Original Article

Prevalance of Obstructive Sleep Apnoea in Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Background. The concomitant occurrence of moderate-to-severe chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea (OSA) is reportedly around 60% attributing to worse prognosis in this subset of population. The present study was undertaken to ascertain the prevalence and implications of OSA in patients of COPD and compare it with those of patients of COPD without OSA.

Methods. Fifty diagnosed patients of moderate-to-severe COPD of age ≥40 years were screened for OSA using a self-reported questionnaire (STOP BANG Questionnaire). Out of these 30 patients who were found to be at risk of OSA (STOP BANG score >2) were included in the study. These 30 patients then underwent (in lab) Type 1 diagnostic polysomnography (PSG) and inflammatory markers interleukin (IL)-4, IL-5,IL-6,IL-13, high sensitivity c-reactive protein [hs-CRP] and fractional exhaled nitric oxide [FeNO] testing. Their quality-of-life was evaluated with St. George's Respiratory Questionnaire (SGRQ) score, body-mass index, airflow obstruction, dyspnoea and exercise (BODE) index and COPD assessment test (CAT) score.

Results. After PSG, OSA apnoea-hypopnoea index (AHI ≥5/hour) was found in 22 (73.3%) out of 30 moderate-to-severe COPD cases. In moderate COPD, 9 (69.2%) out of 13 patients and in severe COPD 13 (76.4%) out of 17 cases were diagnosed to have OSA (P=0.61). On evaluation with the parameters of pulmonary function test (PFT); significantly lower forced vital capacity (FVC) was found in COPD cases with OSA (P=0.03). No statistically significant difference was found for the level of inflammatory marker based on the presence of OSA (P>0.05). The patients of COPD with OSA fared poorly in CAT, BODE index, modified Medical Research Council (mMRC) scale and SGRQ score in comparison to those with COPD alone (P<0.02)

Conclusions. Our study indicates high prevalence of OSA in patients with moderate-to-severe COPD which negatively affects the quality of sleep and symptoms associated with COPD which further leads to poor quality-of-life. Clinicians should maintain a high index of suspicion for OSA while evaluating a patient of poorly controlled COPD.
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Key words: COPD, OSA, CAT, Polysomnography, Inflammatory markers, Pulmonary function, Quality-of-life.

Introduction

Chronic obstructive pulmonary disease (COPD), the most common pulmonary disease worldwide and contribute to significant morbidity and mortality.[1] According to crude estimates there are 30 million COPD patients in India, which is amongst the highest in the world.[2] Similarly, in 2013 the estimated prevalence of OSA was 14% for men and 5% for women and its standard diagnostic test is an overnight polysomnogram (PSG).[3, 4] Their existence in isolation is well studied. However, now-a-days reports regarding the concurrent occurrence of these disorders in varied proportions are emerging. The data from multiple studies observe a bi-directional interaction between OSA and COPD and have attributed to their association beyond random co-existence due to high prevalence.[5]

The concomitant occurrence of COPD and OSA has been termed as 'overlap syndrome' by Flenley.[6] The prevalence of OSA in moderate-to-severe COPD patients was found to be 66%; body mass index (BMI) and pack years were found to be important predictors of OSA.[7] Venkateswaran *et al*[8] reported prevalence of overlap syndrome among COPD patients as 60%. But co-existence of mild obstructive airway disease and sleep disordered breathing appears to be more due to chance than any other mechanism.[9]

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As COPD prevalence is rising to epidemic proportions due to historical smoking trends, the aging of the population and increased air pollution, its association with OSA is being increasingly recognised as a factor responsible for frequent exacerbations.[10] The Sleep Heart Health Study[11] found that patients with both OSA and COPD are at a greater risk of prolonged oxygen desaturation at night than those with OSA but without COPD; the degree of obstruction, as measured by forced expiratory volume in first second/ forced vital capacity (FEV_1/FVC), correlates with the risk of prolonged hypoxaemia. Thus, the identification of their association is imperative as these patients with increased risk of nocturnal hypoxaemia can develop pulmonary hypertension and cor-pulmonale leading to increased morbidity and mortality.[12]

Data on co-existence of COPD and OSA in Indian population is scarce. Therefore, the present study was undertaken to ascertain the implications of OSA in patients of COPD and to compare it with patients of COPD without OSA.

Material and Methods

The study was conducted at the out-patient clinics in Department of Respiratory Medicine at Vallabhbhai Patel Chest Institute, University of Delhi, Delhi after due ethical clearance from the Ethics Committee. Written informed consent was obtained from all patients. Fifty patients diagnosed to have moderate-to-severe COPD presenting to the out-patient clinic during the study year (2015-2016) were screened for OSA using a self-reported questionnaire (STOP BANG questionnaire). Patients with moderate-to-severe COPD and aged ≥40 years, with a smoke exposure of >10 pack-years accumulated, as per GOLD 20[13] were included. Patients who were unable to fill the questionnaire properly, pregnant, lactating women, patients with significant cognitive impairment or poorly controlled psychiatric disorder were excluded from the study. Out of these, 30 patients found to be at risk of having OSA (STOP BANG score >2) were enrolled in the study. Detailed clinical and laboratory evaluation including hemoglobin levels, total and differential leucocyte counts, spirometry with reversibility, absolute eosinophil count, chest radiography followed by in lab (Type 1) diagnostic PSG, inflammatory markers (interleukin [IL]-4, IL-5, IL-6, IL-13, high sensitivity C-reactive protein [hs-CRP] and fractional exhaled nitric oxide (FeNO) testing were done. The measurements of serum inflammatory markers (IL-4, IL-5, IL-13, IL-6, hs-CRP) was measured using commercially available ELISA kits. All patients regardless of their atopic status, underwent measurements of exhaled nitric oxide using NIOX chemiluminescence analyzer (Aerocrine AB, Solna, Sweden) in accordance with the 2005 American Thoracic Society/ European Respiratory Society (ATS/ERS) recommendations[16] using online method. None of our COPD patients were on oxygen supplementation.

The sample size calculation was based on the reported prevalence of OSA in patients who had moderate-to-severe COPD. The computed minimum sample size, calculated using the formula $n = z^2p(1-p)/d^2$, where n is sample size, p is prevalence, z is confidence interval and d is precision, comes to be 24.

As per the American Academy of Sleep Medicine (AASM) guidelines[13], patients with COPD underwent overnight (in laboratory) type 1 diagnostic PSG comprising of 7 channels, namely, elctroencephalography (EEG), electrooculography (EOG), tibialis anterior electromyography (EMG), airflow measured by nasal transducer (hypopnoea) and thermistor (apnoea), pulse oximeter and chest and abdominal effort leads. Polysomnographic recordings were scored manually using the EMBLA 2000 by a certified polysomnographic technologist, with physician's review, both blind to patient's status. A total sleep time >4 hours was required.

Apnoea was defined as complete cessation of airflow for at least 10 seconds. The event is obstructive if during apnoea there is effort to breathe.[14] Hypopnoea was defined as an abnormal respiratory event with at least a 30% reduction in thoraco-abdominal movement or airflow as compared to baseline lasting at least 10 seconds, and with >4% oxygen desaturation.[14] OSA was defined as apnoea-hypopnea index (AHI) ≥5 with symptoms or AHI ≥15 if asymptomatic, as per American Academy of Sleep Medicine (AASM) recommendations.[14] The AHI is calculated by dividing the total number of apnoeas plus hypopneas events by the number of hours of sleep.[14]

After PSG study, patients were classified as per Chicago criteria[15] as normal (AHI <5/hour), with mild OSA (AHI 5-15/hour), moderate OSA (AHI 16-30/hour) and severe OSA (AHI >30/hour).

The symptom control was assessed using COPD assessment test (CAT), BODE index, quality-of-life assessment–SGRQ score. In addition, electrocardiogram, kidney function, liver function tests, arterial blood gas analysis and other appropriate investigations were done as and when required.

Statistical Analysis

Data were entered into Microsoft Office Excel and analysed using Statistical Package for the Social Sciences (SPSS, version 17, USA). Descriptive statistics are reported as mean and standard deviation, proportions. For quantitative data, difference in means between the two groups was compared by student's

t-test (for normal distribution) or Mann-Whitney test (for non-normal distribution). For qualitative data, Chi-square test was used to observe the difference between proportions for independent groups. A P-value of less than 0.05 was considered statistically significant.

Results

Fifty patients diagnosed to have moderate-to-severe COPD presenting to out-patient clinic during a duration of one year (2015-2016) were screened for OSA using a self-reported questionnaire (STOP BANG questionnaire). Of these, 30 patients (25 males) were found to be at risk of OSA (STOP BANG score >2) and included in the study. Their mean age was 49-69 years. After type 1 PSG (in lab) study OSA (AHI ≥5/h) was found in 22 (44.4%) of moderate-to-severe COPD patients.

There were higher number of male patients than female patients and around 70% of them were obese with a mean BMI of around 30kg/m^2. The male gender and BMI are known predisposing factors for OSA. Of the 30 COPD patients, 21 were obese and 9 were non-obese patients. OSA was found in 20/21 (95.2%) obese patients and 2/9 non-obese patients (P=0.01).

Association of OSA with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages (moderate and severe) of COPD is shown in table 1. No significant difference was found between the number of patients with OSA in moderate (9/13, 69.2%) *versus* severe (13/17, 76.4%) COPD cases (P=0.67). The forced vital capacity (FVC) (%) was significantly lower in COPD patients with OSA (P=0.002) compared to those without OSA (Table 2). Other parameters were comparable also (Table 2).

There was no statistically significant difference in sleep period, total sleep time (TST), sleep latency to rapid eye movement (REM) and sleep efficiency between the two groups (Table 3). The sleep efficiency was low (<70%) for both the groups (normal 85%)[17]. The sleep structure was abnormal in all COPD patients with or without OSA as they spent less than 20% of TST in stage N3 sleep and more than 5% of TST in stage N1 sleep. As expected, stage N1 sleep was significantly higher (24.7%) in patients of COPD with OSA as compared to without OSA (10.6%) (P=0.03).

The inflammatory markers (IL-4, IL-5, IL-6, IL-13, hs-CRP and FeNO) were also studied in COPD patients and then analysed according to the presence or the absence of OSA, but the difference was not statistically significant (Table 4). COPD patients with OSA fared poorly in CAT, BODE and SGRQ scores than the patients of COPD alone and the results were statistically significant (Table 5).

Table 1. Stage of COPD against absence or presence of OSA

COPD Stage	Without OSA No. (%)	With OSA No. (%)	P-value
Moderate (N=13)	4 (30.8)	9 (69.2)	
Severe (N=17)	4 (23.5)	13 (76.4)	0.67
Total	7	23	

Definition of abbreviations: COPD=Chronic obstructive pulmonary disease, OSA=Obstructive sleep apnoea, No=Number of patients

Table 2. PFT parameters against absence or presence of OSA

Parameters	COPD With OSA (mean±SD) (N=22)	COPD Without OSA (mean±SD) (N=8)	P-value
FEV_1/FVC	48.8±6.3	55.9±13.02	0.15
FVC	90.1±17.6	71.8±10.8	0.002
FEV_1	51.7±15.9	47.8±12.4	0.48

Definition of abbreviations: PFT=Pulmonary function test, OSA=Obstructive sleep apnoea, SD=Standard deviation, FEV_1=Forced expiratory volume in one second, FVC=Forced vital capacity

Table 3. PSG parameters against GOLD stages of COPD

Parameters	COPD Moderate (mean±SD) (N=13)	COPD Severe (mean±SD) (N=17)	P-value
Sleep period (min)	330.7±130.8	349.3±153.3	0.1
Total sleep time (min)	238.4±101.8	254.5±133.6	1.1
Sleep latency to REM (min)	101.7±45.7	115.3±82.18	0.7
Sleep efficiency (%)	69.2±19.2	65.6±18.03	0.9

Definition of abbreviations: PSG=Polysomnography, GOLD=Global Initiative for Chronic Obstructive Lung Disease, COPD=Chronic obstructive pulmonary disease, SD=Standard deviation, REM=Rapid eye movement

Discussion

In previously done studies[7,8] on overlap syndrome, high prevalence of OSA in COPD ranging from 60%-66% has been reported but more recent studies have suggested that the occurrence of OSA in COPD is by chance alone and such high prevalence does not exist.[9] Hence, the results across various studies are variable.

We found no statistically difference between number of patients with OSA in moderate and severe

Table 4. Inflammatory markers according to the presence of OSA

Marker	COPD With OSA (mean±SD) (N=22)	COPD Without OSA (mean±SD) (N=8)	P-value
IL-4	3.7±4.6	4.5±5.1	0.69
IL-5	1.6±1.9	3.6±5.1	0.31
IL-6	41.6±31.4	40.6±27.5	0.91
IL-13	3.5±5.4	5.9±10.1	0.53
hs-CRP	56.4±57.6	51.2±128.5	0.26
FeNO	14.6±8	17.4±8.2	0.43

Definition of abbreviations: OSA=Obstructive sleep apnoea, COPD=Chronic obstructive pulmonary disease, SD=Standard deviation, N=Number of patients, IL=Interleukin, hs-CRP=High sensitivity C-reactive protein, FeNO= Fractional exhaled nitric oxide

Table 5. SGRQ score, BODE index and CAT in COPD patients

	COPD Without OSA (mean±SD)	COPD With OSA (mean±SD)	P-value
SGRQ (mean) score	61.5±8.7	41.01±14.1	0.000
BODE (mean) index	6.2±0.8	5.0±0.9	0.001
CAT	33.0±1.9	28.1±4.9	0.001

Definition of abbreviations: SGRQ=St. George's Respiratory Questionnaire, BODE=Body-mass index, airflow obstruction, dyspnoea and exercise, CAT=COPD assessment test, COPD=Chronic obstructive pulmonary disease; OSA=Obstructive sleep apnoea; SD=Standard deviation

COPD cases but the FVC was significantly reduced in COPD patients with OSA. This can be attributed to high prevalence of obesity in our study group leading to reduced chest wall compliance.[19] The Sleep Heart Health Study has found that the degree of obstruction, as measured by FEV_1/FVC, correlates with the risk of prolonged hypoxaemia during sleep.[9] Another study[20] suggested that obesity negatively impacts the lung volume. The reduced lung volume can, in turn, increase the upper airway collapsibility[21], a characteristic feature of OSA. OSA impacts lung elasticity properties leading to increased airflow resistance, and hence, this vicious cycle continues.

In the data obtained after full night PSG it was found that the sleep structure was abnormal in all COPD patients with or without OSA as they spent less than 20% of TST in stage N3 sleep and more than 5% of TST in stage N1 sleep. As expected, stage N1 sleep was significantly higher (24.7%) in the cases of COPD with OSA as compared to COPD cases without OSA (10.6%).

The sleep efficiency was poor (<70%) in both moderate and severe COPD cases. This indicates the evidence of disturbed sleep in COPD cases. But the statistically significant difference could not be found between moderate and severe COPD cases in terms of sleep efficiency, sleep period, sleep latency to REM and TST.

No statistically significant difference in the level of inflammatory markers could be found in between patients of COPD with OSA and those with COPD alone. The IL-4, IL-5, IL-13 and FeNO are markers of eosinophilic inflammation.[22] Also, the value of exhaled FeNO is a predictor of steroid responsiveness.[23] Thus, our findings corroborate the findings that OSA causes neutrophilic inflammation of earlier studies[24] of inflammatory markers in patients of OSA.

There were limitations to our study as the sample size was small and duration of the study was limited. Therefore, results of the present study may be generalised with caution.

Conclusions

The present study observed high prevalence of OSA in patients with moderate-to-severe COPD which negatively affects the quality of sleep and symptoms associated with COPD which further leads to poor quality-of-life. Clinicians should maintain a high index of suspicion for OSA while evaluating a patient of poorly controlled COPD.

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