Oxygen desaturation during sleep and exercise in patients with interstitial lung disease

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ABSTRACT The relations between mean and maximum fall in arterial oxygen saturation (Sao_2) during sleep, hypoxaemia during moderate and maximum exercise, and lung mechanics were studied in 16 patients with interstitial lung disease. Mean and minimum Sao_2 during sleep were significantly related to each other and to daytime oxygenation but not to lung mechanics. Although the maximum fall in Sao_2 during sleep was similar to the fall during maximum exercise (a level seldom achieved during normal daily activities), profound hypoxaemic episodes during sleep were rare and brief and therefore contributed little to the mean Sao_2. The fall in mean Sao_2 during sleep was not significant and was considerably less than during moderate exercise (average 0.5 v an estimated 4.5%, p < 0.05). It is therefore concluded that in patients with interstitial lung disease oxygen desaturation during sleep is mild and less severe than hypoxaemia during exercise.

Oxygen desaturation during sleep in chronic obstructive lung disease is well documented, and it has been shown that daytime concentrations of blood gases determine the absolute arterial oxygen saturation (Sao_2) levels during sleep[1,2] as well as the severity of sleep induced fall in Sao_2.[2-4] The conclusions in the few published studies on desaturation during sleep in patients with interstitial lung disease differ. Bye *et al*[5] studied 13 patients with moderately severe disease (mean total lung capacity (TLC) 76% predicted, arterial oxygen pressure (Pao_2) 9·9 kPa (74 mm Hg)). They concluded that the minimum levels of Sao_2 during sleep can be lower than during exercise. Mean levels, however, were not calculated. Perez-Padilla *et al*[6] studied 11 more severely disabled patients (TLC 67% predicted, Pao_2 9·2 kPa (69 mm Hg)) and found "considerable" desaturation during sleep. In contrast, McNicholas *et al*,[7] who studied seven patients (vital capacity (VC) 50% predicted, Pao_2 9·0 kPa (68 mm Hg)), stated that the desaturation during sleep was mild and less severe than in patients with chronic obstructive lung disease.

Previous reports have presented few quantitative data on the relation between daytime concentrations of blood gases and other physiological findings with Sao_2 levels during sleep. We therefore investigated 16 patients with interstitial lung disease and documented desaturation during wakefulness to relate their Sao_2 levels during sleep to daytime concentrations of blood gases at rest and during exercise and to lung volumes and lung resistance.

Methods

From November 1984 to December 1985 we studied all patients referred to our department with stable interstitial lung disease (diffuse fibrosis on x ray examination, reduced lung volumes, and low lung compliance) and daytime hypoxaemia ($Pao_2 \leqslant 8$ kPa (60 mm Hg) at rest or on exercise or a fall in $Pao_2 \geqslant 2·5$ kPa (19 mm Hg) with exercise). Seventeen patients were eligible; none refused to take part in the study but one was excluded because her profound daytime hypoxaemia precluded a sleep study without oxygen supplementation.

Of the 16 patients studied nine had idiopathic pulmonary fibrosis,[8] three had extrinsic allergic alveolitis, two had progressive systemic sclerosis, and one each had alveolar proteinosis and asbestosis. The diagnosis was verified histologically in 10 patients.

The study was approved by the medical ethics committee at the University of Lund.

VC and TLC were measured by body plethysmography.[9] The subjects breathed with a frequency of less than 1 Hz against a closed shutter for determination of thoracic gas volume. Values for VC and TLC are given in table 1 as per cent predicted.[10 11] Lung resistance (RL) was recorded at a regulated flow of 1 l/s and at a static elastic recoil pressure of 7·5 cm H_2O measured with an oesophageal balloon specifically to assess intrinsic bronchial abnormalities.[12] An exercise test was performed on an electrically braked bicycle ergometer (Siemens–Elema) with five minutes at each workload until exhaustion. Samples for arterial blood gas analysis were drawn from an indwelling radial catheter (Venflon, Viggo) at rest in the supine posture and while seated on the bicycle and during exercise at the end of each workload. The blood was analysed immediately using an automatic blood gas analyser (IL 413, Instrumentation Laboratories).

During the sleep study we assessed sleep stage, oronasal airflow, and thoracoabdominal motion during a single night as previously described.[2] Four patients were investigated on a second occasion while receiving oxygen 1–2 l/min through nasal prongs. The continuous sleep recordings were staged conventionally[13] using epochs of 30 seconds.

Oxygen saturation during sleep was measured in the majority of instances using a Biox III ear oximeter.[14] On five occasions a Hewlett Packard 47201A instrument was used and the values thus obtained were adjusted so as to be comparable with the values obtained with the Biox oximeter.[15] The signals from the oximeter were recorded on a Tarkan W + W 600 two channel strip chart recorder, manually synchronised with the electroencephalograph. The Sao_2 recordings were then digitised using 30 s sampling intervals (corresponding to the epochs used for sleep staging) on a plotter (Hewlett Packard 7475A) connected to a microcomputer (IBM PC). Mean Sao_2 was calculated separately for nocturnal wakefulness and non-REM (rapid eye movement) and REM sleep. The sleep induced fall in Sao_2 is presented as fall in mean Sao_2 (difference between mean Sao_2 during nocturnal wakefulness and mean Sao_2 during sleep) and as maximum fall (difference between mean Sao_2 during nocturnal wakefulness and lowest Sao_2 during sleep).

Statistical analysis was carried out with Student's t test for paired and unpaired data or with Pearson's product-moment correlation. In some instances the 95% confidence interval is also presented.

Results

WAKEFULNESS DATA

The patients had a restrictive ventilatory defect with a mean TLC of 65·6% predicted (range 39–91%) (table 1). Airflow limitation was present in about half of the patients, as shown by an abnormally high RL (normal upper limits 3 cm H_2O/l.s for men and 5 cm H_2O/l.s for women[12]), although the FEV_1/VC ratio was within the normal limits in all patients.

In 14 patients the Pao_2 was < 8 kPa (60 mm Hg) at rest or during maximum exercise. Two patients were included only because of a fall in Pao_2 of > 2·5 kPa (19 mm Hg); in these cases the fall in Sao_2 during sleep and exercise was less than the average because they were operating on the flat part of the oxyhaemoglobin dissociation curve. Pao_2 fell on average 0·65 kPa (5 mm Hg) (confidence interval 0·1 to 1·2 kPa; 0·75 to 9 mm Hg) from the supine to the sitting position at rest. The mean fall in Pao_2 from supine rest to moderate exercise (20–50 w depending on the patient's condition) was 1·4 kPa (CI 0·8 to 1·9 kPa; 6 to 14 mm Hg) corresponding to a fall in calculated Sao_2 of 4·5% (CI 1·4 to 7·5%). The mean fall in Pao_2 from supine rest to maximum exercise was 2·1 kPa (16 mm Hg) (CI 1·5 to 2·7 kPa; 11 to 20 mm Hg) and was positively correlated with Pao_2 at rest (r = 0·73, p < 0·01). The average calculated Sao_2[16] during maximum exercise was 87% (range 68–94·5%). There was no correlation between the data on lung mechanics (TLC, VC, RL, or maximum exercise capacity) and level of oxygenation during rest or exercise or fall in Pao_2 with exercise.

Table 1 *Lung function during rest, exercise, and sleep*

	Resting data						Exercise data			Sleeping data				
	TLC (% predicted)	VC (% predicted)	RL M/F (cmH₂O/ l.s)	Pao₂ supine (kPa)	Paco₂ supine (kPa)	Fall in Pao₂ on sitting (kPa)	Fall in Pao₂ with moderate exercise (kPa)	Fall in Pao₂ with maximum exercise (kPa)	WMAX M/F (watt)	Sao₂ awake (%)	Sao₂ non-REM (%)	Sao₂ REM (%)	Fall in mean Sao₂ (%)	Maximum fall in Sao₂ (%)
Mean	66	65	3·5/5·4	9·1	5·0	0·65*	1·35***	2·1***	93/50	91·3	90·9	90·1	0·5 NS	8·3***
(SD)	(16)	(16)	(0·9/1·1)	(1·7)	(0·4)	(1·0)	(1·0)	(1·1)	(45/20)	(3·2)	(3·2)	(4·4)	(0·96)	(4·9)

TLC—total lung capacity; VC—vital capacity; RL—lung resistance; WMAX—maximum workload; Pao₂—arterial oxygen pressure; Paco₂—arterial carbon dioxide pressure; Sao₂—arterial oxygen saturation; REM—rapid eye movement sleep.
NS—not significantly different from zero; *p < 0·05; ***p < 0·001.
Conversion: SI to traditional units—Pao₂, Paco₂; 1 kPa = 7·5 mm Hg.

Table 2 *Correlation between mean and lowest arterial oxygen saturation (Sao₂) during sleep and other variables*

Sao₂	TLC	VC	RL	Paco₂ at rest	Pao₂ at rest	Pao₂ during moderate exercise	Pao₂ during maximum exercse	Sao₂ during nocturnal wakefulness
Mean	−0·044	0·28	0·30	0·45	0·76	0·66	0·74	0·96
	NS	NS	NS	NS	***	**	**	***
Lowest	−0·33	−0·11	0·53	0·09	0·34	0·20	0·43	0·62
	NS	NS	NS	NS	NS	NS	NS	*

TLC—total lung capacity; VC—vital capacity; RL—lung resistance; Paco₂—arterial carbon dioxide pressure; Pao₂—arterial oxygen pressure. NS—not significant; *p < 0·05; **p < 0·01; ***p < 0·001.

SLEEP DATA

The total sleep time was on average 257 minutes, with only 13% spent in stage 3+4 and 11% in REM sleep. One patient had an abnormal number of sleep apnoeas (total 53: 10 apnoeas/h) but the apnoeas were short, mean duration 12 s, and not associated with noteworthy changes in Sao₂.

The overall pattern of oxygenation level during sleep was stable with only a small difference between non-REM and REM sleep (fig 1). Three patients even showed an increase in Sao₂ with sleep owing to hypoxaemic dips during periods of nocturnal wakefulness and stabilisation of Sao₂ during sleep. Oxygen relieved hypoxaemia during sleep to the same extent as it did during wakefulness (fig 2) in the four patients studied.

The average mean Sao₂ during sleep (all stages) was 90·8% compared with 91·3% for wakefulness. The values of mean Sao₂ during sleep were highly significantly correlated with Pao₂ and with mean Sao₂ during (nocturnal) wakefulness (r = 0·96, p < 0·001) (table 2); there were no significant
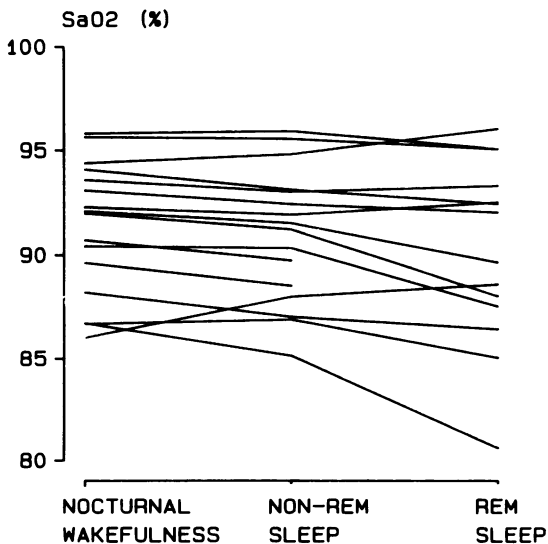

SaO2 (%)

Fig 1 *Mean values of arterial oxygen saturation (Sao₂) during wakefulness and non-REM and REM sleep for all patients.*
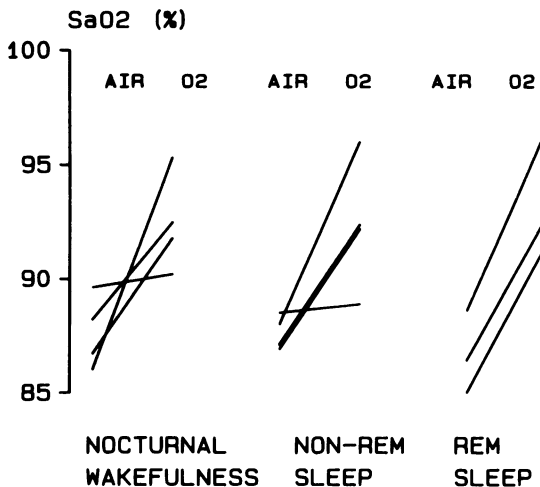

SaO2 (%)

Fig 2 *Arterial oxygen saturation (Sao₂) during wakefulness and non-REM and REM sleep for four patients investigated breathing room air and supplemental oxygen (1–2 l/min). One patient had no REM-sleep.*

relations with awake arterial carbon dioxide pressure (Paco₂), airway resistance, or lung volumes. The nadir values of Sao₂ during sleep averaged 83% (range 70–92%) and were significantly (r = 0·74, p < 0·01) related to mean Sao₂ during sleep, but the hypoxaemic dips were generally short and contributed little to the mean levels.

The fall in mean Sao₂ with sleep was not significant (mean 0·5%, CI −0·01 to 1·01%) and did not correlate with any of the variables, including the Sao₂, during wakefulness. It was significantly less (p < 0·05) than the fall in calculated Sao₂ with moderate exercise (4·5%, CI 1·4 to 7·5). The maximum fall in Sao₂ with sleep was on average 8·3% (CI 5·7 to 10·9%), which is not significantly greater than the average fall in calculated Sao₂ with maximum exercise (6·7%, CI 4·0 to 9·5%).

Discussion

We selected patients with hypoxaemia during rest or exercise because a priori we considered it unlikely that we would find hypoxaemia during sleep in patients

who had no hypoxaemia during the daytime. The average awake Sao_2 calculated[15] from oximeter readings during the sleep study was 92·7%, and Sao_2 calculated[16] from measurements of Pao_2 during the exercise study was 92·5%. A comparison of data from our sleep and exercise studies therefore seems to be justified.

The fall in Pao_2 observed during changing from supine to sitting position may be due to redistribution of blood flow to the basal parts of the lungs, which are often more affected by fibrosis. An alternative explanation is that the fall was exercise induced, since Pao_2 sitting was measured after moving from the couch to the bicycle. The energy demand of normal daily activities, such as washing, dressing, standing, and walking about indoors, corresponds to a workload of approximately 30 w.[17] Moderate exercise was thus defined as 20–50 w, depending on the maximum exercise level for the patient. We estimate that the patients perform at this level for at least six hours every day. We suggest therefore that the comparison of the level of oxygenation at this exercise level with the mean Sao_2 during sleep (six to eight hours every day) probably reflects the relative contributions of exercise and sleep to oxygenation of these patients better than a comparison of transient extreme Sao_2 values.

Desaturation during sleep in our patients was mild when compared with that in patients with chronic airways obstruction;[2 3] episodes of desaturation were brief and seldom profound. The time spent in REM sleep was short (mean 11% of total sleeping time) compared with the normal 21% in this age group,[18] but since the mean Sao_2 in REM sleep was only slightly lower than in non-REM sleep even a considerable increase in REM sleep would have had little effect on the mean Sao_2 (table 1).

Our patients were comparable to those of Perez–Padilla *et al*[6] with respect to TLC and Pao_2 during the daytime but we do not agree with their conclusion that patients with interstitial lung disease may have severe oxygen desaturation during sleep. Although our patients showed smaller falls in Sao_2 during sleep than they reported, in both studies the desaturation was considerably less than is seen in patients with chronic obstructive lung disease.[2 3] On the other hand, our data support the opinion of McNicholas *et al*[7] that oxygen desaturation during sleep in patients with interstitial lung disease is mild.

We conclude that sleep studies are unnecessary in the routine assessment and management of patients with interstitial lung disease.

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