

SHORT REPORT

Prevalence of daytime hypercapnia or hypoxia in patients with OSAS and normal lung function

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Abstract The purpose of this study was to determine factors increasing daytime PaCO_2 or PaO_2 in obstructive sleep apnoea syndrome patients (OSAS) with normal pulmonary function tests. Anthropometric, pulmonary function tests, arterial blood gases and sleep polygraphic data were analysed retrospectively in 218 OSAS patients (apnoea–hypopnoea index $> 15 \text{ h}^{-1}$; 18 females, 55 ± 11 years): 125 patients had abnormal pulmonary function tests, i.e. one or more flow or volume under 80% or above 120% of predictive value (group I) and 93 had normal pulmonary function tests (group II). Hypercapnia was defined as $\text{PaCO}_2 \geq 6.0 \text{ kPa}$ and hypoxia as $\text{PaO}_2 < 9.3 \text{ kPa}$. Patients with abnormal pulmonary function tests were more hypoxic and hypercapnic, more obese, and had a higher apnoea–hypopnoea index ($P < 0.05$). Seventeen patients of group I and four of group II were hypercapnic (13.6% and 4.3%, respectively). Thirty-one patients in group I (24.8%) had a $\text{PaO}_2 < 9.3 \text{ kPa}$ and six (6.5%) in group II. Stepwise multiple regression analysis showed that in group II, only two factors were correlated with PaCO_2 : mean apnoea duration and FRC (respectively: $c=0.228$, $P < 0.001$; $c=0.006$, $P=0.0108$); and only two with PaO_2 : mean apnoea duration: ($c=-0.218$, $P=0.029$) and BMI ($c=-3.72$, $P < 0.0001$). Daytime hypercapnia is present in 4.3% and daytime hypoxia in 6.5% of patients with occlusive sleep apnoea syndrome and normal pulmonary function tests. These alterations in blood gases in OSAS with normal pulmonary function tests should be considered as OSAS severity criteria. © 2001 Harcourt Publishers Ltd

doi:10.1053/rmed.2001.1120, available online at <http://www.idealibrary.com> on IDEAL[®]**Keywords** sleep apnoea syndrome; pulmonary function tests; apnoea index; apnoea duration; hypercapnia; hypoxia.

INTRODUCTION

Obstructive sleep apnoea syndrome (OSAS) refers to occurrence of episodes of complete or partial pharyngeal obstruction during sleep (1,2). In these patients, the night-time blood gas composition fluctuates towards hypoxemia and hypercapnia because of the episodes of apnoeas and hypopnoeas. Therefore, while awake, hypercapnia or hypoxia could be present and is frequently claimed to be the consequence of an associated pulmonary disease (3). These patients have a dramatic increase in the risk of developing respiratory insufficiency, with hypoxemia, hypercapnia and pulmonary hypertension (4). Nevertheless, diurnal hypercapnia or hypoxia could also be present in OSAS patients without any defect in lung function. Actually, there is a lack of data regarding this association and its explanation remains unclear. Therefore, the aim of this study was to describe

the prevalence of daytime hypercapnia or hypoxia and to identify factors predicting an increase in daytime PaCO_2 or PaO_2 in apnoeic patients with normal pulmonary function tests.

SUBJECTS AND METHODS

Subjects

A retrospective analysis was carried out on data collected in 617 patients referred to our sleep laboratory between January 1995 and December 1997. Reference criteria were based only on clinical symptoms, i.e. snoring, obesity, daytime sleepiness and/or hypertension (5). All patients underwent routinely nocturnal polygraphy, arterial blood gas measurements and conventional plethysmography. Two hundred and eighteen patients were diagnosed as OSAS patients according to polysomnographic results [≥ 15 apnoeas and/or hypopnoeas per hour of sleep, $> 80\%$ of which were obstructive in type (6,7)].

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Methods

Measurements

Polygraphy was carried out with a standard sleep recording device (CID I02p, CIDELEC, Saintes Gemmes sur Loire, France) and tracheal sound, abdominal and chest wall displacement, and oxygen saturation were recorded and analysed. In all cases, apnoea index (IA), apnoea-hypopnoea index (AHI), mean apnoea duration (MAD), longest apnoea duration (LAD), mean saturation during the night and time below $SaO_2 < 90\%$ were measured or calculated. Conventional plethysmography (SensorMedics, Yorba Linda, CA, U.S.A.) was performed in all the patients in seated position. Vital capacity (VC), forced expiratory volume in 1 sec (FEV_1), functional residual capacity (FRC), total lung capacity (TLC) were measured and FEV_1/VC was calculated. Reference values used were based on European Community guidelines (8). Arterial blood samples were taken from a radial arterial puncture in a semi-recumbent position and immediately analysed for blood gases (ABL 500, Radiometer, Copenhagen, Denmark). Body mass index (BMI) was calculated as weight height⁻² ratio.

Procedures

Pulmonary function tests were performed in the morning following the sleep recording, and before arterial blood gases sampling.

Data and statistical analysis

Data were expressed by mean and standard deviation. Abnormal lung function was defined as a decrease under 80% or an increase above 120% of predictive value for one or more flow or volume measurements. Hypercapnia was defined as a $PaCO_2 \geq 6$ kPa and hypoxia as $PaO_2 < 9.3$ kPa (75 mmHg) (8). Patients with abnormal pulmonary function tests (henceforth referred to as group I) were compared to the patients with normal pulmonary function tests (henceforth referred to as group II) using a *t*-test for unpaired data. In group II, stepwise multiple regression analysis was performed in attempt to predict the level of independent variable correlated with $PaCO_2$ or PaO_2 . Statistics were calculated using the Statview and SuperAnova softwares (Abacus Concept, Berkeley, CA, U.S.A.) running on an Apple Macintosh computer. Results were considered significant when the probability (*P*) of a type I error was 0.05 or less.

RESULTS

In the 218 patients included in the study (200 males, mean age 55.5 ± 11.2 years), 125 belonged to group I and 93 to group II.

TABLE I. Anthropometric, blood gas, polygraphic and plethysmographic data of patients with abnormal pulmonary function tests (group I) and patients with normal lung function (group II). *P* represents the statistical difference between the two groups.

		Group I	Group II	<i>P</i>
<i>n</i>		125	93	
Age	years	55 ± 11	55 ± 10	NS
BMI	kg m ⁻²	35.3 ± 6.5	31.5 ± 5.2	< 0.0001
$PaCO_2$	kPa	5.3 ± 0.61	5.0 ± 0.47	0.023
PaO_2	kPa	10.3 ± 1.49	11.2 ± 1.60	< 0.0001
AI	n h ⁻¹	26.6 ± 19.1	24.8 ± 17.1	NS
AHI	n h ⁻¹	54.1 ± 25.6	47.1 ± 19.6	0.0288
LAD	s	57.3 ± 33.2	57.9 ± 33.5	NS
MAD	s	18.2 ± 4.8	19.4 ± 6.8	NS
SaO_2m	%	90.2 ± 5.2	92.2 ± 3.8	0.018
T 90% SaO_2	%	28.5 ± 28	18 ± 17	0.0028
VC	% pred	85 ± 17	101 ± 13	< 0.0001
FRC	% pred	80 ± 26	99 ± 19	< 0.0001
TLC	% pred	89 ± 15	104 ± 11	< 0.0001
FEV_1	% pred	81 ± 21	100 ± 14	< 0.0001
FEV_1/VC	% pred	95 ± 13	98 ± 8	0.008

See text for abbreviations.

Comparisons between the two groups are summarized in Table I: patients with abnormal pulmonary function tests were more hypoxic and hypercapnic, more obese and had a higher AHI. As expected, this group of patients had altered pulmonary function tests.

Seventeen patients of group I and four of group II were hypercapnic (13.6% and 4.3% respectively). Thirty-one patients in group I (24.8%) were hypoxic and six (6.5%) in group II (Fig. 1).

Stepwise multiple regression analysis showed that in group II, two factors were correlated with $PaCO_2$: mean apnoea duration and FRC (respectively: $c=0.228$, $P < 0.001$; $c=0.006$, $P=0.0108$) and only two with PaO_2 : mean apnoea duration: ($c=-0.218$, $P=0.029$) and BMI ($c=-3.72$, $P < 0.0001$).

DISCUSSION

This study shows that 4.3% of OSAS patients with normal pulmonary function tests are hypercapnic and 6.5% are hypoxic. Otherwise, mean apnoea duration and decrease in FRC were found to be the main factors determining $PaCO_2$ as mean apnoea duration and BMI were found to be the main factors determining PaO_2 .

Before interpreting these results, some methodological considerations should be discussed. To avoid any bias in this retrospective study, patients were included consecutively, and investigated with the same apparatus for

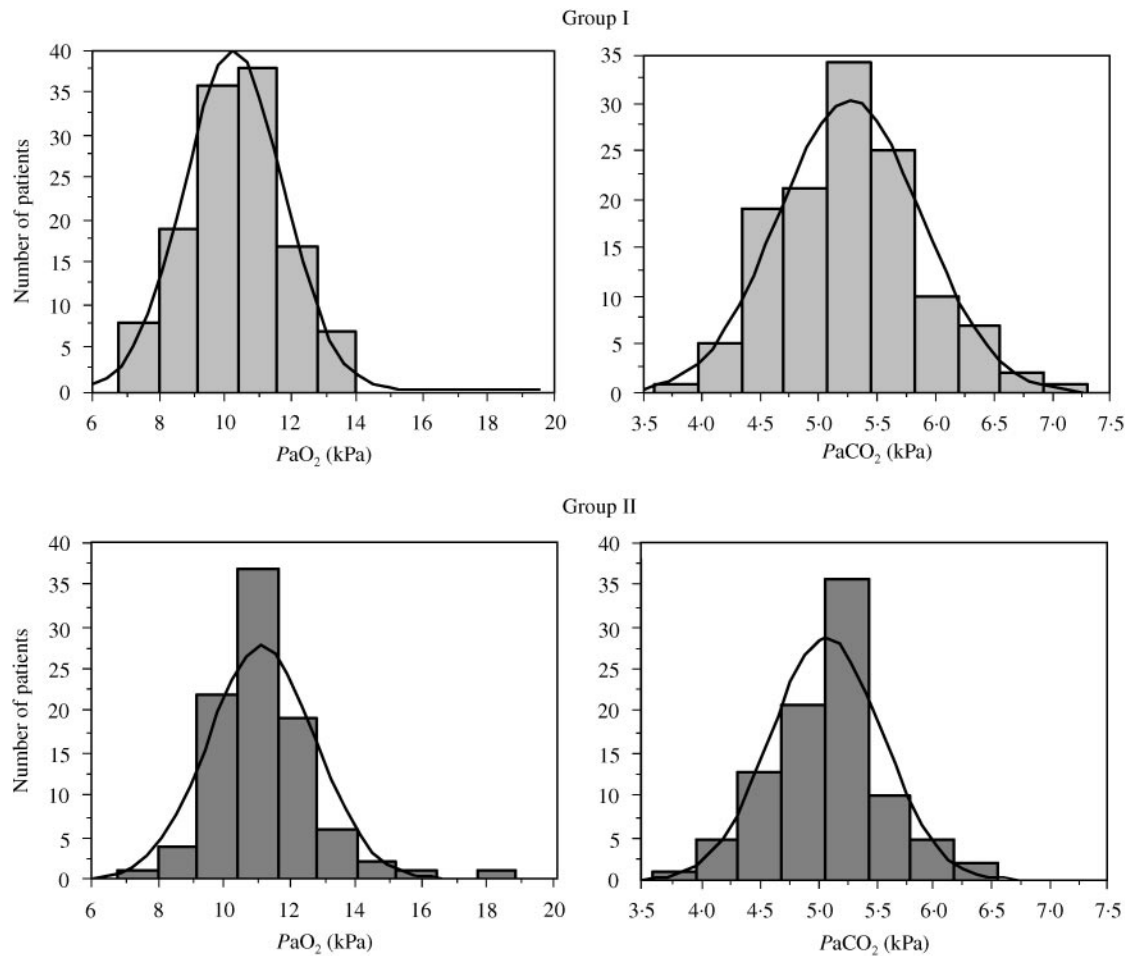


Fig. 1. Histograms of daytime PaCO₂ and PaO₂ in group I (top) and group II (bottom). This figure shows that in group II, daytime hypercapnia or hypoxia could be present.

polygraphy, pulmonary function test and blood gases. Pulmonary function tests were always made in seated patients and not in the supine position. This could influence our results, especially FRC, as that is commonly decreased in supine position. It is reasonable to assume that the influence of FRC in determining PaCO₂ could have been larger if supine FRC values had been measured, but such measurements are not routinely performed during pulmonary function tests, thus making our results more clinically relevant.

All patients had an abbreviated sleep recording and not a polysomnography. As no data regarding sleep fragmentation were available, we only used AHI to establish the diagnosis of OSAS. The accuracy of this recording method has been previously reported by Lloberes *et al.* (9) and MacNicholas *et al.* (7).

To our knowledge, this study is the first one to examine, in OSAS patients with normal pulmonary function tests, determinants of hypercapnia or hypoxia with such a large sample of patients. It demonstrated that alteration in blood gases could exist in a few patients, especially those in which high mean apnoea duration had been measured. This daytime hypercapnia or hypoxia

should be considered as a severity criterion in OSAS, as well as in patients with abnormal pulmonary function tests, because consequences should be the same (respiratory insufficiency or pulmonary hypertension). An impaired process of CO₂ or O₂ clearance during the night, which is compromised by apnoea, or an increased BMI or a decreased FRC, could explain these results, because they alter gas exchanges (10,11). Ventilatory control disturbances, such as impaired ventilatory responses to as inappropriate levels of ventilation in response to hypercapnia, hypoxia, or resistive loading, have been postulated to contribute to the pathogenesis of disordered breathing during sleep (12). Such abnormalities in respiratory drive could not account for the presence of hypercapnia or hypoxia in patients in group II.

In conclusion, the results of the present study suggest that daytime hypercapnia is present in 4.3% and daytime hypoxia in 6.5% of patients with obstructive sleep apnoea syndrome with normal pulmonary function tests. Increase in mean apnoea duration associated with a slight defect in FRC contributed to daytime hypercapnia and increase in mean apnoea duration associated with a high BMI are associated with daytime hypoxia. These altera-

tions in blood gases in OSAS with normal pulmonary function tests remains to be evaluated in further studies, but should be considered as OSAS severity criteria.

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REFERENCES

1. Remmers JE, Degroot WJ, Sauerland EK, Anch AM. Pathogenesis of upper airway occlusion during sleep. *J Appl Physiol* 1978; **44**: 931–938.
2. Guilleminault C, Tikian A, Dement W. The sleep apnea syndromes. *Ann Rev Med* 1976; **27**: 465–484.
3. Chaouat A, Weitzemblum E, Krieger J, Ifoundza T, Oswald M, Kessler R. Association of chronic obstructive pulmonary disease and sleep apnea syndrome. *Am J Respir Crit Care Med* 1995; **151**: 82–86.
4. Krieger J, Sforza E, Apprill M, Lampert E, Weitzenblum E, Ratomaharo J. Pulmonary hypertension, hypoxemia, and hypercapnia in obstructive sleep apnea patients. *Chest* 1989; **96**: 729–737.
5. Strohl KP, Redline S. Recognition of obstructive sleep apnea. *Am J Respir Crit Care Med* 1996; **154**: 279–289.
6. Stradling JR. Sleep studies for sleep-related breathing disorders. *J Sleep Res* 1992; **1**: 265–273.
7. McNicholas WT. Diagnostic criteria for the sleep apnoea syndrome: time for consensus. *Eur Respir J* 1996; **9**: 634–635.
8. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society *Eur Respir J* 1993; **16** (Suppl): 5–40.
9. Lloberes P, Montserrat JM, Ascaso A, et al. Comparison of partially attended night time respiratory recordings and full polysomnography in patients with suspected sleep apnoea/hypopnoea syndrome. *Thorax* 1996; **51**: 1043–1047.
10. Rapoport DM, Norman RG, Goldring RM. CO₂ homeostasis during periodic breathing: predictions from a computer model. *J Appl Physiol* 1993; **75**: 2302–2309.
11. Berger KI, Ayappa I, Sorkin IB, Norman RG, Rapoport DM, Goldring RM. CO₂ homeostasis during periodic breathing in obstructive sleep apnea. *J Appl Physiol* 2000; **88**: 257–264.
12. Zwillich CW, Sutton DJ, Pierson EM, Creagh EM, Weil JV. Decreased in hypoxic ventilatory drive in obesity-hypoventilation syndrome. *Am J Med* 1975; **59**: 343–347.