Role of Nocturnal Oxygen Therapy in Obstructive Sleep Apnea
When Should It Be Used?

Eugene C. Fletcher M.D., F.C.C.P.; and Dominic A. Munafò M.D.†

(Chest 1990; 98:1497-1504)

Obstructive sleep apnea (OSA) is a common disorder of breathing during sleep which, if present for a sufficient period of time, may cause severe daytime hypersomnia, many neuropsychiatric symptoms, pulmonary hypertension and right heart failure, and systemic hypertension. It remains a mystery as to why patients develop these symptoms and hemodynamic abnormalities. In part, they may be due to disruption of sleep: overall decreases in sleep time and shifts in the normal architecture and distribution of sleep stages, or to cardiovascular system stress due to wide fluctuations in inrathoracic pressure from muscular efforts to overcome asphyxia. The most popular theory is that recurrent nocturnal hypoxemia, especially if the desaturations are deep, prolonged, and frequent, causing a low mean nocturnal saturation, is the main contributor to symptoms, systemic hypertension, and right heart cardiopulmonary dysfunction.

Chronic, recurrent hypoxemia is one, if not the primary laboratory manifestation of sleep apnea, and as such, one of the major goals of clinicians involved in treating apnea has been to eliminate or ameliorate this known cause of pulmonary hypertension. We have known since the mid 1950s how to provide supplemental oxygen in a variety of forms to patients who suffer from hypoxemia.1 In some diseases, such as COPD, success has been achieved in alleviating symptoms and partially correcting abnormal hemodynamics that result from chronic hypoxemia.2,3 Unfortunately, in the setting of sleep apnea, sufficient data may not be available to allow us to decide whether oxygen could benefit such patients. Occasional case reports have shown beneficial effects of supplemental oxygen in central apneas, but usually this is in the setting of severe alveolar hypoventilation.4,5 However, in OSA, oxygen may be a two-edged sword, minimizing the degree of hypoxemia while at the same time lengthening apnea duration and worsening respiratory acidosis (Table 1). Faced with such treatment alternatives as tracheostomy or other surgical interventions, medications which may be minimally effective or have substantial side effects, and somewhat cumbersome devices such as nasal continuous positive airway pressure (nCPAP), many practitioners are prescribing home supplemental oxygen as a simple way of treating the hypoxemia of apnea. With an appreciation of the potential benefits and risks involved, where does oxygen therapy currently stand in our armamentarium for treatment of OSA? Is there sufficient evidence that it should receive widespread use? The following review addresses these two questions.

ACUTE EFFECT OF SUPPLEMENTAL OXYGEN ON OBSTRUCTIVE SLEEP APNEA

Due to the inherent difficulty of long-term studies, most of the information on supplemental oxygen in sleep apnea concerns its acute effect. Early investigations involving apnea and nasal supplemental oxygen questioned its safety in this setting. If hypoxic drive is a factor in arousal and apnea termination, then maintenance of a higher oxygen level during apnea could theoretically lengthen the apneas, worsening

Table 1—SUPPLEMENTAL OXYGEN IN OBSTRUCTIVE SLEEP APNEA; POTENTIAL EFFECTS

<table>
<thead>
<tr>
<th>Potential dangers</th>
<th>Potential benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolongation of apnea duration</td>
<td>Improved nocturnal oxygenation</td>
</tr>
<tr>
<td>Increased hypercarbia and acidosis</td>
<td>Improved brainstem function</td>
</tr>
<tr>
<td>Increased ventricular irritability</td>
<td>Improved hemodynamics</td>
</tr>
<tr>
<td></td>
<td>Decreased apnea time</td>
</tr>
<tr>
<td></td>
<td>Decreased symptoms</td>
</tr>
<tr>
<td></td>
<td>Improved sleep quality</td>
</tr>
</tbody>
</table>

†Presently Fellow in Pulmonary Disease, University of California at San Diego.

Reprint requests: Dr. Fletcher, VA Medical Center, 2002 Holcombe Blvd, Houston 77030

From the Department of Medicine, Pulmonary Disease Section, Houston Veterans Administration Medical Center, and Baylor College of Medicine, Houston
CO₂ retention.

Motta and Guilleminault administered 5-10 L/min nasal oxygen intermittently for very short periods to four patients with OSA during rapid-eye-movement (REM) and non-REM sleep. They measured blood gases, apnea duration, and other variables in four apnea patients off and on supplemental oxygen. All four patients achieved arterial PaO₂ tensions above 120 mm Hg. Apnea duration increased by 50 to 90 percent during both NREM and REM apneas. The investigators noted substantial hypercarbia and respiratory acidosis with oxygen administration during REM apneas and warned that this might result in lowering of the ventricular arrhythmia threshold. Problems with this study include the fact that the amount of supplemental oxygen used was excessive and not achievable at home. Also, the oxygen was given for very short periods, making it difficult to evaluate an equilibrium effect of oxygen. The same group published a study in which they administered 1.5 to 3 L/min nasal oxygen during sleep to four patients with "chronic airflow obstruction" and OSA. They again found that apneas were prolonged and one patient showed an increase in atrioventricular block while breathing supplemental oxygen. Although they used more physiologic levels of supplemental oxygen in this study, they measured only five apnea events under each condition. In addition, all of the apneas measured were mixed.

One of the problems with these early studies was that oxygen was administered for only short periods and at variable concentrations. Martin et al provided

<p>| Table 2—Effect of Supplemental Oxygen on Apnea Type, Duration, and Time in Apnea |
|--------------------------------|------------------|------------------|------------------|------------------|
| Air | Total Number | Oxygen | Total Number | Total Number | Air | Total Number |</p>
<table>
<thead>
<tr>
<th>Number</th>
<th>by Type</th>
<th>Number</th>
<th>by Type</th>
<th>Number</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>202</td>
<td>O 131</td>
<td>O 63</td>
<td>O 92</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>M 58</td>
<td>M 5</td>
<td>M 31</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C 18</td>
<td>C 0</td>
<td>C 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration (s)</td>
<td>21.2 + 9s</td>
<td>26.4 + 13s</td>
<td>15.4 + 3s</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% Time in Apnea</td>
<td>41.1 + 18</td>
<td>20.5 + 14</td>
<td>23.0 + 14</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low SaO₂</td>
<td>84.9 + 7</td>
<td>96.7 + 2</td>
<td>85.2 + 7</td>
<td></td>
</tr>
</tbody>
</table>

Effect of supplemental oxygen on apnea number, type, distribution, duration, nadir SaO₂ and percentage of time spent in apnea, in eight patients studied by Martin et al. Data are adapted from their Table 2. O = obstructive apnea, M = mixed apnea, C = central apnea. Important data by administering supplemental oxygen during sleep in a systematic manner. Patients breathed compressed air for 30 min followed by 30 min of 100 percent oxygen, which was then followed by compressed air for another 30 min. Of the eight patients studied (seven men, one woman), three had peripheral edema at the time of study and one had stable reactive airways disease. All subjects had moderate daytime hypoxemia (mean PaO₂ = 66.3 mm Hg, but none had chronic hypoventilation (mean PaCO₂ = 38.9 mm Hg). They found that supplemental oxygen improved nadir oxygenation, reduced apnea frequency, increased apnea duration, but decreased total apnea time (Table 2). Arterial PaCO₂ was not measured, but there was no increase in resting, non-apneic end-tidal CO₂.
during oxygen administration. There was no increase in ventricular irritability. Contrary to what might be expected, the time spent in apnea and apnea nadir SaO₂ changed gradually, not immediately upon application and removal of oxygen (Fig 1). While this was a very complete, systematic evaluation of supplemental oxygen in OSA, it is important to note that patients received 100 percent oxygen from a reservoir bag and therefore achieved much higher concentrations of inspired oxygen than are practical or desirable in the home setting.

Hudgel et al⁹ used a high oxygen concentration (FIO₂ = 50 percent) administered for 8 min periods to examine the effect of supplemental oxygen on apnea frequency and duration. At that level, they found that total apnea time increased from 60±2 percent to 75±5 percent of sleep even though mean nadir SaO₂ increased from 87 percent on ambient air to 96 percent on supplemental oxygen. Again, the level of oxygen used was higher than practical in the home and its effect hard to equate to the clinical setting.

The question of inspired oxygen concentration is important when one is examining the effect of oxygen on apnea duration and apnea time. The effect of low flow nasal oxygen at 3 L/min (approximate FIO₂ 30 percent) may have a different physiologic and clinical effect than very high concentrations such as FIO₂ 100 percent. In addition, such high concentrations can only be achieved in the laboratory setting and therefore have limited clinical applicability.

Some studies have examined the effect of more practical levels of supplemental oxygen on apnea duration and severity. Smith et al¹⁰ studied ten men and two women with OSA in a single-blind cross-over fashion. On the first night, the subjects were given compressed air at 3 L/m and on the second night, oxygen at 3 L/m. The subjects were not severely hypoxemic during the day (mean PaO₂ 80.4 mm Hg) nor were they hypercarbic (mean PaCO₂ 39.0 mm Hg). Nine of 12 showed a decrease in apnea frequency on oxygen. Overall, the group showed a decrease from 69±10 percent to 56±11 percent disordered breathing events/h (apneas plus hypopneas). There was a higher percentage of obstructive events while using oxygen because of a preferential decrease in central and mixed apneas. The mean fall in nadir apnea SaO₂ was reduced by one-half, but the bradycardia frequently seen during apnea was basically unaffected. Sleep architecture showed some improvement with a modest decrease in wake time from 5.3 to 2.6 min/h and decreased number of awakenings. Seven of 12 patients felt better after the oxygen night, but there was no objective improvement in the mean multiple sleep latency time (time from “lights out” to first sleep during multiple daytime naps). Three of four with the most improvement in disordered breathing improved their median daytime sleep latency. The authors concluded that supplemental oxygen was safe in the setting of OSA and was effective in improving symptoms in a subset of subjects, mainly those with a marked decrease in total time spent in apnea while breathing supplemental oxygen.

A later report¹¹ from the same laboratory addressed an important question: does the drop in apnea frequency with oxygen therapy mainly result from a decrease or elimination of central and mixed apneas, or do obstructive apneas also decrease? In this study, 4 L/min of oxygen was administered on the second of two nights to nine patients with predominantly central or mixed apneas as opposed to obstructive (central 51

![Figure 2](http://journal.publications.chestnet.org/pdaccess.ashx?url=/data/journals/chest/21622/ on 06/25/2017)
percent, mixed 33 percent, obstructive 16 percent). The patients were eucapnic (mean PaCO₂, 40 ± 4 mm Hg) except for two who had minimal daytime hypoxemia (mean PaO₂, 83 ± 14 mm Hg). Mean apnea frequency decreased significantly, the mean duration increased slightly, baseline SaO₂ improved, and the fall in SaO₂ during apnea was reduced by about 50 percent. Oxygen therapy greatly decreased the number of central and mixed apneas and caused a relative increase in the number of obstructive apneas (Fig 2).

Various theories were put forth as to why this occurred, but it was felt that oxygen reduces the central controller gain, allowing reduced CO₂ tension to decrease chemical drive and decrease tone to the upper airway muscles. Both of these studies are important from a clinical standpoint because they employed more physiologic levels of supplemental oxygen and applied the oxygen for the entire night.

One study of supplemental oxygen therapy was aimed at a group of milder OSA than previous subjects. Block et al.12 while examining the effect of acute oxygen in patients who snored, found that 20 of 28 snorers had apnea and hypopnea desaturations. Applying room air at 2 L/m for the first half of the night, and nasal oxygen at 2 L/m for the second half, they noted no change in apnea frequency (11 vs 14/h). There was a significant increase in apnea duration (by 7s), mean apnea time in min/h (4.03 vs 6.77 min), and no improvement in overall nadir SaO₂ (72.6 vs 74 percent). One must be careful in interpreting data where events from the first half of the night are compared to events from the second half. Because of a different distribution of sleep stages and perhaps inherent differences in respiratory control as sleep progresses, apnea durations might not be expected to be the same during both halves of the night.

The issue of acidosis and arrhythmia safety with the short-term administration of oxygen to apnea patients with concomitant chronic obstructive pulmonary disease (COPD) was investigated by Alford et al.13 They studied 20 subjects with OSA and COPD, 12 of whom were chronic CO₂ retainers (mean PaCO₂ 45.2 mm Hg) and all of whom had mild to moderate daytime hypoxemia (mean PaO₂ 65.0 mm Hg). These authors demonstrated clear improvement in whole night SaO₂, both during NREM and REM sleep (Fig 3). The price of this improvement was worsening of respiratory acidosis with a decrease in mean end apneic pH from 7.34 on air to 7.28 breathing oxygen (p<0.001). Mean end apneic PaCO₂ increased from 52.5 to 62.3, as did end apneic PaO₂, from 54.7 to 89.6 mm Hg (Fig 4). Despite this worsening of acidosis, there was no increase in PVCs or other potentially lethal arrhythmias. As in other studies, sleep architecture was unaffected by oxygen. It must be kept in mind that the patients in this study had COPD in addition to severe OSA. Thus, respiratory control factors during sleep might be different from patients with OSA alone.

A recent abstract reports the use of transtracheal supplemental oxygen (TTO₂) vs nasal oxygen in five OSA patients.14 Each patient was studied for one whole night on four separate occasions: baseline, nasal cannula oxygen at 2-4 L/min, during nasal CPAP use, and with the application of TTO₂ at 1-2 L/min. The TTO₂ was associated with a fall in apnea index from baseline of 19.2 to 3.8, while nasal oxygen was

**OXYGEN SATURATION DURING REPETITIVE OBSTRUCTIVE APNEAS**

![Graph showing oxygen saturation during repetitive obstructive apneas. Segments of whole night oximeter tracings of the same subject breathing air (top panel) and breathing supplemental oxygen (bottom panel). Note that desaturations are worse during REM sleep on both nights, but that supplemental nasal oxygen improves nadir SaO₂ under both conditions.](image)

**Figure 3.** Oxygen saturation during repetitive obstructive apneas. Segments of whole night oximeter tracings of the same subject breathing air (top panel) and breathing supplemental oxygen (bottom panel). Note that desaturations are worse during REM sleep on both nights, but that supplemental nasal oxygen improves nadir SaO₂ under both conditions. (Reproduced by permission from reference 13.)
associated with an increase in events to 38.2/h. During all therapy, apnea duration was reduced, which contradicts most previous studies. TTO₂ was the best of the three modalities in correcting nadir SaO₂. Unfortunately, there is no information given on the degree of respiratory acidosis associated with the TTO₂. This was a highly select group of patients, having failed previous attempts at nCPAP therapy. No data are given on the amount or difference in sleep architecture between the four conditions.

One article examined the effect of TTO₂ in four patients with OSA who were unable to tolerate CPAP and refused tracheostomy. The mean respiratory disturbance index (RDI) was improved by TTO₂ as were subjective symptoms of daytime hypersomnolence and fatigue (all patients) and depression (one patient). None of the patients had MSLTs to verify objective improvement in hypersomnolence. The authors claim that in three patients who continued to use TTO₂ for up to 7 to 15 months, OSA symptoms remained minimal. Care must be used in interpreting this study. First, three of the four patients had concomitant COPD. Two of these had very low apnea indices (7/h, 9/h) that would not normally be associated with severe hypersomnolence. These two had AHIs of 58/h and 19/h indicating that a large portion of their respiratory disturbances were hypopneas, and hypopneas are a prominent feature of COPD. Thus, the beneficial effect of TTO₂ in two of these subjects may have been a correction of hypoxemia related to COPD rather than obstructive apnea per se. On the other hand, this report is important in that it verifies the safety of TTO₂ in the setting of OSA. Until further reports are forthcoming, the potential role of transtracheal oxygen in OSA must remain speculative.
Effect of Chronic Supplemental Oxygen in Sleep Apnea

To the clinician treating patients with OSA, the long-term clinical outcome of patients treated with nasal supplemental oxygen should be of primary importance. For example, are symptoms improved and are hemodynamic sequelae of apnea reversed?

In their study of the acute effect of supplemental oxygen in apnea, Martin et al. reported follow-up of five patients who used 3-4 L/min nasal oxygen during sleep at home for 30 to 90 days. Each subject was studied one night on room air at the beginning, and one night on oxygen at the end of the study time. They reported a decrease in apnea time and apnea frequency in three of five subjects. The authors state that the patients who showed the greatest reduction of apnea time short-term were the ones with the best subjective improvement long-term. There was mild improvement in sleep efficiency (sleep time/time in bed) from 85.5 to 92.3 percent. Unfortunately, two of the patients showing marked symptom and apnea frequency improvement also showed significant weight loss which could have contributed to or accounted for the difference.

Gold et al.16 conducted a single-blind, non-randomized trial of placebo (compressed air) versus oxygen at 4 L/min, each administered for one month by nasal cannula to eight subjects with OSA. End apneic SaO2 improved during NREM sleep, apnea frequency decreased, and apnea duration increased slightly. Overall there was no consistent subjective or objective improvement in hypersomnolence. Four subjects had improvement in symptoms during the oxygen month, and four had improvement during the placebo month. The two patients who showed the greatest reduction in apnea frequency with acute oxygen administration showed the greatest symptomatic improvement on placebo. There was, however, no change in mean sleep latency time from baseline to placebo to oxygen. Awake ventilation was reduced as evidenced by an increase in mean resting PaCO2 from 40 ± 1 mm Hg to 43 ± 1 mm Hg on oxygen. This was attributed to a chronic metabolic alkalois is induced by recurrent nocturnal respiratory acidosis. Any reduction in apnea frequency or improvement in percentage of time spent in apnea lasted only as long as the oxygen therapy. Cessation of nocturnal oxygen resulted in an immediate return to baseline apnea frequency and duration. The authors interpreted the lack of improvement in hypersomnolence after chronic oxygen administration to mean that factors such as recurrent arousals may be important determinants of hypersomnolence. This is an important study in that it examines the effect of home supplemental oxygen on sleep apnea and its symptoms in a manner similar to the method that would be used to administer home oxygen by most clinicians. Furthermore, objective methods (MSLT) were used to assess the effect of oxygen on daytime hypersomnolence.

A major goal in demonstrating an objective response to chronic nasal oxygen therapy would be to show hemodynamic improvement in sleep apnea patients with cardiovascular abnormalities resulting from recurrent nocturnal hypoxemia. Due to the inherent difficulty of long-term cardiovascular studies, including the invasiveness and time required for long-term follow-up, there are few data available on the long-term effects of oxygen therapy. Interpretation of the data is complicated by the frequent concomitant occurrence of COPD which could further affect cardiopulmonary hemodynamics.

Studies involving hemodynamic follow-up of treated apnea patients are practically non-existent. The only study which examines chronic hemodynamic follow-up of severe sleep apnea patients examines oxygen therapy in a peripheral manner. Fletcher et al.17 followed hemodynamic parameters in 24 patients with severe sleep apnea for up to three years. The patients were divided into three groups: group 1 (N = 9) had severe OSA plus COPD and accepted tracheostomy (cure) at the recommendation of the investigator. Five of these patients were also treated with oxygen. Group 2 (N = 10) had severe OSA plus COPD, but refused tracheostomy upon recommendation. This group accepted non-curative therapy which included nocturnal supplemental oxygen in nine. Group 3 (N = 5) had severe OSA alone which was treated with tracheostomy. The group 2 subjects with OSA and COPD who used home oxygen alone or with other therapies (propritline, N = 2; uvulopalatopharyngoplasty, N = 4) showed no improvement in pulmonary artery pressure or vascular resistance at 12 to 24 months’ follow-up and no improvement in right ventricular ejection fraction (Fig 5). Group 1 and group 3 subjects who accepted tracheostomy showed improvement in all of these parameters at long-term follow-up. In the setting of combined COPD and OSA, supplemental oxygen did not appear to alter cardiopulmonary hemodynamics. In addition, the group 1 patients who received curative therapy for apnea showed improvement in arterial blood gas levels with increased daytime PaO2 from 60 to 73 mm Hg and decreased PaCO2 from 49 to 41 mm Hg.17 The group treated with supplemental oxygen showed no change in room air blood gas levels over a two-year period.

The above study cannot be taken as conclusive evidence against chronic oxygen therapy for sleep apnea, but until further studies are done, it does challenge the efficacy of oxygen as chronic therapy for OSA. Complicating factors in interpreting this study are: 1) it was not randomized and patients were
selected for oxygen therapy because of refusal of tracheostomy; 2) compliance was monitored only by word of the patient; 3) the majority of patients had severe COPD complicating the hemodynamic findings. It could be that fixed pulmonary vascular changes on the basis of COPD had occurred, which supplemental oxygen could not have corrected. Recent studies indicate that about 20 percent of sleep apnea patients will have pulmonary hypertension at the time of diagnosis.8 Most of these will have daytime hypoxemia on the basis of concomitant lung disease. Thus, if oxygen is to be contemplated as a useful chronic therapy for OSA, the clinician should be careful to consider the impact of pre-existing lung disease.

There is one setting in which supplemental oxygen may be beneficial to OSA patients.9 Some patients whose apneas are eliminated with tracheostomy or nCPAP persist in having nonapneic desaturation, especially during REM sleep. This desaturation may be secondary to hypoventilation and a fall in functional residual capacity with ventilation maldistribution and worsening of gas exchange. This is seen mainly in very obese patients with combined COPD and sleep apnea. Low flow oxygen during sleep has been shown to greatly ameliorate this desaturation and could potentially be beneficial in improving pulmonary hemodynamics with chronic use.

CONCLUSIONS

In summary, studies of supplemental oxygen administered for short periods of time (one night) have demonstrated improvement in minimal or nadir SaO2, and some worsening of respiratory acidosis. Generally, there is slight prolongation of mean apnea duration, but overall time spent in apnea during sleep may actually be less in some patients using small amounts of nasal oxygen.

Studies of supplemental oxygen administered for longer periods of time are inconclusive regarding symptomatic improvement. Aside from placebo effect, no objective evidence is at hand to show improvement in daytime hypersomnolence. Work to date on cardiovascular abnormalities of sleep apnea has shown that patients with OSA and COPD (those with the most severe hemodynamic disturbances) who are treated with nocturnal oxygen show no long-term improvement in hemodynamic parameters while on oxygen therapy. This is not the case when the apneas are cured by tracheostomy (or presumably the more recent modality of nCPAP). Although these data are far from conclusive, they do shed some doubt on the efficacy of long-term oxygen therapy in OSA.

Currently, there is little evidence to indicate that supplemental oxygen is useful or beneficial in the treatment of OSA. Because of this, it should only be
used in a setting where other more effective attempts at therapy have failed either because of lack of efficacy or poor patient tolerance. In this setting, the patient should probably not be prescribed home oxygen until polysomnography with acute oxygen demonstrates a decrease in time spent in apnea, there is minimal increase in apnea duration, and no worsening of cardiac arrhythmias.

REFERENCES
1 Barach AL. Ambulatory oxygen therapy: Oxygen inhalation at home and out of doors. Dis Chest 1957; 35:229
14 Elmer JC, Farney RJ, Walker JM, Ord RJ, Viscomi VA. The comparison of transtracheal oxygen with other therapies for obstructive sleep apnea. Am Rev Respir Dis 1989; 137:311A