

Nocturnal desaturation: predictors and the effect on sleep patterns in patients with chronic obstructive pulmonary disease and concomitant mild daytime hypoxemia*

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ABSTRACT

Objective: To determine the nocturnal oximetry pattern in chronic obstructive pulmonary disease patients having no sleep apnea and presenting mild daytime hypoxemia, to identify probable daytime parameters capable of predicting nocturnal desaturation, and to evaluate the influence of nocturnal desaturation on the sleep pattern of these patients.

Methods: Twenty-five patients were divided into two groups: those with nocturnal desaturation and those without.

Results: Comparing the first group (52%) with the second, we found the following: age, 63 + 5 years versus 63 + 6 years; forced expiratory volume in the first second = 53 + 31% versus 56 + 19% predicted; ratio of forced expiratory volume in the first second to forced vital capacity, 49 + 14% versus 52 + 10%; arterial oxygen tension, 68 + 8 mmHg versus 72 + 68 mmHg; and arterial oxygen saturation, 93 + 2% versus 94 + 1%. Patients in the nocturnal desaturation group presented lower daytime arterial oxygen saturation and nocturnal arterial oxygen saturation by pulse oximetry. There was no difference between the two groups in terms of the sleep patterns observed. The ratio of forced expiratory volume in the first second to forced vital capacity was found to correlate with forced vital capacity, daytime arterial oxygen tension and daytime arterial oxygen saturation. In addition, arterial oxygen saturation by pulse oximetry during exercise was found to correlate with nocturnal arterial oxygen saturation by pulse oximetry. However, only daytime arterial oxygen saturation was predictive of nocturnal desaturation. **Conclusion:** The only variable capable of predicting nocturnal desaturation was daytime arterial oxygen saturation. Nocturnal desaturation did not influence the sleep patterns of patients with chronic obstructive pulmonary disease accompanied by mild daytime hypoxemia.

Keywords: Sleep, REM; Pulmonary disease, chronic obstructive; Anoxemia; Spirometry; Wakefulness

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INTRODUCTION

In patients with chronic obstructive pulmonary disease (COPD), the quality of sleep can suffer, and such patients can present a drop in nocturnal levels of blood gases.⁽¹⁻³⁾

There is a consensus that the greatest nocturnal desaturation occurs during rapid eye movement (REM) sleep⁽⁴⁻⁵⁾ and that patients with COPD are more hypoxic during sleep than they are when at rest during the day.⁽⁶⁻⁷⁾ Hypoxemia is also greater during sleep than during maximum exercise.⁽⁸⁾

The principal causes of nocturnal hypoxemia are alveolar hypoventilation⁽⁹⁾ and altered ventilation/perfusion ratio.⁽¹⁰⁾ In addition, there is a correlation between nocturnal hypoxemia and daytime parameters, such as arterial oxygen saturation (SaO₂), arterial oxygen tension (PaO₂)^(6,11) and decreased ventilatory response to hypercapnia.⁽¹²⁾ However, in addition to the differences in methodology, various authors have failed to evaluate the predictive value of each variable,^(11,13) making it difficult to interpret and extrapolate the results presented.

Furthermore, the influence that nocturnal desaturation has on the sleep patterns, pulmonary hemodynamics and life expectancy of patients with COPD (without hypoxemia or with mild daytime hypoxemia) has yet to be clarified in the literature.⁽¹⁴⁾

In view of this, the objectives of this study were as follows: to determine the nocturnal oximetry pattern in patients with COPD with mild daytime hypoxemia and without sleep apnea; to identify probable daytime parameters capable of predicting nocturnal desaturation; and to evaluate the influence of nocturnal desaturation on the sleep patterns of these patients.

METHODS

A cross-sectional study involving patients with COPD was carried out from August of 2003 to April of 2004. The COPD was diagnosed in accordance with the criteria defined by The Global Initiative for Chronic Obstructive Lung Disease.⁽¹⁵⁾

This study included patients admitted to the Pulmonary Rehabilitation Program of the University Hospital of Brasília and the Catholic University of Brasília. All of the patients with COPD were former smokers, smoke-free for at least six months, and

clinically stable for the past four weeks at least, with daytime PaO₂ greater than 60 mmHg and SaO₂ greater than 90%. Patients with sleep apnea syndrome (apnea-hypopnea index \geq 5 events/hour), orthopedic problems or any other problems that might result in sleep disturbance were excluded from the study. All of the patients were using bronchodilators and oral theophylline, and none were being treated with continuous oxygen therapy or corticosteroids.

The patients evaluated were divided into two groups: those who presented nocturnal desaturation (group ND) and those who did not (group NND).

Patients who presented oxygen saturation by pulse oximetry (SpO₂) \geq 90% during \geq 30% of their total sleep time were designated ND group patients.⁽¹⁶⁾

The study was approved by the Ethics Committee of the University Hospital of Brasília. All patients gave written informed consent.

The patients were submitted to the tests described below over a maximum period of one week.

Absolute values of forced vital capacity (FVC), forced expiratory volume in one second (FEV₁) and FEV₁/FVC ratio (%) were determined using a Vmax-22 series spirometer (SensorMedics, Yorba Linda, CA, USA), and the relative values predicted for gender, age and height were calculated based on the values described by Knudson et al.⁽¹⁷⁾ Spirometry was carried out according to the norms established by the American Thoracic Society.⁽¹⁸⁾

Regarding arterial blood gas analysis during wakefulness, values were determined for PaO₂, arterial carbon dioxide tension (PaCO₂) and SaO₂ using a Ciba Corning 278 Gas System (Ciba-Corning, Diagnostics Corp., Medfield, MA, USA).

A 6-minute walk test was administered, immediately after which SpO₂ values were measured with a model 920M pulse oximeter (Healthdyne Technologies, Marietta, GA, USA).

Body mass index, calculated using the formula weight in kilograms/height in square meters, was evaluated.

The following parameters were monitored in all-night polysomnography: electroencephalography; electrocardiography; electromyography; electro-oculography; and nasal/oral airflow thermistry. In addition, body position, snoring, ribcage/abdominal movement and SpO₂ were recorded. These measurements were taken using the Alice 3

computerized polysomnography system (Healthdyne Technologies, Marietta, GA, USA) Traditional polysomnography variables were evaluated in accordance with Rechtschaffen and Kales.⁽¹⁹⁾

Values of the studied variables are presented as means standard deviation. Student's t-test for independent samples was used in the comparative analysis between ND and NND group values. Pearson's correlation test was used to determine the level of correlation between the variables studied during daytime and those evaluated during sleep. (For this analysis, we considered the groups as a whole, regardless of the nocturnal desaturation.) Logistic regression was used to calculate the odds ratios and identify the independent variables that were predictive of nocturnal desaturation. In accordance with this mathematical model the following variables were tested: FVC, FEV₁, FEV₁/FVC, PaCO₂, PaO₂, SaO₂ at rest and SpO₂ during exercise. Values of p < 0.05 were considered statistically significant.

RESULTS

Among the 25 patients studied, 13 (52%) presented nocturnal desaturation (ND group).

Of the 13 ND group patients, two were females, and the mean age was 63 ± 5 years. Of the 12 NND patients, three were females and the mean age was 63 ± 6 years.

Values relating to anthropometry, arterial blood gas, spirometry, and SpO₂ during exercise are presented in Table 1. There were no statistically significant differences between the two groups regarding these values (p < 0.05).

We observed that the ND group patients presented lower SpO₂ values during REM and non-REM (NREM) sleep, as well as lower minimum SpO₂ during sleep and a greater percentage of sleep time with SpO₂ < 90%, than did the NND group patients (p < 0.05) (Table 1).

In the analysis of the study sample as a whole, daytime SaO₂ and PaO₂ correlated positively and significantly with SpO₂ during nocturnal wakefulness, with mean SpO₂ during sleep and with minimum SpO₂ during sleep (Figure 1). Daytime SaO₂ and PaO₂ correlated negatively and significantly with the percentage of sleep time with SpO₂ < 90%. However, there was a positive and significant correlation between the FEV₁/FVC ratio (%) and SpO₂

TABLE 1

Data relating to anthropometry, spirometry, arterial blood gas and SpO₂ - during exercise and during polysomnography - of the groups studied

Variable	ND (n = 13)	NND (n = 12)
BMI (kg/m ₂)	25 + 4	25 + 5
FVC (% of predicted)	84 + 33	86 + 20
FEV ₁ /FVC (%)	49 + 14	52 + 10
FEV ₁ (% of predicted)	53 + 31	56 + 19
PaO ₂ (mmHg)	68 + 8	72 + 6
PaCO ₂ (mmHg)	33 + 5	36 + 3
SaO ₂ (%)	93 + 2	94 + 1
SpO ₂ during exercise (%)	90 + 4	90 + 3
SpO ₂ time < 90% (%)	73.0 + 27.8	9.5 + 6.8*
SpO ₂ (%) - during wakefulness	88.4 + 3.0	91.6 + 1.7*
SpO ₂ (%) - in NREM sleep	87.4 + 3.4	91.3 + 1.7*
SpO ₂ (%) - in REM sleep	85.7 + 4.8	90.1 + 2.1*
SpO ₂ (%) - minimum during sleep	77.2 + 8.6	83.6 + 4.3*

Data expressed as mean standard deviation; *p < 0.05; ND: patients with nocturnal desaturation; NND: patients with no nocturnal desaturation; BMI: body mass index; FVC: forced vital capacity; FEV₁: forced expiratory volume in one second; PaO₂: arterial oxygen tension; PaCO₂: arterial carbon dioxide tension; SaO₂: arterial oxygen saturation; SpO₂: arterial oxygen saturation by pulse oximetry

TABLE 2

Polysomnographic variables of the groups studied

Variable	ND (n = 13)	NND (n = 12)
Apnea-hypopnea index (events/hour)	3.1 + 5.3	1.5 + 1.7
Total sleep time (minutes)	334.0 + 68.8	309.5 + 82.6
Total sleep time/Total time in bed (%)	73.5 + 13.3	72.2 + 14.9
Sleep latency (minutes)	29.0 + 30.7	28.6 + 27.5
REM sleep latency (minutes)	87.9 + 33.0	138.0 + 91.4
Periodic lower limb movement	1.0 + 2.0	1.5 + 4.5
Stage changes	134.5 + 42.6	119.6 + 26.2
Micro-arousals index (events/hour)	31.1 + 11.9	29.6 + 8.3
Stage 1 (%)	20.6 + 6.2	20.7 + 9.0
Stage 2 (%)	47.8 + 6.9	50.2 + 9.6
Delta sleep (%)	9.2 + 2.7	8.3 + 3.3
REM sleep (%)	20.7 + 5.2	19.1 + 7.4

*Results expressed as mean standard deviation; All variables presented p > 0.05; ND: patients with nocturnal desaturation; NND: patients with no nocturnal desaturation; REM; rapid eye movement

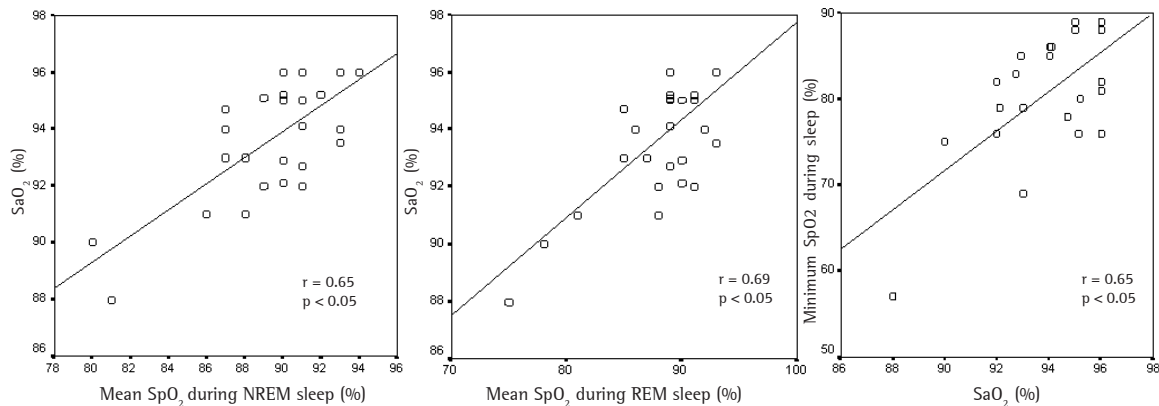


Figure 1 - Correlation between daytime SaO_2 and mean SpO_2 during sleep, and between daytime SaO_2 and minimum SpO_2 during sleep in the 25 patients studied. SaO_2 : arterial oxygen saturation; SpO_2 : arterial oxygen saturation by pulse oximetry

during sleep. In addition, SpO_2 during exercise correlated positively and significantly with SpO_2 during sleep (Figure 2).

Polysomnographic data are presented in Table 2, showing that there were no statistically significant differences between the two groups studied in terms of sleep patterns.

Based on the odds ratios obtained, the only independent predictor of nocturnal desaturation was daytime SaO_2 . We observed that each percentage point increase in daytime SaO_2 reduces the chance of nocturnal desaturation by 49%.

DISCUSSION

Of the 25 patients studied, 13 (52%) presented nocturnal desaturation, according to the definition

adopted,⁽¹⁶⁾ during 30% to 90% of their sleep time. These results are very close to those obtained in another study of patients with COPD with mild hypoxemia,⁽¹⁶⁾ 45% of which were found to present nocturnal desaturation. The results of this study refute the findings of some other authors⁽⁶⁾ who reported that daytime SaO_2 values lower than or equal to 93% always result in nocturnal desaturation, since two of our NND group patients presented daytime SaO_2 values of 91% and 92%, respectively.

The literature presents controversial results regarding the impact of nocturnal desaturation, in isolation, on patients with COPD. It has been reported that nocturnal desaturation promotes an increase in pulmonary arterial pressure.⁽⁷⁾ However, other authors have stated that, among patients with mild daytime hypoxemia, pulmonary arterial

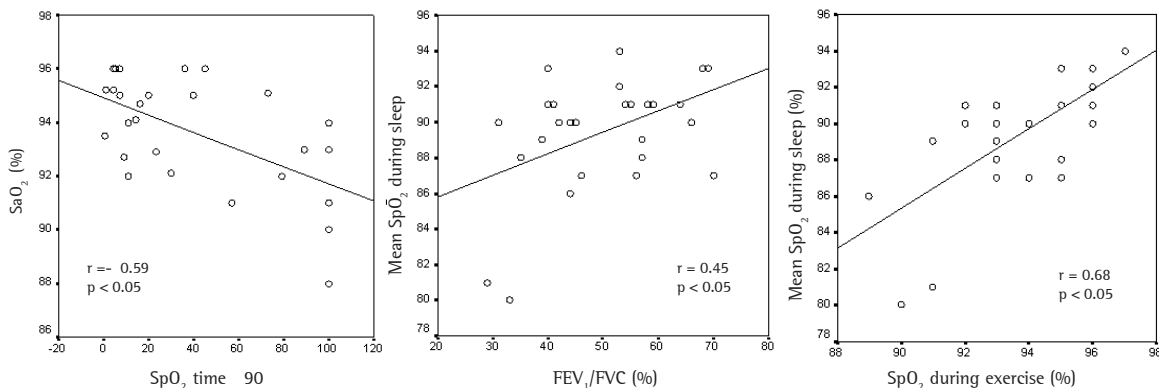


Figure 2 - Correlation between daytime SaO_2 and sleep time with $SpO_2 < 90\%$, between FEV_1/FVC ratio and mean SpO_2 during sleep, and between SpO_2 during exercise and mean SpO_2 during sleep in the 25 patients studied.

SaO_2 : arterial oxygen saturation; SpO_2 : arterial oxygen saturation by pulse oximetry; FEV_1 : forced expiratory volume in one second; FVC: forced vital capacity

pressure was the same for those presenting nocturnal desaturation as for those not presenting such desaturation.⁽²⁰⁾ The survival of these patients is also an object of controversy. A recent review of the literature⁽¹⁴⁾ indicates that there is no scientific evidence of the deleterious effect of nocturnal hypoxemia, in isolation, on the survival of these patients.

The present study demonstrated that, although SpO₂ during sleep correlates with the FEV₁/FVC ratio (%), daytime SaO₂, daytime PaO₂ and SpO₂ during exercise, only daytime SaO₂ was a predictor of nocturnal desaturation. This finding corroborates those of other authors.^(6,21)

The literature presents different results on the predictive parameters of nocturnal desaturation. Some authors found that SpO₂ during sleep correlates positively with daytime FEV₁⁽²¹⁾, SaO₂ and PaO₂.^(6,11) In addition, it has been observed that the greater the nocturnal desaturation, the lower the ventilatory response to hypercapnia and hypoxemia.⁽¹²⁾ Regarding exercise, a situation of ventilatory and cardiac stress, the lower the SaO₂ during exercise, the lower the SpO₂ during sleep.^(6,8,13) Furthermore, we found nocturnal SpO₂ to correlate negatively with functional residual capacity,⁽⁶⁾ PaCO₂^(6,13) and daytime sleepiness.⁽¹²⁾ However, of all the factors that correlated with nocturnal SpO₂, only SaO₂,^(6,21) daytime sleepiness⁽¹²⁾ and daytime PaO₂^(8,12) were independent predictors of desaturation during sleep.

The discrepancy in the results presented in the literature can result from the differences in the methodology used, including the innumerable definitions of nocturnal desaturation used in the studies, such as a drop in SpO₂ greater than 4% in relation to baseline for a minimum of five minutes⁽⁶⁾ and 30% or more of total sleep time with an SpO₂ below 90%.^(13,16) In this study, we adopted the definition proposed by Levi-Valensi et al.⁽¹⁶⁾ due to its greater clinical importance.

As a response to hypoxemia and/or hypercapnia, patients with COPD present increased ventilation and respiratory effort, often resulting in awakening.⁽²²⁾ According to some authors,⁽²³⁾ desaturation is accompanied by awakenings and/or sleep stage changes.

In this study, there were no statistically significant differences between the ND group and the NND group in any polysomnography parameters

except for oximetry. Therefore, the number of awakenings, sleep stage changes, or movements during sleep, was not altered by nocturnal desaturation. This result corroborates those of other authors,^(12,14,24) Some of whom⁽²⁴⁾ stated that nocturnal desaturation is not the only factor that can cause sleep alterations in patients with COPD.

In conclusion, 52% of the patients studied presented nocturnal desaturation, and the only variable capable of predicting such desaturation was daytime SaO₂. Furthermore, nocturnal desaturation does not influence the sleep pattern of patients with COPD accompanied by mild daytime hypoxemia.

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