factors in

patients of OSA and put forward only the observations. Large, long term, prospective, randomized controlled studies are necessary to fully evaluate CPAP and to study the effect of CPAP in obstructive airway disease patients on sleep architecture.

Conclusions

COPD and asthma remains a major public health problem and has considerable morbidity and mortality. Prevalence of OSA and overlap syndrome is also on a rise. These diseases were affecting quality of sleep and hence quality of life. In the present study, polysomnography was used to find sleep disturbance and OSA in study population. Polysomnography was also used to find out correlation between OSA and patients having COPD and asthma in resource limited settings. Use of auto-CPAP was found to be well tolerated and effective in OSA patients with overlap syndrome.

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*All correspondences to: Dr. Sachinkumar S. Dole. Associate Professor, Department of Respiratory Medicine, Dr. D.Y. Patil Medical College, Hospital & Research Centre, Sant Tukaram Nagar, Pune-411018, Maharashtra, India. E-mail: sachindole85@gmail.com