

Supplemental oxygen and quality of sleep in patients with chronic obstructive lung disease

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ABSTRACT The hypothesis that supplemental oxygen could improve the quality of sleep was tested in 23 consecutive patients (14 male, nine female; age 42-74 years) with chronic obstructive lung disease (mean (SD) FEV₁ 0.81 (0.32) litre, FEV₁/FVC 37% (12%). Patients breathed compressed air or supplemental oxygen via nasal cannulas on consecutive nights in a randomised, double blind, crossover trial. Quality of sleep was assessed by questionnaire and by electroencephalographic sleep staging. The study had a power of 80% to detect, at the 0.05 level, a 20% improvement in total sleep time. Seventeen patients slept for two nights in the laboratory. Oxygenation during sleep was improved by oxygen administration, but there was no improvement in quality of sleep. There was an acclimatisation effect with better sleep on the second night. Six patients spent an additional acclimatisation night in the laboratory as well as the two study nights. There was no difference in sleep quality between the second and third nights or between the compressed air and the oxygen nights in these patients. Subgroups of patients with an arterial carbon dioxide tension of over 43 mm Hg (5.7 kPa) (n = 12) and arterial oxygen saturation of less than 90% (n = 11) while awake did not show any improvement in quality of sleep on the oxygen night. It is concluded that supplemental oxygen improves nocturnal oxygenation but does not immediately improve the quality of sleep in the laboratory in patients with chronic obstructive lung disease.

Introduction

Patients with chronic obstructive lung disease experience falls in arterial oxygen saturation (Sao₂) during sleep¹⁻³ and have poorer quality sleep than healthy, control subjects of a similar age.¹ Whether supplemental oxygen improves the quality of their sleep, however, is uncertain. Three studies suggested an improvement,⁴⁻⁶ but the number of patients studied was small; a larger study did not show improved sleep quality.⁹ We therefore studied 24 patients with chronic obstructive lung disease who received compressed air or supplemental oxygen on consecutive nights in a randomised, double blind, crossover trial. We planned to compare quality of sleep between the compressed air and the oxygen night and also between the first and the second night.

Methods

The subjects were outpatients with chronic obstructive

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lung disease (FEV₁ <70% predicted, FEV₁/FVC <60%, with no significant change in spirometric measurements after a nebulised bronchodilator). No patient had asthma, left ventricular failure, or symptoms suggesting obstructive sleep apnoea. All patients gave informed consent for the study.

CLINIC VISIT

Patients were seen in the clinic, where a history was taken and physical examination and routine pulmonary function testing were carried out. The patients rested in the sitting position and arterial blood was drawn from the radial artery for analysis of pH, oxygen tension (Po₂) and carbon dioxide tension (PCO₂) (Radiometer ABL-2). Sao₂ was measured with an ear oximeter (Biox IIA, Ohmeda, Colorado) and haemoglobin concentration from a venous blood sample.

SLEEP STUDIES

Eighteen patients were studied during sleep on two consecutive nights in the sleep laboratory. In one patient, the EEG recording was not adequate for staging sleep, so results are presented for only 17 patients. A further six patients were studied for three

consecutive nights, consisting of an acclimatisation night and two study nights. Patients received compressed air or supplemental oxygen by nasal cannula in a double blind, randomised, crossover design. Neither the patient nor the person who staged the EEG recordings knew the order in which the gas mixtures had been inhaled. On the compressed air night the flow rate was 1 l/min throughout the night. On the oxygen night the flow rate was started at 0.5 l/min and increased by 0.5 l/min every 10 minutes until Sao_2 was at least 90%. It was further increased in 0.5 l/min steps during sleep if Sao_2 fell below 90% for at least 10 minutes, the aim being to keep Sao_2 above 90% throughout the night.

Sleep stage was monitored with cup electrodes in standard positions for electroencephalography, chin electromyography and electro-oculography.¹⁰ Arterial oxygen saturation was continuously monitored by an ear oximeter (Biox IIA). Movements of chest and abdomen were measured by an inductance plethysmograph (Respitrace Corporation, Ardsley, New York). Airflow at the nose and mouth was measured by thermocouples attached to nasal prongs. All signals were recorded on a 12 channel ink pen recorder (Model 78 Grass Instruments, Quincy, Massachusetts). The oximeter signal was also processed and stored by a desk top computer (Hewlett Packard 47804A, Waltham, Massachusetts) for analysis of the percentage of time spent below 85% Sao_2 ($\text{TST}_{<85}$).¹¹

Sleep was staged by the method of Rechtschaffen and Kales¹⁰ on the basis of 30 second epochs. During analysis the Sao_2 record was masked. Total sleep period (TSP) was the time from the first occurrence of stage 2 (sleep onset) to final awakening. Total sleep time (TST) was TSP minus stage awake (W). An arousal was defined as a change in the EEG to either alpha rhythm or a low voltage, mixed frequency pattern and included arousals to wakefulness (more than 15 seconds of any epoch) and briefer arousals (less than 15 seconds of any epoch). After sleep staging was completed, the lowest arterial saturation during sleep was determined directly from the record.

A 16 item questionnaire¹² was administered to each patient after awakening to assess the quality of the previous night's sleep. Patients were asked to nominate which study night they preferred and to compare their sleep in the laboratory with their usual sleep at home.

STATISTICAL METHODS

Mean differences between nights were compared by paired *t* tests and 95% confidence intervals for the differences were calculated.¹³ The power of the study was calculated by a standard formula.¹⁴ Wilcoxon's signed rank test for paired data was used to analyse the

questionnaires. The two period crossover trial was analysed for treatment effects, period effects, and interactions.¹⁵

Results

Twenty three patients (14 male, 9 female; age range 42–74 years) had sleep studies that were adequate for sleep staging. No patient had obstructive sleep apnoea. Three patients had clinical and radiological evidence of bronchiectasis; five had chronic bronchitis with normal carbon monoxide gas transfer and 15 had a reduced carbon monoxide gas transfer. Table 1 shows the mean age, haemoglobin concentration, arterial blood gas tensions, and pulmonary function of the group. Four patients were current cigarette smokers, 18 were ex-smokers, and one had never smoked. Nine patients had a Pao_2 less than 56 mm Hg (7.5 kPa), of whom seven had a history of right heart failure. Four patients had a Pao_2 in the range 56–60 mm Hg (7.5–8.0 kPa), of whom two had had right heart failure. Twelve patients had hypercapnia ($\text{Paco}_2 > 43$ mm Hg) (5.7 kPa). Seven of the nine patients with a history of right heart failure had ECG evidence of right ventricular hypertrophy or a dilated right ventricle from echocardiography. Six patients had secondary polycythaemia.

SLEEP STUDIES

In the 17 patients who spent two nights in the sleep laboratory there were no significant differences between the compressed air and oxygen nights in the amount of time spent in any sleep stage (fig 1, upper

Table 1 Characteristics of the patients

	Mean	SD	Range
Age (y)	63.1	9.6	42–74
Body mass index (kg/m ²)*	23.0	3.9	17–29
Haemoglobin (g/dl)	15.7	2.2	11.4–19.4
Packed cell volume	0.47	0.7	0.35–0.61
pH	7.43	0.04	7.35–7.56
Pao_2 (kPa)	7.7	1.2	5.5–10.9
Paco_2 (kPa)	5.9	1.2	4.1–8.3
HCO_3^- (mmol/l)	29.2	5.7	21.8–39.6
Sao_2 (%)	89	4	80–96
FEV_1 (l)	0.81	0.32	0.45–1.50
FEV_1 (% pred)	32	12	17–62
FVC (l)	2.26	0.68	1.00–3.85
FVC (% pred)	67	17	35–121
RV (% pred)	202	62	100–334
TLC (% pred)	119	24	80–183
Tlco (% pred)	57	35	6–120

*Body mass index = weight (kg)/height² (m²). 20–25 = normal, 26–30 = overweight, > 30 = obese.
 Pao_2 —arterial oxygen tension; Paco_2 —arterial carbon dioxide tension; HCO_3^- —bicarbonate; Sao_2 —arterial oxygen saturation; FEV_1 —forced expiratory volume in one second; FVC—forced vital capacity; RV—residual volume; TLC—total lung capacity; Tlco—carbon monoxide transfer factor.

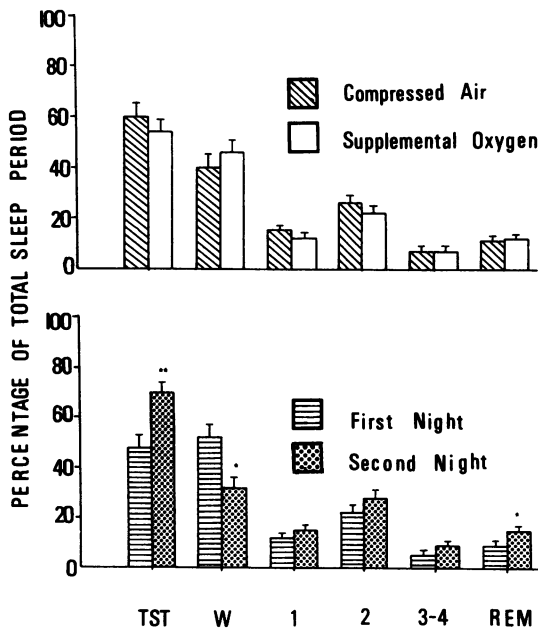


Fig 1 Sleep stage distributions for 17 patients who spent two nights in the laboratory, comparing the compressed air with the oxygen night and the first with the second night. Means and standard errors (bars) are shown. * $p < 0.01$; ** $p < 0.001$.

panel). Mean (SEM) sleep latency on the oxygen night was longer than on the compressed air night (70 (17) v 45 (7) min; $p < 0.02$; 95% confidence interval (CI) for the difference between means 6–44 min). There was no significant difference between the nights in the number of arousals (fig 2) or in the number of sleep state changes. The mean lowest SaO_2 (%) during sleep on the oxygen night was higher than on the compressed air night (86 (3) v 77 (2); $p < 0.01$; 95% CI for difference between means 3–15%). The mean % time spent below 85% SaO_2 on the oxygen night was less than on the compressed air night (4 (2) v 41 (11); $p < 0.01$;

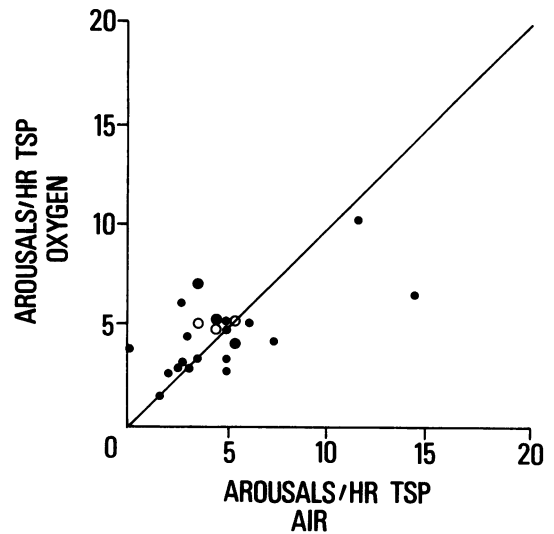


Fig 2 Arousals per hour of total sleep period on the compressed air and oxygen nights. ● Two night group; ○ three night group. The line of identity is shown.

95% CI for difference between means 13–55%). Eleven patients did not require any increase in oxygen flow rate as SaO_2 remained at or above 90% with the initial flow rate (1 l/min) before they went to sleep. In the remaining six patients at least one increment in oxygen flow rate before sleep onset was needed. Mean sleep latency in these six patients did not differ significantly from that found in the group receiving 1 l/min oxygen before sleep onset (45 (11) v 83 (14) min).

On the second night TST was longer than on the first night and there was more REM sleep (fig 1, table 2). There were no significant differences between the two nights in sleep latency, arousals, lowest SaO_2 during sleep, or % TST_{<85}. There were no significant interactions between treatment and period effects (table 2).

Analysis of the questionnaire data showed no

Table 2 Mean treatment responses and period effects for 17 patients who spent two nights in the laboratory

	Treatment		Period	
	Effect (O_2 -CA)	Significance (p)	Effect (N1-N2)	Significance (p)
Sleep latency (min)	25	<0.02	10	NS
Total sleep period (TSP; min)	-15	NS	-23	NS
Total sleep time (% TSP)	-5	NS	-18	<0.01
Stage awake (% TSP)	5	NS	17	<0.01
Stage I (% TSP)	3	NS	-3	NS
Stage II (% TSP)	4	NS	-5	NS
Stages III and IV (% TSP)	0	NS	-4	<0.05
Stage REM (% TSP)	1	NS	-6	<0.01
Arousals (per hour TSP)	0.1	NS	-0.4	NS

O_2 —oxygen night; CA—compressed air night; N1—night 1; N2—night 2.

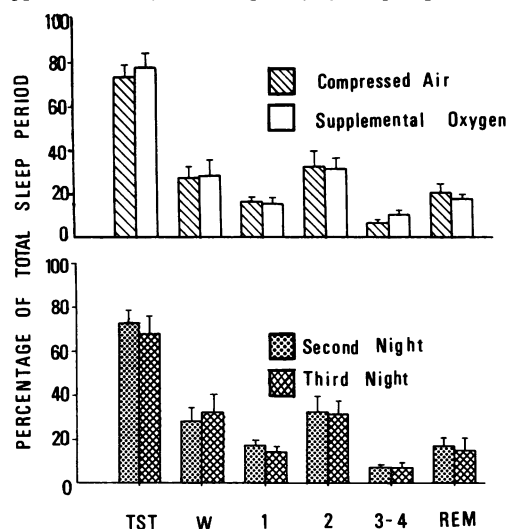


Fig 3 Sleep stage distributions for six patients who spent three nights in the laboratory, comparing the compressed air with the oxygen night and the second with the third night. Means and standard errors (bars) are shown. TST—total sleep time; W—awake; REM—rapid eye movement sleep.

differences between the compressed air and oxygen nights for the 17 patients. When asked which night they preferred, nine patients chose the compressed air night and eight the oxygen night. There were, however, some significant differences between the first and second nights, favouring the second night: patients reported deeper sleep ($p = 0.006$) and fewer awakenings ($p = 0.03$), and thought that they slept better ($p = 0.003$) and that the second night was more like their usual sleep at home ($p = 0.01$). Two patients preferred the first night and 15 preferred the second night.

In the six patients who spent three nights in the laboratory there were no significant differences between the second and third nights in sleep stages (fig 3), sleep latency, arousals, lowest Sao_2 during sleep, or % TST_{<85}. There were also no significant differences between the compressed air and oxygen nights in sleep stages (fig 3), number of sleep state changes, sleep latency, or arousals (fig 2). The mean lowest Sao_2 (%) on the oxygen night was higher than on the compressed air night (86 (4) v 75 (5); $p < 0.001$; 95% CI for the difference 6–16%). The mean % TST_{<85} on the oxygen night was less than on the compressed air night (1 (1) v 45 (18); $p < 0.05$; 95% CI for the difference 1–88%).

Analysis of the questionnaire data for these six patients showed greater difficulty in going to sleep on the oxygen night ($p = 0.01$) but no other significant differences between the compressed air and oxygen nights. There were no significant differences between the second and third nights in the laboratory.

The group was stratified according to Paco_2 (> 43 mm Hg) (5.7 kPa) and Sao_2 ($< 90\%$). There were no differences between the compressed air and oxygen nights in sleep stages or arousals for either subgroup.

Discussion

In 23 hypoxaemic patients with chronic obstructive lung disease supplemental oxygen did not improve the quality of sleep significantly when compared with placebo, as assessed by questionnaire or by sleep staging. There was an acclimatisation effect with improved quality of sleep on the second night. Even in the subgroup, however, who spent an additional acclimatisation night in the laboratory oxygen did not improve sleep quality significantly when compared with placebo.

An acclimatisation effect has been described in normal subjects undergoing EEG monitoring during sleep.¹⁶ In that study less wakefulness and stage 1 sleep and more REM sleep were found on the second night than on the first night. There were no further changes over the next two nights of the study. Acclimatisation to the laboratory may have reduced our chances of showing an improvement with oxygen. There was, however, no significant improvement in quality of sleep with supplemental oxygen in the subgroup who had an acclimatisation night. In the study of Fleetham *et al*⁹ the oxygen night was always preceded by a placebo night, maximising the chances of finding an improvement with oxygen. Despite this, these workers failed to find any improvement in quality of sleep on the oxygen night.

The quality of sleep of our patients was poorer than that reported previously for patients with chronic obstructive lung disease whose breathing was monitored during sleep;^{6,18} in particular, our patients had more wakefulness and less stage 2 sleep. Their quality of sleep was, however, similar to that of similarly aged patients with chronic obstructive lung disease previously reported from our laboratory.¹ The present study had a power of 80% to detect, at the 0.05 level, a 20% increase in TST (% TSP), a 25% increase in stage 2 (% TSP), and a 36% decrease in stage W (% TSP) with oxygen administration. These changes with oxygen would have resulted in near normal sleep architecture according to the findings of Carskadon and associates,¹⁷ who studied breathing and oxygenation during sleep in healthy elderly subjects. The longer sleep latency with oxygen is unexplained. On the oxygen night there was no difference in sleep latency between those patients who did and did not have adjustments made to flow rate before sleep onset. Thus, although the pattern of gas flow differed between the nights, increments in flow rate occurring on the oxygen night but not on the compressed air

night, this seems unlikely to explain the difference in sleep latency that was observed.

Our negative findings contrast with the results of studies of patients with chronic obstructive lung disease in which sleep quality was felt to have been improved by supplemental oxygen.⁶⁻⁸ In the study of Kearley and associates the protocol was not optimal as only one night of sleep was studied; seven patients received room air followed by oxygen and only four patients received the gases in the reverse order. Goldstein and associates⁷ studied patients on two consecutive nights with oxygen always on the first night. Total sleep time improved on the oxygen night but this difference did not achieve statistical significance. Calverley and associates⁶ studied six patients who had an acclimatisation night followed by two nights breathing compressed air or supplemental oxygen at 2 l/min from nasal cannulas in a randomised, double blind, crossover trial. On the oxygen night there was a significant reduction in stage 0 + 1/TSP (%) (27% versus 15%) and an increase in stage REM/TSP (%) (11% versus 17%). The number of patients who received oxygen on the second study night was not reported.

The differences between the studies of Calverley *et al*⁶ and Fleetham *et al*⁹ were discussed in a recently published monograph on chronic obstructive lung disease.¹⁹ The authors¹⁹ suggested that hypercapnic patients were more likely to benefit from supplemental oxygen than eucapnic patients, noting that patients in the former study were hypercapnic (mean $Paco_2$ = 50 mm Hg (6.7 kPa)) compared with those in the latter study (mean $Paco_2$ 44 mm Hg (5.9 kPa)). Our findings are against this interpretation because we found no significant improvement in quality of sleep with supplemental oxygen regardless of $Paco_2$. Moreover, the level of arterial oxygen saturation when patients are awake does not appear to influence the effect of oxygen on sleep quality as stratification of our patients according to whether or not Sao_2 was below 90% did not show differences between the groups.

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