Incidence of Nocturnal Desaturation While Breathing Oxygen in COPD Patients Undergoing Long-term Oxygen Therapy*

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Study objective: It is suggested that oxygen flow be increased by 1 L/min during sleep in COPD patients undergoing long-term oxygen therapy (LTOT) in order to avoid nocturnal desaturations. The purpose of this study was to investigate the occurrence of nocturnal desaturations while breathing oxygen in COPD patients receiving LTOT.

Setting: Inpatient/university hospital.

Patients: We studied 82 consecutive COPD patients. Their functional characteristics were as follows (mean ± SD): FVC, 2.15 ± 0.69 L; FEV1, 0.87 ± 0.33 L; PaO2, 51.6 ± 5 mm Hg; and PaCO2, 47 ± 8 mm Hg.

Measurements: Overnight pulse oximetry (PO) was performed twice: (1) while breathing air and (2) while breathing supplemental oxygen assuring satisfactory diurnal resting oxygenation (mean PaO2 during oxygen breathing, 67 ± 6 mm Hg; mean arterial oxygen saturation [SaO2] during oxygen breathing, 93%).

Results: PO performed while patients were breathing air showed a mean overnight SaO2 of 82.7 ± 6.7%. Patients spent 90% of the recording time with an SaO2 of <90%. While breathing oxygen, 43 patients (52.4%) remained well oxygenated. Their mean overnight SaO2 while breathing oxygen was 94.4 ± 2.1%, and time spent with saturation <90% was 6.9 ± 8.6%. Thirty-nine patients (47.6%) spent >30% of the night with an SaO2 of <90% while breathing supplemental oxygen. Their mean overnight SaO2 while breathing oxygen was 87.1 ± 4.5%, and time spent with an SaO2 of <90% was 66.1 ± 24.7% of the recording time. Comparison of ventilatory variables and daytime blood gases between both groups revealed statistically significantly higher PaCO2 on air (p < 0.001) and on oxygen (p < 0.05), and lower PaO2 on oxygen (p < 0.05) in the group of patients demonstrating significant nocturnal desaturation.

Conclusions: We conclude that about half of COPD patients undergoing LTOT need increased oxygen flow during sleep. Patients with both hypercapnia (PaCO2 ≥ 45 mm Hg) and PaO2 < 65 mm Hg while breathing oxygen are most likely to desaturate during sleep.

Key words: COPD; long-term oxygen therapy; nocturnal desaturation; overnight pulse oximetry; oxygen flow

Abbreviations: BMI = body mass index; LTOT = long-term oxygen therapy; OSAS = obstructive sleep apnea syndrome; PAP = pulmonary artery pressure; PO = pulse oximetry; Q = quality index of pulse oximetry recording; SaO2 = arterial oxygen saturation; T85 = the percentage of total recording time spent with pulse oximeter saturation of <85%; T90 = the percentage of total recording time spent with pulse oximeter saturation of <90%

There is a general agreement that patients with COPD who are developing respiratory failure benefit from long-term oxygen therapy (LTOT) at home.1,2 When LTOT is started, the oxygen flow is individually adjusted to increase PaO2 to > 60 mm Hg.3,4 Such a flow may be insufficient during sleep. We demonstrated earlier that some COPD patients undergoing LTOT desaturate during sleep despite breathing oxygen.5 Fletcher et al6 and Levi-Valensi et al7 demonstrated that COPD patients with diurnal PaO2 > 60 mm Hg while breathing air may also desaturate during sleep. Block et al8 and Flenley9 hypothesized that nocturnal hypoxemia may precip-
itate development of cor pulmonale. Recent American Thoracic Society guidelines for diagnosis and treatment of COPD recommended increasing oxygen flow by 1 L/min during sleep in patients undergoing LTOT to prevent nocturnal oxygen desaturation. However, those recommendations were not supported by any formal study demonstrating frequency of nocturnal desaturation in COPD patients breathing oxygen.

The aim of this study was to evaluate overnight oxygen saturation in a large nonselected group of COPD patients who were eligible for LTOT and were breathing oxygen at a flow assuring satisfactory oxygenation at rest and while awake (PaO₂ ≥ 60 mm Hg; arterial oxygen saturation [SaO₂] > 90%).

**Materials and Methods**

We studied 82 consecutive COPD patients (54 men and 28 women; mean age, 60.2 ± 8.2 years) who were eligible for LTOT. Diagnosis of COPD was established based on commonly accepted criteria. Indications for LTOT were stable hypoxemia, defined as (1) PaO₂ < 55 mm Hg, or (2) PaO₂ between 55 and 59 mm Hg if hypoxemia coexisted with one of the following signs: signs of pulmonary hypertension on chest radiograph (15 patients), signs of right ventricle hypertrophy on ECG (16 patients), or elevated hematocrit (10 patients). In all patients, spirometric and arterial blood gas measurements were performed in a steady state. Spirometry showed severe airway obstruction (mean FEV₁, 0.87 ± 0.33 L). The results of arterial blood gas measurements revealed hypoxemia (mean PaO₂, 51.6 ± 5 mm Hg) and hypercapnia (mean PaCO₂, 47.5 ± 8.3 mm Hg). Details of patients’ characteristics are shown in Table 1.

**PO** was performed twice. During the first night, patients breathed ambient air. During the second PO session, they breathed oxygen through nasal prongs at a flow ranging from 1 to 2.5 L/min, assuring good oxygenation at rest and while awake (PaO₂ ≥ 60 mm Hg). 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. PO was conducted between 10:00 pm and 6:00 am. We used two models of transcutaneous pulse oximeters: Pulsox 7 (Minolta; Osaka, Japan) and Biox 3700 (Ohmeda Monitoring Systems Group; Boulder, CO). Close attention was paid to proper fixation of the oxygen sensing device to a patient’s finger to ensure stable recording. Both pulse oximeters have built-in memory allowing for ≥ 8 h of oxygen saturation recording. To assure good-quality recording, the pulse oximeters were powered by an alternating-current electricity source. The software checked the SaO₂ signal. Artifacts such as an interruption of electricity supply or displacement of the measuring cell were recorded and influenced the quality index (Q). Q was considered an expression of the ratio of artifacts to effective recording time. The mean Q was 0.99 and 0.98, respectively, for the Pulsox 7 and Biox 3700 devices. Recorded data were analyzed using computer software (Proxan, version 1.0;
M. Lagosz, Warsaw, Poland, as described elsewhere. From multiple variables measured and calculated, we retained the following: mean overnight $S_T O_2$, minimum $S_T O_2$, the percentage of total recording time spent with pulse oximeter saturation of $90\%$ (T90), the percentage of total recording time spent with saturation of $85\%$ (T85), and Q. The protocol of the study was approved by the Ethics Committee of the Institute. All patients gave informed consent.

Statistical Analysis

Results of lung function tests and PO recordings were presented as mean value ± SD. The unpaired Student's t-test or Mann-Whitney rank sum test (when the t-test failed) was used to compare results in two analyzed subgroups (SigmaStat, version 2.0; SPSS Inc; Chicago, IL).

Results

As expected, all patients desaturated during the night while breathing air, and the T90 was 90\% (Table 2). While breathing oxygen, the mean overnight $S_T O_2$ in the group as a whole was satisfactory (90.9 ± 5.0\%). However, we found that many patients spent an important part of the night in desaturation ($S_T O_2 < 90\%$). Using a cut-off point of a T90 of $< 30\%$, we divided the study group into “non-saturators” (43 subjects, 52.4%) and “saturators” (39 subjects, 47.6%). Functional characteristics and results of both PO sessions in the two groups are shown in Table 3. Typical PO tracings in one of the saturators are shown in Figure 1.

We tried to find relationships between daytime lung function variables and nocturnal desaturation. Comparison of daytime blood gases and spirometric variables revealed significantly higher $P_{CO_2}$ while breathing air ($p < 0.001$) and while breathing oxygen ($p < 0.05$) in the desaturators (Table 4). A significant relationship between both groups was present in the 36 patients with $P_{CO_2} > 45$ mm Hg and $P_{O_2} > 65$ mm Hg while breathing oxygen. Table 4 shows the lung function characteristics in the two subgroups.

Table 4—Lung Function Characteristics in the Two Subgroups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Nondesaturators (n = 43)</th>
<th>Desaturators (n = 39)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>60.1 ± 6.9</td>
<td>60.4 ± 9.5</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.1 ± 5.2</td>
<td>24.9 ± 4.4</td>
<td>NS</td>
</tr>
<tr>
<td>FVC, L</td>
<td>2.21 ± 0.75</td>
<td>2.09 ± 0.64</td>
<td>NS</td>
</tr>
<tr>
<td>FEV₁, L</td>
<td>0.86 ± 0.33</td>
<td>0.87 ± 0.35</td>
<td>NS</td>
</tr>
<tr>
<td>$P_{O_2}$ on air, mm Hg</td>
<td>52.4 ± 4.5</td>
<td>50.7 ± 5.3</td>
<td>NS</td>
</tr>
<tr>
<td>$P_{CO_2}$ on air, mm Hg</td>
<td>44.6 ± 6.5</td>
<td>50.6 ± 9.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>$P_{O_2}$ on oxygen, mm Hg</td>
<td>68.8 ± 6.8</td>
<td>65.7 ± 5.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>$P_{CO_2}$ on oxygen, mm Hg</td>
<td>416 ± 153</td>
<td>294 ± 50</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

* Data are presented as mean ± SD. See Table 3 for abbreviation.
breathing oxygen predicted nocturnal desaturation in 18 of 22 patients who presented both signs (81.8%).

**Discussion**

We found that almost half of COPD patients eligible for LTOT desaturated during sleep despite breathing oxygen at an airflow ensuring good oxygenation at rest and while awake. To our best knowledge, our study is the first to assess the incidence of nocturnal desaturation in such a large nonselected group of COPD patients. Previous observations were based on much smaller groups.

As early as 1977, Flick and Block first reported nocturnal desaturation in COPD patients receiving oxygen. Of 10 oxygen-breathing patients (2 L/min) who were all well oxygenated during the day (mean SaO₂, 97 ± 2%), 6 patients desaturated at night (mean SaO₂, < 90%) despite oxygen supplementation.

Carroll et al studied 10 COPD patients who had severe airway obstruction (mean FEV₁, 0.53 L). They had been receiving oxygen at home for ≥ 6 months. Their awake PaO₂ was > 8 kPa, and their SaO₂ was ≥ 90% while breathing oxygen. Four patients demonstrated significant oxygen desaturation during sleep while breathing oxygen.

Śliwiński et al found important nocturnal desaturation in 19 out of 34 COPD patients receiving long-term oxygen supplementation. This phenomenon was more frequent in the “blue bloater” type of patients. Morrison et al studied 11 COPD patients receiving LTOT (mean FEV₁, 0.6 L; PaO₂, 48 mm Hg; PaCO₂, 54 mm Hg) with satisfactory oxygenation while breathing oxygen (PaO₂ > 60 mm Hg). Three of these patients spent < 75% of the night with an SaO₂ of > 90% despite breathing oxygen. Servella et al observed nocturnal desaturation in 5 of 34 COPD patients eligible for LTOT. A 0.5-L/min increase in oxygen flow abolished nocturnal desaturation.

The present study has one important limitation. Multiple arterial blood desaturations during sleep are a typical feature of obstructive sleep apnea syndrome (OSAS). However, we made all possible efforts to exclude subjects with OSAS. All subjects who reported snoring were excluded. The history of nonsnoring was taken from bed partners and confirmed by the nurse on duty. Obese subjects (BMI > 30 kg/m²) and subjects with a shirt-collar size of > 39 cm were also excluded. All PO analog recordings were carefully checked. All episodes of desaturation below the initial saturation level were rather long (Fig 1), with a gradual SaO₂ decrease over several minutes typical for COPD patients. We did not find in any analog tracing the saw-tooth pattern of desaturations typical in patients with OSAS. We are confident that patients with OSAS were excluded from the analyzed material.

There are several mechanisms that may be responsible for nocturnal desaturations in patients with COPD. The minute ventilation decreases during sleep similarly in both normal subjects and COPD patients. The majority of desaturations appear during rapid eye movement sleep. Irregular breathing, especially shallow rapid breathing that increases physiologic dead space ventilation, and hypoventilation are responsible for that phenomenon. The decreased activity of intercostal muscles and the increase of upper and lower airway resistance additionally decrease alveolar ventilation. Resetting of respiratory control to higher PaCO₂ and lower PaO₂ during sleep also reduces ventilatory response to blood gas disorders.

The absence of a cough reflex during sleep in patients with disturbed mucociliary clearance increases the ventilation/perfusion imbalance due to mucus retention in the small airways. Hypoventilation and the increase of the ventilation/perfusion ratio results in transient hypoxemic episodes, mainly during rapid eye movement sleep. The clinical importance of nocturnal desaturation in COPD patients is still under debate. Fletcher and coworkers devoted a series of papers to this problem. They found that about 25% of COPD patients with daytime PaO₂ > 60 mm Hg experienced nocturnal desaturation. Desaturators had higher pulmonary artery pressure (PAP) at rest and during exercise. During a 3-year follow-up period, desaturators treated with oxygen during sleep showed a decrease in PAP, contrary to desaturating control patients in whom PAP increased and who also had a shorter survival rate.

However, a paper by Chaouat et al did not confirm that nocturnal desaturations in COPD patients with diurnal PaO₂ > 55 mm Hg resulted in a permanent increase of PAP.

Generally, it was found that the level of PaO₂ during the day correlates well with nocturnal desaturations. However, there are large individual variations in nocturnal hypoxemia in COPD patients. Our data confirm that it is rather difficult to predict nocturnal desaturations from spirometric indexes and from the diurnal PaO₂. The best predictor of nocturnal desaturation was diurnal PaCO₂. In the linear regression analysis, only PaCO₂ correlated with T₉₀ while breathing oxygen (r = − 0.43; p < 0.001).

Patients who significantly desaturate during sleep should have their oxygen flow increased during sleep. In hypercapnic patients, this may lead to an
increase in Paco₂ during sleep, up to dangerous levels. Servera et al.¹⁴ found that adding 0.5 L/min of oxygen flow in desaturators was sufficient to prevent nocturnal desaturation. Apparently, all those patients were hypercapnic during the day. The authors did not provide data on the arterial blood gases in the morning following nocturnal increase in oxygen flow.

In summary, around half of COPD patients undergoing LTOT experience nocturnal hypoxemia even though they are breathing oxygen at a flow that ensures satisfactory oxygenation during the day. The desaturation during sleep may be expected in patients with a Paco₂ of > 45 mm Hg and a PaO₂ of < 65 mm Hg while breathing oxygen. However, the "gold standard" for recognizing nocturnal desaturation remains overnight PO. We would suggest that PO be performed in all patients who are eligible for LTOT and present with hypercapnia.

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