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Correlates and management of sleep related breathing disorders in COPD patients

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Abstract

COPD is characterized by chronic airflow obstruction secondary to chronic bronchitis and/or emphysema. COPD patients reportedly have significant degree of nocturnal sleep symptoms. Some of the sleep related breathing disorders seen in patients with COPD include Obstructive sleep apnea, sleep related hypoventilation and REM related nocturnal oxygen desaturation syndrome. It is a longitudinal observational study. 60 patients both males and females above the age of 40yrs having COPD were randomly selected and distributed into mild moderate and severe grades based in FEV1 and FEV1/FVC ratio following pulmonary function testing. It is found that out of 60 patients following sleep study, proportion of patients with abnormal Apnea hypopnea index were more among grade 2,3,4 (chi square 26.33, p-0.0001) <0.001 which was statistically significant. Also proportion of patients with abnormal Oxygen desaturation index was more as the severity of grading of COPD increased. Early CPAP treatment helped to reduce the severity of sleep disorders and the reduction of AHI and ODI indices.

Keywords: Chronic obstructive pulmonary disease (COPD),obstructive sleep apnea(OSA),apnea hypopnea index(AHI),oxygen desaturation index (ODI)

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is defined as a preventable and treatable disease with pulmonary component characterized by airflow limitation that is of not fully reversible which is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases and some significant extrapulmonary effects that may contribute to the severity in individual patients. It includes emphysema, Chronic Bronchitis, Small airway disease[1-3].

AECOPD (acute exacerbation of COPD) condition is defined as a sustained worsening of the patient's condition from the stable state (in the patient's baseline dyspnoea and cough or sputum or both and beyond normal day to day variation that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD as per Gold guideline[4].It is characterized by presence of increased sputum volume, sputum purulence and dyspnoea.Chronic obstructive pulmonary disease (COPD) is associated with significant morbidity and mortality, with the World Health Organization estimating its rise from being the fourth to the third leading cause of death by 2030. The mortality rates are supposed to increase by 30% every decade[5].

Almost 95% of mortality due to chronic respiratory disease in India can be assigned to COPD. Exacerbations of COPD have considerable impact on health care system at both primary and tertiary care levels as they are the major reason for antibiotic use and admissions.

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WHO has estimated that 600 million people worldwide have COPD. Additionally, exacerbations lead to indirect costs because of days lost from work. COPD affects 30% of patients seen in chest clinics and constitutes 1-25% of hospital admissions all over India[6].AE-COPD is a common cause of emergency room (ER) visits and is a major cause of morbidity and mortality[7, 8].

The natural history of COPD is characterized by frequent exacerbations with an increase of cough, purulent sputum production and breathlessness. Majority of exacerbations are infectious in etiology. Childhood infections are probably a risk factor for the development of COPD. Chronic infections may lead to recurrent chronic inflammation for chronic bacterial colonization of the airways. It can potentially predispose to loss of lung function as well as increase the risk of exacerbation[8, 9].

Three classes of pathogens responsible for acute exacerbations of COPD by infecting lower respiratory tract are respiratory viruses, aerobic gram-positive and gram- negative bacteria and atypical bacteria[10].

Patients with frequent exacerbations appear to lose lung function at an accelerated rate and exacerbations of COPD increase the rates of hospitalization and mortality and decrease the quality of life and increase economic burden[8].

This condition is highly serious in our country. Air pollution and smoking are the highest risk factors in India which are the main causes of COPD that lead to increase in microbial infection[9].

Methodology

Patients underwent Spirometric analysis and those with post bronchodilator FEV1 < 40% are asked for willingness to participate in the study. Those who are willing to participate are screened for inclusion into the study. Informed Consent was obtained from all the patients.

Detailed History, symptoms of nocturnal cough, wheeze, history of lifetime alcohol, smoking and clinical examination of patients done.

Height and weight were measured and BMI calculated, Neck circumference, Waist circumference measured. Respiratory Rate, Pulse rate, Blood pressure, Day time Oxygen saturation measured.

Patient was advised to avoid intake of caffeine on the day of study. He/She is refrained from having nap at daytime on the day of study.

Patient was asked to go to bed one hour before the usual sleep time, hooking up of the polysomnogram instrument was completed and the lights are off at the usual sleep time and the recording was started. Full attended polysomnography was performed with Medicaid systems, Sleep care SC 32 Polysomnogram.

Polysomnography was done and the following sleep variables according to American Academy of Sleep Medicine (AASM) criteria are recorded.

- Total Bed Time (TBT).
- Total Sleep Time (TST).
- Sleep efficiency.
- Sleep latency.
- Sleep stages in minutes and as percentage of TST.
- Arousal index.
- Respiratory event (apnoea and hypopneas) were measured in seconds.
- Apnoea-hypopnea index.
- Minimal nocturnal oxygen saturation.
- Mean nocturnal oxygen saturation.
- Patients with nocturnal desaturation are recorded.

Cheyne Stokes Breathing is diagnosed if there are at least 3 consecutive cycles of crescendo decrescendo change in breathing amplitude and at least 1 of the following Five or more Central apnoeas or hypopneas per hour.

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The cyclical crescendo decrescendo breathing has duration of atleast10 consecutive minutes.

Total Bed Time (TBT): Is the time from Lights out to Lights on
Total Sleep Time (TST): Is Total Stages N1, N2, N3, REM (in minutes) Total Sleep Time =Total Bed Time (TBT)-Total Wake Time.
Wake after Sleep Onset (WASO): Is the total amount of wake time after the first epoch of Sleep.
Sleep Efficiency (%): Is the percentage of time asleep compared to the time spent in bed.
Sleep Efficiency (%) = Total Sleep Time (TST) ÷ Total Bed Time (TBT) x 100%

% of Sleep Stages
% of Sleep Stages is the Total Time of a particular sleep stage divided by Total Sleep Time (TST) this is calculated for Stages N1, N2, N3 & REM.
% Stage N1= Total Stage N1 (in minutes) ÷ TST x 100%
% Stage N2= Total Stage N2 (in minutes) ÷ TST x 100%
% Stage N3= Total Stage N3 (in minutes) ÷ TST x 100%
% REM= Total REM (in minutes) ÷ TST x 100

Sleep latency: Is lights out to first epoch of any sleep stage in minutes.
Arousal: Is the total number of awakenings associated with transient desaturation compared to the preceding two-minute period per hour of sleep.
Arousal index: Is the average number of arousals per hour of sleep.
Nocturnal desaturation: Is defined by Patients with Oxygen saturation below 90 for> 30% of total sleep time.

Criteria for obstructive sleep apnoea
Individuals must fulfil criterion A or B, plus criterion C to be diagnosed with OSA:
A. Excessive daytime sleepiness that is not explained by other factors.
B. Two or more of the following that are not explained by other factors:
- Choking or gasping during sleep.
- Recurrent awakenings from sleep.
- Unrefreshing sleep.
- Daytime fatigue.
- Impaired concentration.

Overnight monitoring demonstrates 5 to 10 or more obstructed breathing events per hour during sleep or greater than 30 events per 6 hours of sleep. These events may include any combination of obstructive apnoea, hypopnea.

Results

Table 1: Distribution according to age and GOLD criteria

		Grade 1		Grade 2		Grade 3		Grade 4		Total
		No	%	No	%	No	%	No	%	
Age in years	40-50	6	22.2	6	27.3	3	30.0	0	0.0	15
	51-60	6	22.2	8	36.4	2	20.0	0	0.0	16
	61-70	12	44.4	8	36.4	5	50.0	1	100.0	26
	> 70	3	11.1	0	0.0	0	0.0	0	0.0	3
	Total	27	100.0	22	100.0	10	100.0	1	100.0	60

Majority of the patients i.e. 12(44.4%) were from 61-70 years from Grade 1 whereas 36.4% each were from 51-60 and 61-70 years from Grade 2, 50% from 61-70 years from Grade 3 and all i.e. 100% from 61-70 years from Grade 4 of GOLD criteria.

Table 2: Distribution according to gender and GOLD criteria

		Grade 1		Grade 2		Grade 3		Grade 4		Total
		No	%	No	%	No	%	No	%	
Gender	Male	11	40.7	18	81.8	9	90.0	1	100.0	39
	Female	16	59.3	4	18.2	1	10.0	0	0.0	21
	Total	27	100.0	22	100.0	10	100.0	1	100.0	60

Chi square test-13.0, p-0.005(<0.05), Significant.

Proportion of males were more in number in grade 2, 3 and 4 i.e. 81.8%, 90% and 100% respectively whereas proportion of females (59.3%) were more in grade 1 of GOLD criteria. This difference in the proportion of males and females was significantly higher (<0.05). It means gender has predilection for severity of COPD in our study.

Table 3: Distribution according to AHI and GOLD criteria

		Grade 1		Grade 2		Grade 3		Grade 4		Total
		No	%	No	%	No	%	No	%	
AHI	Normal	16	59.3	0	0.0	0	0.0	0	0.0	16
	Abnormal	11	40.7	22	100.0	10	100.0	1	100.0	44
	Total	27	100.0	22	100.0	10	100.0	1	100.0	60

Chi square test-26.66, p-0.0001(<0.001), highly significant.

Proportion of patients with abnormal AHI were more in number in grade 2, 3 and 4i.e. 100% each compared to proportion of 40.7% in grade 1 of GOLD criteria.
This difference in the proportion of patients was significantly higher (<0.05). It means AHI raised significantly with severity of COPD in our study.

Table 4: Distribution according to ODI (oxygen desaturation index) and GOLD criteria

		Grade 1		Grade 2		Grade 3		Grade 4		Total
		No	%	No	%	No	%	No	%	
ODI	Normal	18	66.7	0	0.0	0	0.0	0	0.0	18
	Abnormal	9	33.3	22	100.0	10	100.0	1	100.0	42
	Total	27	100.0	22	100.0	10	100.0	1	100.0	60

Chi square test-31.42, p-0.0001(<0.001), highly significant.
Proportion of patients with abnormal ODI were more in number in grade 2, 3 and 4i.e. 100% each compared to proportion of 33.3% in grade 1 of GOLD criteria.

This difference in the proportion of patients was significantly higher (<0.05). It means ODI raised significantly with severity of COPD in our study.

Table 5: Correlation between BMI and AHI

		BMI
AHI	Pearson Correlation	0.891
	value	0.0001
	Inference	Positive correlation

We found statistically significant positive correlation between AHI and BMI in ourstudy.

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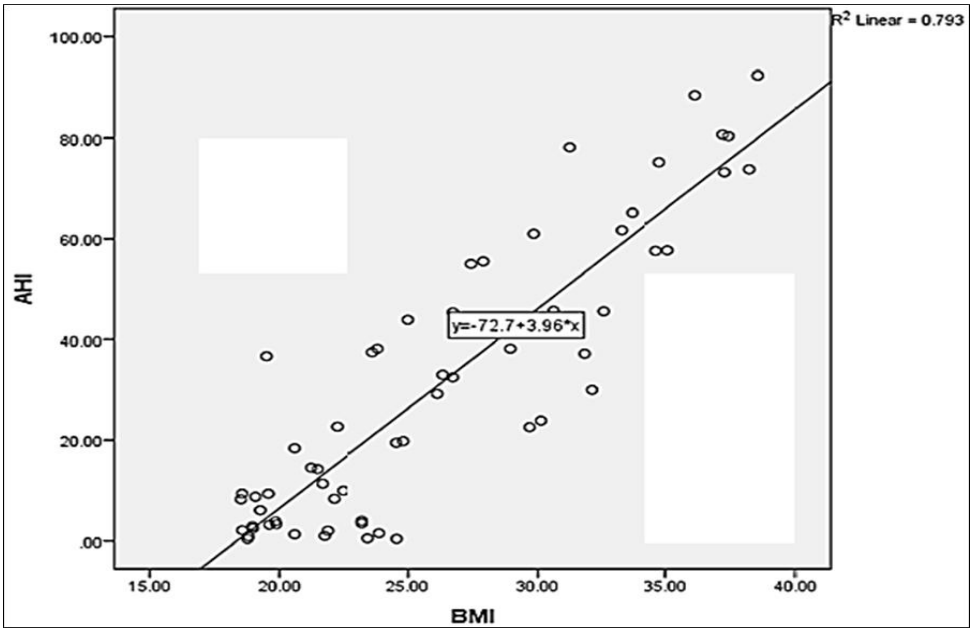

Graph 1: Scatter diagram showing Correlation between BMI and AHI

Table 6: Correlation between BMI and ODI

		BMI
ODI	PearsonCorrelation	.893**
	p value	0.0001
	Inference	Positivecorrelation

We found statistically significant positive correlation between ODI and BMI in ourstudy.

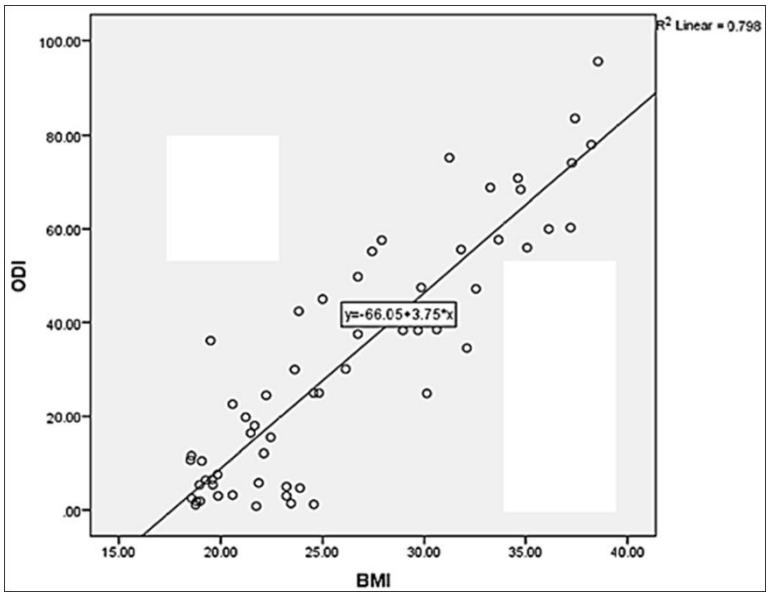

Table 7: Effect of treatment on ODI

		N	**Mean**	**Std.Deviation**	**t**	**p**	**Inference**
ODI	Pre-treatment	60	31.29	26.00	2.82	0.007	Significant
	Post-treatment	60	17.75	42.32		(<0.05)	

Mean ODI before treatment in our study was 31.29±26 whereas it was 17.75±42.32 after treatment.

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The difference in the mean ODI before and after treatment was found to be statistically significant (<0.05)
It means oxygen desaturation index is significantly reduced after treatment in our study.

Table 8: Effect of treatment on AHI

		N	Mean	Std.Deviation	t	p	Inference
AHI	Pre-treatment	60	30.17	27.57	9.28	0.0001 (<0.001)	Highly significant
	Post-treatment	60	12.29	13.79			

Mean apnoea hypo apnoea index before treatment in our study was 30.17±27.57 whereas it was 12.29±13.79 after treatment.
The difference in the mean ODI before and after treatment was found to be statistically significant (<0.001).
It means apnoea hypo apnoea index (AHI) is significantly reduced after treatment in our study.

Discussion

Insomnia is primarily a clinical diagnosis. Patients should be asked about theduration, frequency, and severity of their sleep symptoms. The course andprecipitants of the symptoms, and relationship to the symptoms of the lung disorder (cough, sputum production, dyspnea) should be assessed. Inquiries should be made regarding daytime habits that might contribute to insomnia (e.g., nicotine use,alcohol, and caffeine intake), sleep hygiene and possible daytime consequences of sleep problems, including fatigue, sleepiness, andqualityoflife. Patientsshould also be asked about any other disorders that could contribute to insomnia. Physical exam should be targeted towards assessing comorbidities[11].
Sleep logs can help provide relatively objective evidence of presence and course of sleep disturbance. Scales such as the Insomnia Severity Index can help quantify the severity of insomnia at baseline as well as provide objective evidenceof improvement with therapies. Actigraphy is largely limited to the research arena, but may be used clinically if history is not clearly indicative of type or severity of sleep problems.
Several interventions improve sleep quality in COPD patients. Optimal treatment of COPD to minimize symptoms such as cough, secretions, and dyspnea will likely lead to better sleep quality. Smoking cessation should be strongly encouraged. Organic sleep disorders including RLS and sleep disordered breathing (SDB) should be optimally treated. Oxygen may theoretically have several salutary effects on sleep in COPD. Larger studies are needed to assess effects of long-term oxygen supplementation on sleep in these patients[12, 13].
Cognitive behavioral therapy for insomnia (CBT-I) is aneffectivetherapyin primary insomnia and appears to be superior to sedatives in thelong term. CBT-Ialso appears to be beneficial in insomnia comorbid with cancer, human immunodeficiency virus infection, chronic pain, psychiatric disorders such as depression. A small study suggests feasibility and efficacy of performing CBT-I in COPD patients. In view of the potential adverse effects of pharmacotherapy inCOPD, larger trials need to be conducted assessing CBT in COPD. Other interventions, such as stimulus control therapy alone, may also be beneficial[14].
Therapy of attendant anxiety and depression may help improve sleep. One randomized, controlled trial reported significant improvements notonlyindepressive symptoms after CBT, but also improved sleep efficiency at 8-month follow-up in patients with COPD and depression.
Despite concerns regarding their respiratorydepressanteffects,benzodiazepines have been assessed for treatment of insomnia in COPD.
Medications may be required to improve sleep when nonpharmacologic measures prove inadequate. One week of temazepam 10 mg therapy in 14 patients with stable, severe, normocapnic COPD did not cause a significant increaseincarbon dioxide tension during sleep or worsen dyspnea or sleepiness. However, decrease in minute ventilation, worsening of

diaphragmatic endurance and decreasein oxygen saturations have been reported withtraditionalbenzodiazepines, suggesting need for caution. Furthermore, tolerance, dependence, cognitive impairment and abnormal sleep-related behaviors are concerns with both benzodiazepines and nonbenzodiazepine benzodiazepine receptor agonists[15].

Melatonin can also improve sleep quality in COPD. Use of the MT(1)/MT(2) melatonin receptor agonist ramelteon 8 mg for one night in 25 subjects (≥ 40 years) with moderate to severe COPD resulted in a significant increase in total sleep and sleep efficiency without causing respiratory depression or worse hypoxemia. The likelihood of cognitive impairment and abuse liability is also lower than that with benzodiazepine receptor agonists. However, more clinical trials need to be done to assess the effects of ramelteon on diverse physiological and polysomnographic parameters in persons with COPD.

Doxepin is a histamine-1 receptor antagonist that has been shown to alleviate psychophysiological insomnia[63].The sleep promoting effect is seen primarily at low doses (3 mg or 6 mg), in contrast to the higher doses (10 mg or more) required for antidepressant action. However, efficacy of other antihistaminic agents in insomnia has not been demonstrated

consistently. Furthermore, these agents can be limited by their anticholinergic adverse effects which include precipitating narrow angle glaucoma or urinary retention. Trazodone is commonlyusedforinsomnia.However, its efficacy, especially in the long-term is not clear. Mirtazapine binds to 5-HT_{2A} and 5-HT_{2C} in addition to the H_1 receptor and may have a role in promoting weight gain apart from its effects on sleep. Thus, it may have a potential role in a subset of COPD patients where both these benefits would bedesirable.Nevertheless, it needs to be reiterated that these agents have not been systematically evaluated in COPD.

Finally, it is plausible that antioxidants and anti-inflammatoryagents, if proven effective, may improve sleep by improving thesymptoms of COPD as wellas decreasing sympathetic activity.

We found statistically significant positive correlation between AHI and BMI in our study. We also found statistically significant positive correlation between ODI and BMI in our study.

Our findings are consistent with the findings of other studies[16].

Conclusion

- Statistically significant positive correlation was seen between AHI and BMI as well as between ODI and BMI in our study.
- CPAP treatment is useful to reduce the oxygen desaturation index (ODI) and AHI.

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