Role of oxygen and continuous positive airway pressure therapy in chronic obstructive pulmonary disease patients with nocturnal oxygen desaturation

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Introduction Sleep has a significant effect on respiration, even in healthy individuals. Breathing difficulties in chronic obstructive pulmonary disease (COPD) patients during sleep are one of the most common symptoms in these patients. Nocturnal desaturation may occur in COPD in the absence of severe daytime hypoxemia. Nocturnal desaturation may contribute to the development of pulmonary hypertension, nocturnal cardiac arrhythmias, and death during sleep. However, the optimal treatment for patients with isolated nocturnal hypoxemia remains uncertain.

Aim of the work The aim of this study was to assess the role of oxygen and continuous positive airway pressure (CPAP) therapy in COPD patients with nocturnal oxygen desaturation (NOD).

Patients and methods This study was conducted on 40 male COPD patients. The included patients were classified into two groups: group 1 included normoxic or mildly hypoxic patients with day time SpO\textsubscript{2}≥91\% defined as NOD by fall of greater than 4\% from awake SpO\textsubscript{2}, and group 2 included moderate and severely hypoxic patients with daytime SpO\textsubscript{2}≤90\% who showed a pulse oximetric plot with at least 5 min with SpO\textsubscript{2}≤90\% and a peak of SpO\textsubscript{2}≤85\% and were considered as nocturnal desaturator. The two groups were subjected to full history taking, clinical examination, the Epworth sleepiness scale, anthropometric measurements, pulmonary function tests (spirometry), radiological examination using chest radiograph, and SpO\textsubscript{2} using pulse oximetry. SpO\textsubscript{2} evaluation using pulse oximetry was carried out for four nights: the first night while breathing room air, the second night while giving low-flow humidified oxygen (2 l/min) overnight, the third night with patients on noninvasive ventilation using autoset CPAP mask, and the fourth night with patients on noninvasive ventilation using autoset CPAP mask with low-flow humidified oxygen (2 l/min).

Results The included patients had moderate, severe, and very severe COPD according to the GOLD spirometric classification. The highest mean value of oxygen saturation was seen in cases that received CPAP with oxygen, followed by cases that received low-flow humidified nasal oxygen, and the lowest mean value was on CPAP. In group 1, there was no significant difference between mean values of oxygen saturation on oxygen and CPAP, but there was a highly significant difference between mean values of oxygen saturation on oxygen and CPAP with oxygen, as well as on CPAP and CPAP with oxygen. In group 2, there was a significant difference between mean values of oxygen saturation on oxygen and CPAP, on nocturnal oxygen and CPAP with oxygen, as well as on CPAP and CPAP with oxygen.

Conclusion In group 1, it is better to prescribe nocturnal CPAP with oxygen than nocturnal oxygen alone or nocturnal CPAP alone to COPD patients with NOD in this group, whereas in group 2 it is better to prescribe nocturnal CPAP with oxygen, followed by nocturnal oxygen alone, compared with nocturnal CPAP alone to COPD patients with NOD in this group.

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nocturnal desaturation [5]. Supplemental oxygen is the mainstay of treatment for those with daytime and nocturnal hypoxemia. Noninvasive ventilation has been used as an adjunct to COPD rehabilitation, as it increases ventilation, allows the respiratory muscles to unload during rest and physical exercise, and reduces symptoms of dyspnea [6].

Aim of the work
The aim of this study was to investigate the effect of nocturnal oxygen therapy and continuous positive airway pressure (CPAP) as a treatment of NOD in COPD patients.

Patients and methods
This study was conducted on 40 COPD male patients. The study protocol was approved by local ethical committee and informed consent was taken.

Study design
The included patients were classified into two groups:

Group 1: Normoxic or mildly hypoxic patients with daytime $\text{SpO}_2 \geq 91\%$ defined as NOD with a fall of greater than 4% from awake baseline.

Group 2: Moderate and severely hypoxic patients with daytime $\text{SpO}_2 \leq 90\%$ who showed a pulse oximetric plot with at least 5 min with $\text{SpO}_2 \leq 90\%$ and a peak of $\text{SpO}_2 \leq 85\%$ were considered as nocturnal desaturators according to Fletcher definition [7].

Inclusion criteria
All patients included in the study fulfilled the criteria of COPD according to the GOLD classification [1].

Exclusion criteria
(1) COPD patients with exacerbation within 4 weeks.
(2) COPD patients with coexisting illness (renal impairment, liver impairment, etc.).
(3) COPD patients with no NOD.

However, we made all possible efforts to exclude individuals with obstructive sleep apnea syndrome (OSAS). Epworth sleepiness scale: The patients were asked to evaluate sleepiness (how likely are you to doze off or fall asleep in the following situations) [8]:

(1) Sitting and reading.
(2) Watching television.
(3) Sitting inactive in a public place (e.g. theater).
(4) As a car passenger for an hour without break.
(5) Lying down to rest in the afternoon.
(6) Sitting and talking to someone.
(7) Sitting quietly after lunch without alcohol.
(8) In a car, while stopping for a few minutes in traffic.

The following scale was then used to choose the most appropriate number for each situation:

0 = would never doze.
1 = slight chance of dozing.
2 = moderate chance of dozing.
3 = high chance of dozing.

The patients with a total score of 10 or above were considered abnormal and were also excluded. Moreover, all participants who reported snoring were excluded. The history of nonsnoring was taken from bed partners and confirmed by the nurse on duty. Each patient was subjected to the following:

(1) Full history taking.
(2) Full clinical examination.
(3) Laboratory examination.
(4) Radiological examinations: chest radiograph (posteroanterior and lateral views).
(5) Pulmonary function tests: spirometry was performed using master screen care fusion.
(6) Oxygen saturation measurement using pulse oximetry. Arterial $O_2$ saturation ($\text{SpO}_2$) was continuously recorded with a pulse oximeter. Measurements were taken during daytime (awake) and the nighttime by positioning the sensor on the second finger of the hand in the supine position. Pulse oximetry was conducted between 10:00 p.m. and 6:00 a.m. for four nights. Close attention was paid to proper fixation of the oxygen sensing device to a patient’s finger to ensure stable recording using the transcutaneous pulse oximetry equipment (Rossmax, 11545 Sorrento Valley Rd, Suite 308 San Diego, CA. 92121 USA) model to assess the basic nocturnal oxygen desaturation as these patients were not on a domiciliary oxygen therapy before enrollment.

(a) The first night while breathing on room air.
(b) The second night when a low-flow humidified oxygen (2 l/min) overnight was given through nasal prongs. The position of the nasal prongs was checked every hour by a nurse on duty, and on no occasion were prongs found out of place.
(c) The third night with patients on noninvasive ventilation using autoset CPAP with a full face mask (CPAP).
(d) The fourth night with patients on noninvasive ventilation using autoset CPAP with a full face mask (CPAP) with low-flow humidified oxygen (2 l/min).

(7) Noninvasive ventilation: Noninvasive ventilation was delivered through an autoset - CPAP...
device (ResMed, 3F Iwamotocho Bldg., 3-2-4 Iwamotocho, Chiyoda-ku, Tokyo 101-0032, Japan), which was administered through a comfortably fitting face mask. During noninvasive ventilation, the participants were instructed to relax, breathe calmly, and maintain a respiratory rate similar to spontaneous breathing. During CPAP ventilation, SpO2 was continuously monitored using portable pulse oximetry and recorded every hour of sleep hours. CPAP device was administered for two nights, one night without supplemental oxygen and the other night with a low-flow humidified oxygen (2 l/min).

Statistical analysis of the results
Data were statistically described in terms of mean±SD, median and range, or frequencies (number of cases) and percentages, when appropriate. Comparison of numerical variables between the study groups was made using the Mann–Whitney U-test for independent samples. For comparing categorical data, the χ²-test was performed. An exact test was used instead when the expected frequency is less than 5. Correlations between different study variables were made using the Spearman Rank correlation test. Accuracy was represented in terms of sensitivity and specificity. P values less than 0.05 were considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, Illinois, USA) version 21 for Microsoft Windows.

Results
The mean age of patients in group 1 (10 patients) was 63.28 years, and that in group 2 (30 patients) was 64.43 years, and all were male (Table 1).

Comparison between group 1 and group 2 showed a highly statistically significant difference as regards the mean values of nocturnal oxygen saturation on room air, low-flow nasal oxygen, CPAP alone, and CPAP with oxygen. However, Fig. 1 revealed that the highest mean value of nocturnal oxygen saturation in both groups was in cases that received CPAP with oxygen, followed by cases on low-flow nasal oxygen and cases on CPAP, and the lowest mean value was on room air.

Table 2 and Fig. 2 show that the highest mean value of nocturnal oxygen saturation in moderate, severe, and very severe cases was seen in cases that received CPAP with oxygen, followed by cases on low-flow nasal oxygen followed by cases on CPAP only; moreover, it showed a highly statistically significant difference as regards the mean values of oxygen saturation on room air, low-flow nasal oxygen, and CPAP alone. However, there was a

![Figure 1](image1)

Comparison between mean values of oxygen saturation on room air, low flow nasal oxygen, continuous positive airway pressure (CPAP) alone, and CPAP with oxygen in group 1 and group 2.

![Figure 2](image2)

Comparison between the mean values of oxygen saturation on room air, low-flow nasal oxygen, continuous positive airway pressure (CPAP) alone, and CPAP with oxygen in moderate, severe, and very severe stages of chronic obstructive pulmonary disease (COPD).

|                  | Group 1 (n=10) (mean±SD) | Group 2 (n=30) (mean±SD) | P value |
|------------------|--------------------------|--------------------------|---------|
| Mean SpO2 (RA)   | 89.56±1.53               | 78.87±4.80               | <0.001*** |
| Mean SpO2 (O2)   | 94.86±1.46               | 90.81±3.81               | 0.002**  |
| Mean SpO2 (CPAP) | 93.92±2.53               | 89.39±4.26               | 0.003**  |
| Mean SpO2 (CPAP+O2) | 96.21±1.54          | 92.37±3.66               | 0.003**  |

CPAP, continuous positive airway pressure; RA, room air. *P<0.05 (nonsignificant), **P<0.05 (significant), ***P<0.01 (highly significant).

***P<0.001 (extremely significant).
significant difference between mean values of oxygen saturation on CPAP with oxygen in moderate, severe, and very severe stages of COPD (Table 3).

**Group 1**

(1) There was no significant difference between mean values of nocturnal oxygen saturation on nocturnal oxygen and nocturnal CPAP.

(2) However, there was a highly significant difference between mean values of nocturnal oxygen saturation on nocturnal oxygen and nocturnal CPAP with oxygen. Moreover, there was a highly significant difference between mean values of nocturnal oxygen saturation on nocturnal CPAP and nocturnal CPAP with oxygen.

**Group 2**

(1) There was a significant difference between mean values of nocturnal oxygen saturation on nocturnal oxygen and nocturnal CPAP. Moreover, there was a significant difference between mean values of nocturnal oxygen saturation on nocturnal oxygen and nocturnal CPAP with oxygen.

(2) Moreover, there was an extremely significant difference between the mean values of nocturnal oxygen saturation on nocturnal CPAP and nocturnal CPAP with oxygen (Table 4).

**Very severe stage**

(1) There was no significant difference between the mean values of nocturnal oxygen saturation on nocturnal oxygen and nocturnal CPAP.

(2) However, there was a significant difference between the mean values of nocturnal oxygen saturation on nocturnal oxygen and nocturnal CPAP with oxygen.

(3) Moreover, there was an extremely significant difference between the mean values of nocturnal oxygen saturation on nocturnal CPAP and nocturnal CPAP with oxygen.

**Severe stage**

(1) There was no significant difference between the mean values of nocturnal oxygen saturation on nocturnal oxygen and nocturnal CPAP, or between mean values of nocturnal oxygen saturation on nocturnal oxygen and nocturnal CPAP with oxygen.

(2) However, there was a highly significant difference between the mean values of nocturnal oxygen saturation on nocturnal CPAP and nocturnal CPAP with oxygen.

**Moderate stage**

(1) There was no significant difference between the mean values of oxygen saturation on nocturnal oxygen and nocturnal CPAP or between the mean values of oxygen saturation on nocturnal oxygen and nocturnal CPAP with oxygen.
between the mean values of oxygen saturation on nocturnal CPAP and nocturnal CPAP with oxygen.

**Group 1**
As regards FVC\% pred, there was a positive correlation with mean values of oxygen saturation on low-flow nasal oxygen, whereas there was a negative correlation with mean values of oxygen saturation on room air, CPAP alone, and CPAP with oxygen. As regards FEV\(_1\)% pred, there was a positive correlation with mean values of oxygen saturation on room air and low-flow nasal oxygen, whereas there was a negative correlation with mean values of oxygen saturation on CPAP alone and CPAP with oxygen.

As regards FEV\(_1\)/FVC, there was a positive correlation, with mean values of oxygen saturation on room air, low-flow nasal oxygen, and CPAP with oxygen, whereas there was a negative correlation with mean values of oxygen saturation on CPAP alone and CPAP with oxygen.

**Group 2**
As regards FVC\% pred, there was a positive correlation with mean values of oxygen saturation on room air, low-flow nasal oxygen, CPAP alone, and CPAP with oxygen. Moreover, as regards FEV\(_1\)% pred, there was a positive correlation with mean values of oxygen saturation on room air and low-flow nasal oxygen CPAP alone, and CPAP with oxygen.

As regards FEV\(_1\)/FVC, there was a positive correlation with mean values of oxygen saturation on room air and CPAP with oxygen, whereas there was a negative correlation with mean values of oxygen saturation on low-flow nasal oxygen and CPAP alone.

**Discussion**
It is well known that people with normal lungs can desaturate during sleep [9]. More than 75% of patients with COPD report poor sleep quality, night-time symptoms, and sleep disturbances, which are generally not considered in the clinical management of the disease [10]. Breathing difficulties in COPD patients during sleep are the most common symptoms after dyspnea and fatigue [11]. Multiple mechanisms may contribute to nocturnal hypoxia, including alterations in ventilation perfusion [12], reduced functional residual capacity, reduced respiratory drive, and alveolar hypoventilation [13] possibly as a consequence of intercostal muscle hypotonia [7]. Nocturnal hypoxemia in COPD patients is characterized by bad quality of sleep; these episodes cause an increase in pulmonary arterial pressure, arrhythmias, and in the long-term they are responsible for reduced survival [14]. Nocturnal desaturation may occur in COPD in the absence of severe daytime hypoxemia. The prevalence of such ‘isolated’ nocturnal desaturation has previously been reported [15].

Valipour et al. [15] reported that, even in the absence of significant awake hypoxemia, nocturnal hypoxemia occurs, and furthermore it contributes to the development of pulmonary hypertension; this is in agreement with our study results in group 1. Moreover, they confirmed that patients with COPD who are hypoxemic during wakefulness become more hypoxic during sleep as in group 2 of our study, and they reported that this hypoxemia also causes a reduction in the amount and quality of sleep in COPD patients compared with healthy controls.

In this study, the results are in agreement with those of Lewis et al. [16], who studied the prevalence of isolated nocturnal desaturation in COPD. They found that significant nocturnal desaturation was common in patients with mild-to-moderate daytime hypoxemia (\(\text{PaO}_2=56–70\ \text{mmHg}\)) and that patients with resting...
saturations of less than 95% had the worst level of nocturnal oxygen saturation. This is in agreement with our findings, in which group 2 (moderate and severely hypoxic patients) had a lower level of nocturnal oxygen saturation compared with group 1 (normoxemic or mildly hypoxic).

Kinsman et al. [17] reported that the NOD in COPD patients is determined by the daytime arterial saturation. This is not in agreement with our study, as we found that patients with normal daytime arterial oxygen saturation desaturate at night and were diagnosed as nocturnal desaturators. Lacasse et al. [18] found that a significant proportion (38%) of patients with moderate-to-severe COPD who do not qualify for home oxygen therapy based on their daytime PaO₂ have NOD without evidence of sleep apnea, which is also supporting our results.

In 70 hospitalized patients affected by COPD, night pulse oximetry was performed by De Angelis et al. [19]; they found that 54 (77.15%) of them were night desaturators (NOD), whereas 16 (22.85%) were not desaturators. The night desaturators had a FEV₁% pred of 37±16, but it was found that only patients with FEV₁ less than 49% resulted to desaturate, which is not matching our study. This difference in result can be attributed to the wide range of FEV₁ (moderate, severe, and very severe) we studied. FEV₁ values were found to be 39±10 in group 1 and 27±8 in group 2.

Fleetham et al. [20] reported that COPD patients with mean FEV₁ less than 26% were night desaturators. This result is not in agreement with our results, as above and below these values patients were desaturators, as in our study the mean FEV₁% pred in group 1 was 39.20±10 and that in group 2 was 27.70±8. Eugene et al. [21], in their study on 37 patients (27%) of the remaining 135 COPD patients with arterial oxygen tensions above 60 mmHg, showed nocturnal oxyhemoglobin desaturation in normoxemic patients, as in group 1 of this study.

Correlation of spirometric values with nocturnal oxygen saturation in group 1 is presented in Table 5. As regards FVC% pred, there was a positive correlation with mean values of nocturnal oxygen saturation on nocturnal low-flow nasal oxygen, whereas there was a negative correlation with mean values of nocturnal oxygen saturation on room air, nocturnal CPAP only, and nocturnal CPAP with oxygen. However, as regards FEV₁% pred there was a positive correlation with mean values of nocturnal oxygen saturation on room air and nocturnal low-flow nasal oxygen, whereas there was a negative correlation with mean values of nocturnal oxygen saturation on room air and nocturnal CPAP with oxygen. As regards FEV₁/FVC, there was a positive correlation with mean values of nocturnal oxygen saturation on room air, nocturnal low-flow nasal oxygen, and nocturnal CPAP with oxygen, whereas there was a negative correlation with mean values of nocturnal oxygen saturation on CPAP only. Correlation of these values with nocturnal oxygen saturation in group 2 is presented in Table 6. As regards FVC% pred, there was a positive correlation with mean values of nocturnal oxygen saturation on room air, nocturnal low-flow nasal oxygen, and nocturnal CPAP with oxygen. Moreover, as regards FEV₁% pred, there was a positive correlation with mean values of nocturnal oxygen saturation on room air and nocturnal low-flow nasal oxygen, nocturnal CPAP only, and nocturnal CPAP with oxygen.

### Table 5 Correlation between mean values of nocturnal oxygen saturation on room air, low-flow humidified nasal oxygen, CPAP alone, and CPAP with oxygen saturation in different spirometric parameters (FVC – FEV₁ – FEV₁/FVC) in group 1

| Group 1 | FVC% pred | FEV₁% pred | FEV₁/FVC |
|---------|-----------|------------|---------|
| Mean SpO₂ (RA) | r-Coef = -0.189, P = 0.602 | 0.009, Positive | 0.181, Positive |
| Mean SpO₂ (O₂) | r-Coef = 0.086, P = 0.812 | 0.159, Positive | 0.108, Positive |
| Mean SpO₂ (CPAP) | r-Coef = -0.143, P = 0.694 | -0.299, Negative | -0.120, Negative |
| Mean SpO₂ (CPAP+O₂) | r-Coef = -0.335, P = 0.344 | -0.071, Negative | 0.165, Positive |

CPAP, continuous positive airway pressure; RA, room air.
However, as regards FEV₁/FVC, there was a positive correlation with mean values of nocturnal oxygen saturation on room air and nocturnal CPAP with oxygen, whereas there was a negative correlation with mean values of oxygen saturation on nocturnal low flow nasal oxygen and nocturnal CPAP only.

Zanchet and Viegas [22] found that there was a positive and significant correlation between the FEV₁/FVC ratio (%) and SpO₂ during sleep on room air in COPD patients with nocturnal desaturation.

Bradley et al. [23] studied COPD patients who were not hypoxemic while awake, who showed nocturnal hypoxemia with a significant drop from baseline awake SpO₂. Baseline awake SpO₂ correlated well with mean nocturnal SpO₂; moreover, they confirmed that FEV₁ had a positive correlation with mean nocturnal SpO₂. Chaouat et al. [24] found that nocturnal desaturators had a lower FEV₁/FVC ratio (P=0.04) and lower FEV₁ in agreement with our study (but the difference was not statistically significant).

De Angelis et al. [19] confirmed a significant correlation between FEV₁ and mean nocturnal SpO₂% (the worse the FEV₁, the lower the mean nocturnal SpO₂%). This is in agreement with our study as they demonstrated that the more the respiratory function is impaired, the more likely these individuals will be night-time hypoxemic.

### Conclusion and recommendations

In group 1, there was no significant difference between mean values of oxygen saturation on nocturnal oxygen and nocturnal CPAP, and hence it is equal to prescribe each of them to COPD patients with NOD in this group. Moreover, there was a highly significant difference between mean values of oxygen saturation on nocturnal oxygen and nocturnal CPAP with oxygen, and hence it is better to prescribe nocturnal CPAP with oxygen than nocturnal oxygen to COPD patients with NOD in this group. Moreover, there was a highly significant difference between mean values of oxygen saturation on nocturnal CPAP and nocturnal CPAP with oxygen, and hence it is better to prescribe nocturnal CPAP with oxygen than nocturnal CPAP alone to COPD patients with NOD in this group. As regards patients in group 2, there was a significant difference between the mean values of oxygen saturation on nocturnal oxygen and nocturnal CPAP, and hence it is better to prescribe nocturnal oxygen than nocturnal CPAP alone to COPD patients with NOD in this group. Moreover, there was a significant difference between mean values of oxygen saturation on nocturnal oxygen and nocturnal CPAP with oxygen, and hence it is better to prescribe nocturnal CPAP with oxygen than nocturnal oxygen to COPD patients with NOD in this group. Moreover, there was an extremely significant difference between mean values of oxygen saturation on nocturnal CPAP and nocturnal CPAP with oxygen, and hence it is better to prescribe nocturnal CPAP with oxygen than nocturnal CPAP alone to COPD patients with NOD in this group.

Patients with very severe pulmonary function tests showed no significant difference between mean values of oxygen saturation on nocturnal oxygen and nocturnal CPAP, and hence it is equal to prescribe each of them to COPD patients with NOD in this stage. Moreover, there was a significant difference between mean values of oxygen saturation on nocturnal oxygen and nocturnal CPAP with oxygen, and so it is better to prescribe nocturnal CPAP with oxygen than nocturnal oxygen to COPD patients with NOD in this group. Moreover,
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there was an extremely significant difference between mean values of oxygen saturation on nocturnal CPAP and nocturnal CPAP with oxygen, and hence it is better to prescribe nocturnal CPAP with oxygen than nocturnal CPAP alone to COPD patients with NOD in this stage. However, in severe cases there was no significant difference between mean values of oxygen saturation on nocturnal oxygen and nocturnal CPAP, and hence it is equal to prescribe each of them to COPD patients with NOD in this stage. Moreover, there was no significant difference between mean values of oxygen saturation on nocturnal oxygen and nocturnal CPAP with oxygen, and so it is equal to prescribe each of them to COPD patients with NOD in this stage. Moreover, there was no significant difference between mean values of oxygen saturation on nocturnal oxygen and nocturnal CPAP with oxygen, and hence it is equal to prescribe each of them to COPD patients with NOD in this stage.

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**Conflicts of interest**

There are no conflicts of interest.

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