

Sleep-related O₂ desaturation and daytime pulmonary haemodynamics in COPD patients with mild hypoxaemia

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ABSTRACT: It has been hypothesized but not firmly established that sleep-related hypoxaemia could favour the development of pulmonary hypertension in chronic obstructive pulmonary disease (COPD) patients without marked daytime hypoxaemia.

We have investigated the relationships between pulmonary function data, sleep-related desaturation and daytime pulmonary haemodynamics in a group of 94 COPD patients not qualifying for conventional O₂ therapy (daytime arterial oxygen tension (P_{a,O_2}) in the range 7.4–9.2 kPa (56–69 mmHg)). Nocturnal desaturation was defined by spending $\geq 30\%$ of the recording time with a transcutaneous O₂ saturation $< 90\%$. An obstructive sleep apnoea syndrome was excluded by polysomnography.

Sixty six patients were desaturators (Group 1) and 28 were nondesaturators (Group 2). There was no significant difference between Groups 1 and 2 with regard to pulmonary volumes and P_{a,O_2} (8.4 ± 0.6 vs 8.4 ± 0.4 kPa (63 ± 4 vs 63 ± 3 mmHg)) but arterial carbon dioxide tension (P_{a,CO_2}) was higher in Group 1 (6.0 ± 0.7 vs 5.3 ± 0.5 kPa (45 ± 5 vs 40 ± 4 mmHg); $p < 0.0001$). Mean pulmonary artery pressure (P_{pa}) was very similar in the two groups (2.6 ± 0.7 vs 2.5 ± 0.6 kPa (19 ± 5 vs 19 ± 4 mmHg)). No individual variable or combination of variables could predict the presence of pulmonary hypertension.

It is concluded that in these patients with chronic obstructive pulmonary disease with modest daytime hypoxaemia, functional and gasometric variables (with the noticeable exception of arterial carbon dioxide tension) cannot predict the presence of nocturnal desaturation; and that mean pulmonary artery pressure is not correlated with the degree and duration of nocturnal hypoxaemia. These results do not support the hypothesis that sleep-related hypoxaemia favours the development of pulmonary hypertension.

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The worsening of hypoxaemia during sleep in patients with chronic obstructive pulmonary disease (COPD) has been documented since the early 1960s [1], and has since been confirmed by polysomnographic studies [2, 3], which have included continuous monitoring of oxygen saturation from the late 1970s [4–10]. It must be emphasized that most of these studies have included patients with severe COPD exhibiting marked daytime hypoxaemia. Is sleep-related hypoxaemia present in patients with less severe COPD with mild or absent daytime hypoxaemia? Several studies of the literature [11–13] have shown that a relatively high percentage of these COPD patients exhibit significant nocturnal hypoxaemia, which naturally raises the question: Does this hypoxaemia, limited to sleep, deserve treatment with nocturnal oxygen? Such a treatment could be justified if nocturnal hypoxaemia had deleterious effects on life expectancy, which is rather controversial [14, 15], and on pulmonary

haemodynamics. It has been hypothesized [16, 17] that isolated nocturnal hypoxaemia, occurring in patients without significant daytime hypoxaemia, could lead to permanent (daytime) pulmonary hypertension, but this hypothesis has not, so far, been demonstrated. Recent studies have suggested that, among COPD patients with daytime arterial oxygen tension (P_{a,O_2}) ≥ 8.0 kPa (60 mmHg), those who exhibit sleep-related hypoxaemia have an increased risk of developing pulmonary hypertension [12, 18], but the differences between nocturnal desaturators and nondesaturators were in fact rather small in both studies.

The present study is a part of a large multicentric study devoted to the long-term effects of nocturnal O₂ therapy in COPD patients not qualifying for conventional O₂ therapy. The aim was, firstly, to assess whether daytime functional and gasometric variables could allow the prediction of nocturnal desaturation, and, secondly,

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to investigate the relationships between nocturnal desaturation and pulmonary daytime haemodynamics. The study included 94 patients (66 desaturators and 28 controls), who all underwent sleep studies and right heart catheterization.

Methods

Patients were included in this prospective multi-centric study if they fulfilled the following criteria: a diagnosis of COPD based on usual clinical and functional grounds; forced expiratory volume in one second/vital capacity (FEV₁/VC) ratio <60%; total lung capacity (TLC) >80% of the predicted values; daytime P_{a,O_2} 7.4–9.2 kPa (56–69 mmHg) for two measurements separated by 4 weeks, in patients free of acute exacerbation, and in a stable state of the disease. Arterial carbon dioxide tension (P_{a,CO_2}) could be high (≥ 6.0 kPa (45 mmHg)), normal or low (≤ 4.8 kPa (36 mmHg)). Arterial blood samples were drawn from the patient whilst breathing ambient air, in the morning, after a 15 min resting period in the supine position.

Patients were excluded from the study if they had left heart or congenital heart diseases, associated lung diseases, such as interstitial lung diseases, bronchiectasis, lung carcinoma, or other severe diseases that could influence survival (hepatic cirrhosis, chronic renal failure). In addition, patients were excluded if they had obstructive sleep apnoea syndrome, defined by an apnoea-hypopnoea index (AHI) ≥ 10 events·h⁻¹. Finally, patients were excluded if they were receiving almitrine bismesylate or other respiratory analeptics.

Since the presence of obstructive sleep apnoea was an exclusion criterion, patients had to undergo a conventional polysomnography in a sleep laboratory. Standard techniques, including electroencephalogram (C4/A1; C3/A2), bitemporal electro-oculogram and submental electromyogram were used. Nasal and oral airflows were detected by thermistors. Rib cage and abdominal movements were detected using pneumobelts connected to pressure transducers. Arterial O₂ saturation (S_{a,O_2}) was continuously recorded with a pulse oximeter. The baseline S_{a,O_2} was measured with the subject awake, in the supine position during the 30 min preceding the onset of sleep. The mean nocturnal S_{a,O_2} and the percentage of recording time with an S_{a,O_2} <90% were calculated by computer software.

Sleep stages were scored using scoring episodes of 20 s, according to usual criteria [19]. Time in bed (TIB) was defined as the total time of recording. Total sleep time (TST) was defined as TIB less sleep latency + intrasleep wakefulness. The minimal TST required for a satisfactory analysis of sleep recording was 2 h.

Pulmonary volumes were measured by conventional spirometry. Static volumes were measured by the helium-dilution method. Reference values were those of the European Respiratory Society [20].

Right heart catheterization was separated from polysomnography by no more than 1 week, and was performed as reported previously [21]. Briefly, patients were investigated in the supine position, in the morning, after a light breakfast. Either balloon-tipped Swan-Ganz catheters or small Grandjean floating catheters [22] were

introduced percutaneously. Systolic, diastolic and mean pressures were averaged over five respiratory cycles. The zero reference was at mid-thoracic level. A catheter was introduced into the radial artery for measurement of arterial blood gas tensions. Cardiac output was calculated according to the Fick principle applied to oxygen, measurements being obtained during the last minute of a 15 min resting period. In most of the patients (54 of the 94), measurements could also be obtained during the last minute of a 7 min steady-state exercise performed on an ergometric bicycle, in the supine position; the load being 40 W, or less in patients who were too breathless. The modalities of exercise testing have been described previously [23].

Informed consent was obtained from each individual patient, and the study protocol was approved by the Ethics Committee of the University Hospital of Strasbourg.

Statistical analysis

All data were expressed as mean \pm SD. The group of nocturnal desaturating patients and the group of non-desaturators (defined below) were compared using Student's t-test for unpaired data. The correlations between the mean S_{a,O_2} , the nocturnal time spent in desaturation, the mean pulmonary artery pressure (\bar{P}_{pa}) and several anthropometric, spirometric, gasometric and sleep variables were calculated using the Pearson correlation coefficient (with a two-tailed significance). A multiple regression analysis with stepwise variable selection was performed, attempting to predict the level of two dependent variables: mean nocturnal S_{a,O_2} and \bar{P}_{pa} . A logistic regression analysis was also performed, attempting to predict the presence or absence of pulmonary hypertension (defined by a $\bar{P}_{pa} \geq 2.7$ kPa (20 mmHg)), and of significant nocturnal desaturation (defined below). In all statistical tests, a p-value of 0.05 was accepted as the level of significance.

Results

A significant nocturnal desaturation was defined, as in a previous study [12], by spending $\geq 30\%$ of the recording time (TIB) with an S_{a,O_2} <90%. Our previous study [12] showed that TIB is strongly correlated with TST ($r=0.9$), and that 30% of TIB spent with an S_{a,O_2} <90% corresponds approximately to 40% of TST spent with an S_{a,O_2} <90%. From the 94 patients included in the study, 66 were nocturnal desaturators (Group 1) and 28 were nondesaturators (Group 2).

Comparisons of anthropometric data, pulmonary volumes, daytime arterial blood gas values and polysomnographic data between the two groups are presented in tables 1–3. Nondesaturators weighed less when compared to desaturators ($p=0.02$), but the difference did not achieve significance when comparing the body mass index (BMI) (table 1). Pulmonary volumes were identical in the two groups, but the FEV₁/VC ratio was smaller in Group 2 ($p=0.04$) (table 1). Whereas daytime P_{a,O_2} was similar in the two groups (table 2) daytime P_{a,CO_2} was significantly higher in desaturators (6.0 ± 0.7 vs $5.3 \pm$

Table 1. – Anthropometric data and pulmonary volumes

	Desaturators (n=66)	Nondesaturators (n=28)	p-value [‡]
Sex M/F	59/7	23/5	-
Age yrs	64±8	65±9	NS
Height m	1.7±0.09	1.6±0.08	NS
Weight kg	76.0±13.4	66.7±18.5	0.02
BMI kg·m ⁻²	27.0±4.9	24.7±5.5	NS
VC L	2.84±0.92	2.77±0.94	NS
FEV ₁ L	1.09±0.45	0.95±0.45	NS
FEV ₁ /VC	0.40±0.12	0.35±0.10	0.04
TLC L	6.58±1.65	6.71±1.89	NS

Values are presented as mean±SD. [‡]: for comparison between the two groups. M: male; F: female; BMI: body mass index; VC: vital capacity; FEV₁: forced expiratory volume in one second; TLC: total lung capacity; NS: nonsignificant.

Table 2. – Arterial blood gas tensions and pulmonary haemodynamics

	Desaturators (n=66)	Nondesaturators (n=28)	p-value [‡]
<i>P</i> _{a,O₂ kPa}	8.4±0.6	8.4±0.4	NS
mmHg	62.8±4.4	62.9±2.9	
<i>P</i> _{a,CO₂ kPa}	6.0±0.7	5.3±0.5	<0.001
mmHg	44.7±5.3	39.6±3.8	
\bar{P} _{pa} kPa	2.6±0.7	2.5±0.6	NS
mmHg	19.4±5.3	18.7±4.4	
<i>P</i> _{wp} kPa	1.04±0.47	1.05±0.47	NS
mmHg	7.8±3.6	7.9±3.5	
<i>Q'</i> L·min·m ⁻²	2.97±0.76	3.06±0.82	NS
\bar{P} _{pa} exercise kPa	5.0±1.2 (n=36)	4.9±1.2 (n=18)	NS
mmHg	37.4±8.7	36.5±8.8	

Values are presented as mean±SD. [‡]: for comparison between the two groups. *P*_{a,O₂: arterial oxygen tension; *P*_{a,CO₂: arterial carbon dioxide tension; \bar{P} _{pa}: mean pulmonary pressure; *P*_{wp}: pulmonary artery wedge pressure; *Q'*: cardiac output. NS: nonsignificant.}}

Table 3. – Nocturnal data

	Desaturators (n=66)	Nondesaturators (n=28)	p-value [‡]
TST min	303±101	271±64	NS
REM %	13±10	12±8	NS
AHI events·h ⁻¹	2.8±3.5	2.3±2.6	NS
Mean <i>S</i> _{a,O₂ %}	88±2	92±1	<0.001
<i>t S</i> _{a,O₂ <90% %}	69±24	8±11	<0.001

Values are presented as mean±SD. [‡]: for comparison between the two groups. TST: total sleep time; REM: duration of rapid eye movement sleep (% of TST); AHI: apnoea + hypopnoea index; *t S*_{a,O₂ <90%: time spent with an arterial oxygen saturation <90% (% of the recording time); NS: nonsignificant.}

0.5 kPa (44.7±5.3 vs 39.6±3.8 mmHg); *p*<0.001). Hypercapnia, defined by a *P*_{a,CO₂ ≥6.0 kPa (45 mmHg) was present in only 2 of the 28 Group 2 patients compared to 33 of the 66 Group 1 patients, and the difference was significant (*p*<0.001).}

\bar{P} _{pa} was identical in the two groups (2.59±0.71 kPa (19.4±5.3 mmHg)) in Group 1 vs 2.49±0.59 kPa (18.7±4.4 mmHg) in Group 2), and this was also true for exercising \bar{P} _{pa} (table 2). The distribution of individual values of resting \bar{P} _{pa} is shown in figure 1. It can be

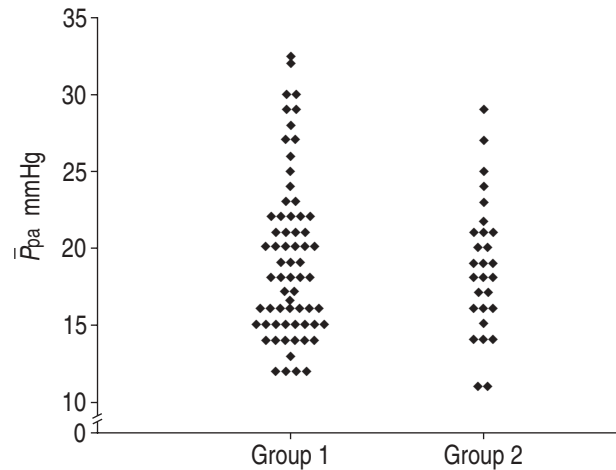


Fig. 1. – Individual values of mean pulmonary artery pressure (\bar{P} _{pa}) in desaturators (Group 1) and nondesaturators (Group 2). It can be seen that abnormally high (≥2.7 kPa (20 mmHg)) and normal (<2.7 kPa (20 mmHg)) values of \bar{P} _{pa} were equally distributed in the two groups (see text). (1 mmHg = 0.133 kPa).

seen that pulmonary hypertension (which was defined by a resting \bar{P} _{pa} ≥2.66 kPa (20 mmHg)) was present in 29 of the 66 Group 1 patients vs 11 of the 28 Group 2 patients (NS). Exercising \bar{P} _{pa} was ≥4.0 kPa (30 mmHg) (upper limit of the normal) in 27 out of 36 patients in Group 1 vs 14 out of 18 patients in Group 2 (NS).

By definition, the mean nocturnal *S*_{a,O₂ and the percentage of the recording time with an *S*_{a,O₂ <90% (*t S*_{a,O₂ <90%) were markedly different in Groups 1 and 2 (table 3). It can be seen from table 3 that in the nocturnal desaturators, sleep-related hypoxaemia was generally not severe, since the mean nocturnal *S*_{a,O₂ was 88±2 vs 92±1% in the nondesaturators. As desaturators spent, as a mean, 69±24% of the recording time with an *S*_{a,O₂ <90%, this means that their nocturnal *S*_{a,O₂ was most often in a narrow range (86–90% in many patients).}}}}}}

The mean nocturnal *S*_{a,O₂ was correlated only with diurnal *P*_{a,CO₂ (*p*<0.001) and BMI (*p*<0.02) (table 4). Surprisingly, it was not correlated with diurnal *P*_{a,O₂. Similarly, *t S*_{a,O₂ <90% was related only to *P*_{a,CO₂ (*p*<0.001), BMI (*p*<0.02) and FEV₁/VC ratio (*p*<0.05) (table 4). In a logistic regression analysis, only two variables could contribute to the prediction of nocturnal desaturation (*t S*_{a,O₂ <90% for ≥30% of the recording time): *P*_{a,CO₂ (*p*=0.0001); and FEV₁ (0.02). Of the patients as a whole, 82% could be correctly classified. In a multiple regression analysis, attempting to predict the mean nocturnal *S*_{a,O₂, the only independent variable}}}}}}}}

Table 4. – Prediction of mean nocturnal *S*_{a,O₂, *t S*_{a,O₂ <90% and \bar{P} _{pa}: univariate analysis}}

	Mean nocturnal <i>S</i> _{a,O₂}		<i>t S</i> _{a,O₂ <90%}		\bar{P} _{pa}	
	r	p-value	r	p-value	r	p-value
BMI	-0.26	<0.02	0.25	<0.02		
VC					-0.29	<0.01
FEV ₁					-0.22	<0.05
FEV ₁ /VC			0.22	<0.05		
<i>P</i> _{a,CO₂}	-0.39	<0.001	0.34	<0.001		

Only the significant correlations have been indicated. For definitions see legends to tables 1–3.

Table 5. — Prediction of mean nocturnal Sa_aO₂, *t* Sa_aO₂ <90% and \bar{P}_{pa} : multivariate analysis

Mean nocturnal Sa_aO₂: multiple regression analysis Mean nocturnal Sa _a O ₂ (%) = 97.4 - 0.025 × Pa _a CO ₂ (kPa) Only predictive variable = Pa _a CO ₂ (r ² = 0.15; p<0.001)
<i>t</i> Sa_aO₂ <90%: logistic regression analysis (prediction of nocturnal desaturation defined by a <i>t</i> Sa _a O ₂ <90% for ≥30% of the recording time) Two variables contribute to the prediction: Pa _a CO ₂ (p<0.001), FEV ₁ (p<0.02)
\bar{P}_{pa}: multiple regression analysis \bar{P}_{pa} (kPa) = 3.13 - (0.199 VC (L)) Only predictive variable = VC (r ² = 0.08; p=0.01)
\bar{P}_{pa}: logistic regression analysis (prediction of pulmonary hypertension defined by a \bar{P}_{pa} ≥2.7 kPa (20 mmHg)) No variable significantly contributes to the prediction

For definitions see legends to tables 1–3.

which could be included was Pa_aCO₂ (p<0.001), but the r² was only 0.15 (table 5).

Very few variables were correlated with \bar{P}_{pa} (table 4): VC, FEV₁ and the percentage of time spent in rapid eye movement (REM) sleep; and the correlation coefficients were rather weak. Diurnal Pa_aO₂ and Pa_aCO₂ were not correlated with \bar{P}_{pa} , nor were the mean nocturnal Sa_aO₂ and *t* Sa_aO₂ <90%. In a logistic regression analysis, no individual variable could predict the presence of pulmonary hypertension (\bar{P}_{pa} ≥2.67 kPa (20 mmHg)). In a multiple regression analysis, attempting to predict \bar{P}_{pa} , the only variable included was VC (p=0.01), and the r² was particularly low (0.08) (table 5).

Discussion

The two major findings of the present study are that: 1) functional and arterial blood gas data, with the noticeable exception of Pa_aCO₂, cannot predict the presence of significant nocturnal desaturation in COPD patients with mild-to-moderate daytime hypoxaemia; and 2) the level of \bar{P}_{pa} is not correlated with the degree nor the duration of nocturnal hypoxaemia.

Prediction of nocturnal desaturation

The present results have been observed in a rather homogeneous population of COPD patients, and we do not know whether they apply to COPD patients with marked daytime hypoxaemia, *i.e.* those who qualify for conventional oxygen therapy (Pa_aO₂ ≤7.3 kPa (55 mmHg)), or to COPD patients without significant daytime hypoxaemia (Pa_aO₂ ≥9.3 kPa (70 mmHg)). This study is, in fact, part of a larger study devoted to the effects of nocturnal oxygen therapy on pulmonary haemodynamics and survival in COPD patients not fulfilling the usual criteria for conventional oxygen therapy, since their diurnal Pa_aO₂ was >7.3 kPa (55 mmHg). An upper limit for daytime Pa_aO₂ of 9.2 kPa (69 mmHg) was chosen, since the comparison of some recent studies [11–13] indicated that significant nocturnal desaturation is rather common in patients who are in the range 8.0–9.2 kPa (60–69 mmHg), but not in patients with very mild or absent daytime hypoxaemia. As a consequence, the

range of diurnal Pa_aO₂ was narrow: Pa_aO₂ was required to range 7.5–9.2 kPa (56–69 mmHg), but in fact it was most often 8.0–8.7 kPa (60–65 mmHg) (in 54 of the 94 patients). The average values were 8.35 and 8.37 kPa (62.8 and 62.9 mmHg) in Groups 1 and 2, respectively; with standard deviations of 0.59 and 0.39 kPa (4.4 and 2.9 mmHg), respectively, indicating that the dispersion of the individual results from the average values was limited.

This probably explains why, in the present study, diurnal Pa_aO₂ did not appear to be a good predictor of nocturnal desaturation. In contrast, several studies have clearly indicated that diurnal Pa_aO₂ was significantly correlated with the mean nocturnal Sa_aO₂ [13, 14, 24–26], and that daytime Pa_aO₂ was the best predictor of nocturnal hypoxaemia in COPD patients [27], which can be explained, at least partly, by the influence of the presleep position on the oxyhaemoglobin dissociation curve. The differences between these studies and the present one is that they covered a very large range of Pa_aO₂ values, which was not the case in the present study.

In our patients with mild-to-moderate daytime hypoxaemia, Pa_aCO₂ was the only predictor of the mean nocturnal Sa_aO₂, but, in fact, Pa_aCO₂ accounted for only 15% of the variance of mean nocturnal Sa_aO₂. Several studies have found that patients with hypercapnia whilst awake are more likely to exhibit nocturnal oxygen desaturation [11, 13, 14, 24–26, 28], but most of these studies have indicated that daytime Pa_aCO₂ was not, in fact, an independent predictor of Sa_aO₂ during sleep [13, 14, 24, 25]. We found that Pa_aCO₂ whilst awake was an independent predictor of nocturnal Sa_aO₂. Pa_aCO₂ was significantly (p<0.001) higher in desaturators (6.0±0.7 kPa (45±5 mmHg)) than in nondesaturators (5.3±0.5 kPa (40±4 mmHg)), whereas Pa_aO₂ and lung volumes were nearly identical in the two groups. This is in good agreement with the data of BRADLEY *et al.* [26], who also noticed that Pa_aCO₂ whilst awake was an independent predictor of mean nocturnal Sa_aO₂ in a series of 48 COPD patients, with a wide range of daytime Pa_aO₂. They observed that the occurrence of sustained nocturnal hypoxaemia was closely related to the presence of daytime hypercapnia in those patients who were only mildly hypoxaemic (awake Sa_aO₂ 89–92%). BRADLEY *et al.* [26] performed polysomnography in only 6 out of 48 patients, and we could confirm their results, when performing polysomnography and respiratory monitoring in all of the present patients, which enabled us to exclude apnoeic events and to be confident of sleep status and the presence of REM sleep in all patients.

Our results suggest that patients who hypoventilate when awake (hypercapnic) are also those who are most likely to hypoventilate during sleep. Unfortunately, the multicentric protocol of the present study did not require the continuous measurement of transcutaneous carbon dioxide tension (P_{tc}CO₂), and we do not know whether it increased more markedly during sleep in desaturators than in nondesaturators. MULLOY and McNICOLAS [13] found a similar rise in P_{tc}CO₂ both among normocapnic and hypercapnic patients, and concluded that an identical degree of hypoventilation was present during sleep in all patients, regardless of Pa_aCO₂, but their series was limited to 19 patients.

We noticed that the nondesaturators (n=28) weighed less when compared to desaturators (table 1), they had a lower FEV₁ (but the difference was not statistically significant) and a lower FEV₁/VC ratio (p=0.04) (table 1). Their average P_{a,CO₂} was normal, in contrast with the desaturators (table 2). We believe that most of these patients belong to the "pink and puffer" type of COPD, whereas a number of desaturators were probably of the "blue and bloated" type. It has been shown previously that "blue bloated" COPD patients are likely to desaturate more during sleep [9, 10, 28], but these studies concerned patients with a very wide range of P_{a,O₂} levels whilst awake, most of them exhibiting marked daytime hypoxaemia. Of interest, the same observation can be drawn from a series with a narrow range of P_{a,O₂}, not including patients with severe daytime hypoxaemia. Comparative measurements of the ventilatory responses to hypoxia and hypercapnia in desaturators and nondesaturators would be of great interest.

Nocturnal desaturation and daytime (permanent) pulmonary hypertension

Isolated nocturnal desaturation, *i.e.* in the absence of significant daytime hypoxaemia (P_{a,O₂} >8.0 kPa (60 mmHg)), could induce, with time, the development of permanent pulmonary hypertension. This has been hypothesized by FLENLEY [16] and BLOCK *et al.* [17], but never firmly established. Two previous studies [12, 18] have compared awake pulmonary haemodynamics in nocturnal desaturators and nondesaturators, with daytime P_{a,O₂} >8.0 kPa (60 mmHg). \bar{P}_{pa} was somewhat higher in the desaturators, but the differences were rather small and there was a marked overlapping of individual results between the subgroups. In the study by FLETCHER *et al.* [18], the average \bar{P}_{pa} was 3.1±0.6 kPa (23.3±4.8 mmHg) in desaturators (n=36) vs 2.7±0.6 kPa (20.4±4.2 mmHg) in nondesaturators (n=13) (p<0.05). The difference between the two groups was more pronounced for pulmonary vascular resistance (p<0.0001). In the study by LEVI-VALENSI *et al.* [12], the average \bar{P}_{pa} was 2.5±0.6 kPa (19.1±4.7 mmHg) in 18 desaturators vs 2.2±0.25 kPa (16.8±1.9 mmHg) in 22 nondesaturators (p<0.05), but again there was an important overlapping of individual values between the two groups.

The present study, which has included more patients than these two previous ones taken together [12, 18], has shown no difference in \bar{P}_{pa} between desaturators (2.6±0.7 kPa (19.4±5.3 mmHg)) and nondesaturators (2.5±0.6 kPa (18.7±4.4 mmHg)). Exercising \bar{P}_{pa} , measured in 54 patients, was also similar in the two groups, in contrast to the results of FLETCHER *et al.* [29]. Furthermore, \bar{P}_{pa} was not significantly correlated with the mean nocturnal S_{a,O₂}, nor with *t* S_{a,O₂} <90%. Pulmonary hypertension was present in 43% of the patients, was generally mild (3.2±0.5 kPa (23.8±3.8 mmHg)), and was equally distributed between desaturators (29 out of 66) and nondesaturators (11 out of 28). In fact, the present results do not differ markedly from the earlier studies mentioned above [12, 18], since the statistical differences were hardly significant and, even in the desaturating group, the average \bar{P}_{pa} was <2.7 kPa (20 mmHg) [12] or hardly >2.7 kPa (20 mmHg) [18].

The present results do not support the hypothesis [16, 17] that isolated nocturnal hypoxaemia is sufficient to induce the development of permanent (daytime) pulmonary hypertension in COPD patients. This finding is in keeping with the observations that have been made in the obstructive sleep apnoea syndrome [30–32]: pulmonary hypertension is not observed in patients with isolated night-time hypoxaemia, but supposes the presence of an associated daytime hypoxaemia. Pulmonary hypertension, which was not uncommon in the present patients (40 out of 94), was mild in all cases (\bar{P}_{pa} ranging 2.7–4.3 kPa (20–32 mmHg)), and certainly had a multifactorial origin, including, in particular, the consequences of emphysema (particularly in Group 2 patients) and a variable contribution of daytime hypoxaemia and nocturnal worsening of arterial blood gas tensions.

We must emphasize the fact that the data presented here do not, at present, lead to the conclusion that nocturnal oxygen therapy is of no interest in sleep desaturators. In fact, the nocturnal desaturators in the present study have been randomly allocated either to nocturnal oxygen therapy or no oxygen therapy, and they are being followed-up for at least 2 yrs. A second haemodynamic investigation will be performed at that time in all the patients. Nocturnal oxygen therapy could have favourable effects on the pulmonary haemodynamic evolution, as suggested by the elegant study of FLETCHER *et al.* [33], which included 18 desaturating and 19 nondesaturating subjects with a follow-up of 3 yrs. Nocturnal oxygen therapy could also favourably influence the prognosis in the desaturating patients [15], and the answer to this question is one of the major aims of the ongoing part of this study.

We conclude that in these patients with chronic obstructive pulmonary disease with mild-to-moderate daytime hypoxaemia (arterial oxygen tension most often 8.0–8.6 kPa (60–65 mmHg)) functional and arterial blood gas variables, with the noticeable exception of arterial carbon dioxide tension, cannot predict the presence of nocturnal desaturation, and that pulmonary arterial pressure is not correlated with the degree and duration of nocturnal hypoxaemia. These results do not support the hypothesis that isolated sleep-related hypoxaemia favours the development of pulmonary hypertension, but do not exclude a possible favourable effect of nocturnal oxygen therapy in desaturating patients.

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