Nocturnal pulse oximetry studies in patients with COPD

Part I: A clinical review

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Introduction

During the past thirty years, pulse oximetry has been used in chronic obstructive pulmonary disease (COPD) cases in several settings. Most commonly, oximetry has been used with the titration of oxygen therapy, with acute exacerbation in patients hospitalized in the intensive care unit, and with sleep studies in the stable state of the disease. The latter will be reviewed in this article.

For more than 40 years, it has been understood that sleep can accentuate hypoxemia in patients with COPD [1]. The earliest nocturnal polygraph studies of patients were in 1975, and include intermittent blood gas tension measurements during sleep [2]. However, it was only with the advent of reliable pulse oximeters in 1976 that the respiratory "events" occurring during sleep could be clearly defined. After the landmark study by Flick and Block in 1977 [3], several groups went on to show that patients with COPD experienced a worsening of hypoxemia particularly during REM sleep [4,5,6].

The initial studies focused almost entirely on patients having severe disease, and who were clearly hypoxemic during the day. Publications studying nocturnal hypoxemia in patients with little or no daytime hypoxemia (i.e. arterial oxygen tension, PaO2 > 60mmHg) appeared only later [7,8,9].

In this short review, we will present the characteristics of nocturnal hypoxemia in COPD patients, its mechanisms and consequences, and we will consider the treatment options currently available. Finally, practical issues about pulse oximetry during nocturnal studies will be exposed.

Oximetric desaturation during sleep in COPD

Healthy subjects have a mean nocturnal SpO_2 of above or equal to 96%. Particularly in REM sleep, there may be short periods of a physiological drop with a SpO_2 between 93 and 96 percent [10]. The small decline has hardly any effect on *arterial* oxygen saturation (SaO_2) with normal subjects, as the change takes place on the horizontal portion of the oxyhemoglobin dissociation curve (Figure 1).

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Episodes of oxygen desaturation are characterized by their number, duration, and severity (i.e. lowest SpO_2 reached). Most software used for analyzing pulse oximeter stored data provides access to representative parameters of nocturnal desaturation, such as:

- Mean nocturnal SpO_2 - reflecting the mean desaturation level during the night
- The time (or percent of time) spent in sleep below a given saturation threshold, like 90% or 80%

Episodes of oxygen desaturation during sleep are frequent in patients with advanced COPD. Desaturation episodes can be defined by a fall in pulse oximetric saturation (SpO_2) of more than 4%, compared to the baseline level of SpO2 during stable respiration, and immediately preceding the hypoxemic episode.

Patients with severe COPD and with mild to moderate daytime hypoxemia (i.e. PaO_2 between 55 and 70 mmHg) have a mean nocturnal SpO_2 of approximately 90%. Finally, when daytime hypoxemia is severe, or PaO_2 below 55 mm Hg, mean nocturnal SpO_2 may reach as low levels as 75 to 80 %.

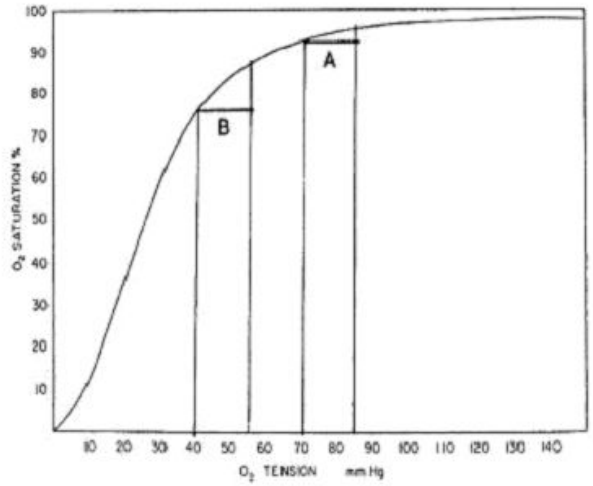

Figure 1. Oxyhemoglobin Dissociation Curve. *Points A and B demonstrate effect of identical drops of PaO_2 (15 mm Hg) on O2 saturation (SpO2) in two different situations. In A, the decrease from normal baseline PaO_2 (85 mm Hg) results in minimal change in SpO2. In B, due to the S-shaped hemoglobin dissociation curve, the markedly decreased PaO_2 (55 mm Hg) level results into substantial drop of SpO2 along the steep part of the curve.*

The most prolonged and severe episodes of desaturation occur during REM sleep. They may last from a few minutes to half an hour. However, desaturation is not only specific to REM sleep, but may also occur during unstable periods during the onset of sleep that correspond to light, non-REM sleep (NREM stages 1-2). However, it must be stressed that episodes of desaturation during NREM may be relatively short. They usually last for only a few minutes, and they are not as intense as episodes recorded during REM sleep [4,5].

Patients with COPD but without daytime hypoxemia may have a similar pattern of nocturnal SpO_2 tracing. Daytime PaO_2 is clearly the best predictive indication of nocturnal SpO_2, but significant correlation in series of patients has nevertheless failed to accurately predict nocturnal desaturation in individual cases.

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COPD patients may have a PaO2 as low as 50 mmHg while awake, pinpointed at the steep portion of the hemoglobin dissociation curve. Hence, decreases in PaO_2 would result in oxygen desaturation, which may vary greatly depending on whether the subject has minimal, little, or marked hypoxemia.

For patients with minimal daytime hypoxemia (PaO_2 > 60 mmHg), but with significant airway obstruction (forced expiratory volume in one second, FEV1, < 50 % of the predicted value), the following definitions for detection of nocturnal desaturation have been suggested:

- Over 30% of the recording time showing a SpO_2 < 90% [8]
- Over 5 minutes recorded with a SpO_2 < 90% and the lowest desaturation is 85% or less [7]

According to the first definition, the proportion of patients with sleep-related hypoxemia in COPD is 25-50 % of all having daytime PaO_2 from 55 to 70 mmHg [8]. However, the latter definition does not appear to be tight enough to differentiate “desaturators” from “non-desaturators” [7].

In a community-based study of 884 subjects with a mild obstructive airway disease and without symptoms of sleep apnea, 11.4 % of patients spent over 5 % of the total sleep time with SpO_2 below 90 %. That number is remarkably high compared to a significantly lower value of 6.3 % of subjects without obstructive airway disease. Nevertheless, individuals with mild COPD without sleep apnea symptoms have only minimally perturbed sleep [11].

Sleep-related mechanisms of hypoxemia

Two main mechanisms explain the accentuation of sleep hypoxemia: alveolar hypoventilation (which predominates in REM sleep), and ventilation-perfusion mismatching. In nocturnal hypoxemia associated with COPD, apnea is not a feature. Hence, it needs to be differentiated from the obstructive sleep apnea syndrome (OSAS) [5], although sometimes the two conditions may coexist.

As alveolar hypoventilation sometimes can take place in healthy subjects [10], it is hardly surprising to find it in patients with respiratory symptoms and COPD, alveolar hypoventilation is related to the rise in $PaCO_2$, or a decrease in minute ventilation [12,13]. The "hypopneas" observed in these patients during sleep correspond to alveolar hypoventilation. Such episodes are often characterized by decreased ventilation associated with increased hypoxemia and a drop in respiratory effort.

The role of alveolar hypoventilation appears to predominate in determining hypoxemia, especially in REM sleep [12,14,15]. Alveolar hypoventilation is explained by a reduction in "central command" linked to the diminished sensitivity to hypoxia and hypercapnia, by increased upper airway resistance, and by less activity of the intercostal muscles and accessory respiratory muscles, during phasic REM sleep [15].

Ventilation-perfusion mismatching is the other nocturnal desaturation mechanism. Its presence or accentuation is suggested by a sometimes observed discrepancy between a marked fall in SpO_2 and a lack of rise in $PaCO_2$ [16], as well as by an increase in the arterial-alveolar difference in PO_2 and venous return [17]. In fact, it is difficult to perform detailed studies of gas transfer during sleep. The published data oftentimes refer to only a limited number of patients.

Reduced ciliary clearance of mucus results in accumulation of bronchial secretions and may be associated with ventilation-perfusion mismatching. It may also be associated with decreased functional residual capacity (FRC) in the supine position during REM sleep [18]. Decreased FRC results in the closure of the small airways in the lower parts of lungs and increased shunting.

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Consequences of sleep-related hypoxemia

Hemodynamic effects in the pulmonary circulation: Acute alveolar hypoxemia, which characterizes severe episodes of nocturnal desaturation, typically causes vasoconstriction of the small pulmonary arteries and a rise in mean pulmonary arterial pressure (mPAP). Episodes of nocturnal hypoxemia, especially when marked and protracted, can lead to pulmonary hypertensive jolts.

As the measurement of pulmonary artery pressures is an invasive technique, only a few attempts have been made to study pulmonary hemodynamics during sleep. However, they consistently show that episodes of hypoxemia, particularly in REM sleep, tend to be accompanied by substantial increases in mPAP [16,19,20,21].

Only a few sleep studies assessing pulmonary hemodynamics have been carried out on patients with complex COPD, presenting daytime pulmonary hypertension, as well. The question remains as to whether their results can be applied to subjects with minor hypoxemia while awake, but with normal mPAP levels while awake.

One tempting hypothesis has been published, suggesting that a daytime pulmonary hypertension might begin as a result of episodes of nocturnal desaturation. Transient increases in mPAP may then gradually result into pulmonary hypertension, even though daytime hypoxemia may still remain low or non-existent [22].

However, a European multi-center study failed to confirm this hypothesis, and as of today we do not have clear evidence. The study reported mPAP to be identical for patients with and without nocturnal desaturation [9].

Tachycardias and other cardiac dysrhythmias have been observed in COPD patients during sleep [23]. Supraventricular (SV) and ventricular (VE) extrasystolic beats appear to be particularly frequent between the times of 3 and 5 in the morning [24]. The study on 42 severely affected COPD patients showed that VE occurred during sleep in 60 % of them. VE were more frequent in cases of severe nocturnal desaturation (SpO_2 < 80 %) [25]. The frequency and impact of these findings remains controversial, although one may assume that some unexplained night time deaths may be due to severe dysrhythmias, aggravated by profound hypoxemia.

Coronary circulation and the myocardium. Episodes of nocturnal hypoxemia lead to a strong increase in myocardial oxygen consumption. In roughly 30% of severely ill COPD patients, the maximum myocardial blood flow during sleep may exceed that observed during a significant daytime effort [26]. Nighttime hypoxic myocardial stress may be associated with the higher incidence of nocturnal mortality of COPD patients. This is only an unconfirmed hypothesis. Due to a limited number of published researches, it can't be confirmed, and nocturnal hypoxemia cannot be claimed as direct cause of COPD mortality.

COPD associated with obstructive sleep apnea syndrome

COPD is a common condition in patients. Obstructive sleep apnea syndrome (OSAS) is common, as well. OSAS affects approximately 5% of middle-aged adult males. Subsequently, the association between COPD and OSAS is far from unusual, although there is no causal link. In a study carried out on 265 OSAS patients, 30 cases (11%) had an associated COPD diagnosis [27].

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In COPD patients, the additional diagnosis of OSAS must be suspected in the presence of clinical symptoms such as:

- Sleepiness in a subject who snores
- Breathing pauses reported by the partner
- Marked nocturnal hypoxemia persisting under oxygen therapy

Generally speaking, the clinician should always be suspicious when the observed picture of respiratory failure and cardiac repercussions seems to be related to *only moderate* ventilatory deficiency.

Elevated risk may indicate polysomnography. When compared with "OSAS-only" patients, those affected by both COPD and OSAS have an elevated risk of daytime respiratory failure and pulmonary hypertension. Hence, early identification of patients with combined COPD and OSAS is important. In this state, the prompt ordering of a polysomnography may be indicated, although it is not normally indicated for just COPD. Polysomnography is often regarded as a time-consuming and expensive test, but it may be very informative, and it includes a continuous nocturnal pulse oximetry test, as well.

Treatment of nocturnal hypoxemia, and practical case examples

Published in part II as a separate clinical appendix to this review article.

Conclusion.

Pulse oximeters are invaluable tools for care patients with severe and very severe COPD. Patients with COPD and normal arterial blood gases usually have the same pattern of nocturnal SpO_2 tracing compared with healthy subjects. On the contrary patients, having COPD and the presence of chronic respiratory failure experience episodes of oxygen desaturation as low as 75-80 % lasting from a few minutes up to even 30 minutes during REM sleep. Therefore, the author recommends a continuous nocturnal monitoring of SpO_2 at a first evaluation of a patient with COPD and chronic respiratory failure. Such recordings may be helpful to monitor treatment titration of long-term oxygen therapy and if necessary, additional ventilatory support. For similar reasons, nocturnal oximetry may be of use in these patients during yearly follow-up evaluation.

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