

Arterial oxygenation during sleep in patients with right-to-left cardiac or intrapulmonary shunts

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ABSTRACT We have studied arterial oxygen saturation (SaO_2), breathing patterns, and electroencephalographic (EEG) sleep stage during nocturnal sleep in six patients with right-to-left cardiac or intrapulmonary shunts and six patients with chronic bronchitis and emphysema, chosen because they were equally hypoxaemic when awake (SaO_2 during wakefulness: bronchitis 74-90%, mean 83%; shunt 77-89%, mean 83%). The patients with bronchitis had far greater falls in SaO_2 when asleep than those with shunts (maximum fall in SaO_2 during sleep: bronchitis 14-47%, mean 29%; shunt 5-10%, mean 8%; $p < 0.01$). Significant episodes of hypoxaemia (defined as SaO_2 falls $> 10\%$) occurred in all six bronchitic patients, from once to seven times per night, but in none of the patients with shunts ($p < 0.05$). Twenty-four of the 27 episodes of hypoxaemia occurred in rapid-eye-movement (REM) sleep and 24 were associated with hypopnoea. The two groups of patients had similar EEG sleep patterns and the same amount of hypopnoea during sleep. Thus the level of arterial oxygenation when the patient is awake is not the sole determinant of the degree of nocturnal hypoxaemia; the pathological process is also important.

Transient hypoxaemia occurs during sleep in patients with a variety of respiratory diseases, including chronic bronchitis and emphysema,¹⁻⁵ asthma,⁶⁻⁷ and cystic fibrosis.^{8,9} Furthermore, at high altitude even healthy people have considerable falls in arterial oxygen saturation (SaO_2) during sleep.^{10,11} If severe, such nocturnal hypoxaemia may be important in the development of secondary polycythaemia¹² and pulmonary hypertension.^{12,13} Most of these hypoxaemic episodes result from hypoventilation rather than sleep apnoea, and we have recently shown that the degree of arterial oxygen desaturation in sleep is largely determined by the level of arterial oxygenation when the patient is awake,^{4,14} as those who are most hypoxaemic when awake start the night on the steep part of the oxyhaemoglobin dissociation curve.

We have now sought to explore this relationship between daytime and nocturnal hypoxaemia in patients whose daytime hypoxaemia arises from right-to-left pulmonary or intracardiac shunts and not primary disease of pulmonary airways.

Methods

We have studied six patients with right-to-left shunts (one man and five women) and six patients with chronic bronchitis and emphysema (two men and four women). The bronchitic patients—mean age 56 years, range 47-62—were older than the patients with shunts—mean age 43 years, range 30-57 ($p < 0.05$); but the resting SaO_2 during wakefulness (measured for 15 minutes with the subject sitting in bed immediately before each study) was similar in the two groups, ranging from 74% to 90% (mean 83%) in the patients with shunts and from 77% to 89% (mean 84%) in the bronchitic patients. They all had secondary polycythaemia, the packed cell volume ranging from 0.51 to 0.60 (mean 0.55) in the patients with shunts and from 0.44 to 0.61 (mean 0.52) in the patients with bronchitis. One of the patients with shunts had pulmonary arteriovenous fistulas in association with hereditary haemorrhagic telangiectasia and the other five had congenital abnormalities of the heart or great vessels (table 1). All the bronchitic patients had severe irreversible airways obstruction with a forced expiratory volume in one second (FEV_1) of less than 1.0 l and they had the "blue and bloated" (type B) pattern of the disease,¹⁵ being hypoxic, with an arter-

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Accepted 10 January 1983

Table 1 Clinical details of patients studied

Patient No	Age	Sex	SaO ₂ awake (%)	FEV ₁ l	% predicted	FVC l	% predicted	Diagnosis
Right-to-left shunt								
1	30	F	90	2.8	105	3.2	100	Transposition of great vessels, pulmonary stenosis Partial drainage of inferior vena cava to left atrium Pulmonary arteriovenous fistulas Tetralogy of Fallot Eisenmenger's syndrome (patent ductus arteriosus) Tricuspid atresia, atrial and ventricular septal defects
2	50	M	87	3.8	100	4.8	100	
3	57	F	86	1.2	67	1.7	77	
4	36	F	82					
5	42	F	80	1.8	78	2.1	80	
6	43	F	74	1.9	83	2.9	100	
Chronic bronchitis and emphysema								
7	62	F	89	0.8	27	1.4	51	
8	52	M	85	0.9	23	1.9	47	
9	59	F	85	0.5	24	1.0	35	
10	47	M	84	0.7	20	2.5	56	
11	52	F	79	0.8	29	1.2	52	
12	62	F	77	0.6	27	1.2	50	

SaO₂—arterial oxygen saturation (ear oximeter); FEV₁—forced expiratory volume in one second; FVC—forced vital capacity.

ial oxygen tension (PaO₂) less than 8 kPa (60 mm Hg), and hypercapnic, with an arterial carbon dioxide tension (PaCO₂) greater than 6.6 kPa (50 mm Hg), when awake, with pulmonary hypertension (mean pulmonary arterial pressure 28–48 mm Hg, mean 38 mm Hg). All the patients had been in a stable clinical state for at least six weeks before the study; all were within 20% of their ideal weight,¹⁶ and none was receiving hypnotics, sedatives, or respiration stimulants. Each patient gave informed consent to the study, which was approved by the hospital ethical committee.

Each subject slept in a quiet, darkened room on two consecutive nights. On the first, the "familiarisation" night, all the equipment was in place but data were not recorded. Ear oxygen saturation (SaO₂) was recorded by a Hewlett Packard 47201A ear oximeter,¹⁷ anteroposterior chest wall movement by magnetometers at the level of the third intercostal space anteriorly, air flow at the nose and mouth by thermocouples mounted on nasal prongs, electroencephalogram (EEG) by two midline frontoparietal electrodes, electro-oculogram by four electrodes outside and above the outer canthi, and electromyogram by two submental electrodes.

The SaO₂, breathing pattern, and EEG traces were recorded on separate time-based recorders linked by time marks every 15 minutes and were analysed separately. Ear oximeter readings below 65% were corrected as the oximeter then underestimates SaO₂.¹⁷ The EEG was analysed by standard criteria.¹⁸ Apnoea was defined as complete cessation of air flow at nostrils and mouth for 10 seconds or longer, and was classified as obstructive or central.¹⁹ Hypopnoea was defined as an episode lasting at least

10 seconds in which the amplitude of chest wall movement was less than half the mean amplitude during the preceding period of regular breathing, despite continuation of airflow at nose and mouth.² Most episodes of apnoea or hypopnoea occurred repetitively, so creating easily recognised *periods* of irregular breathing. Such a period was defined as starting with either apnoea or hypopnoea and ending with the next full two-minute period of regular breathing. Each such period was dominated by one breathing pattern. The periods were summed to give the total duration of irregular breathing in each subject. Differences between values were analysed by the Wilcoxon rank sum test. Values are given as means and ranges.

Results

Details of sleep and of irregular breathing and oxygen desaturation during sleep for all the patients are shown in table 2.

Both the duration and the quality of sleep were similar in the patients with shunts and the patients with bronchitis. There was no difference between the two groups in the total time asleep (mean 324 min, range 181–494 min), the duration of rapid-eye-movement (REM) sleep (56 min, 9–124 min), or the duration of non-REM sleep (239 min, 139–320 min).

Irregular breathing occupied, on average, 26 minutes (1–78 min) of the total time asleep. There was no significant difference between the patients with shunts and those with chronic bronchitis in the total duration of irregular breathing, the duration of any type of irregular breathing, or the number of

Table 2 *Electroencephalographic sleep stages, irregular breathing, and oxygen desaturation during sleep in six patients with right-to-left cardiac or intrapulmonary shunts and six patients with chronic bronchitis and emphysema*

	Sleep time (min)*			No of apnoeic episodes per night	Total irregular breathing (min)	Maximum fall in SaO ₂ from "awake" level (%)	No of hypoxaemic episodes† per night
Patient No	Total	Non-REM	REM				
Right-to-left shunt							
1	329	255	36	0	1	5	0
2	412	272	100	4	75	6	0
3	190	177	9	0	31	10	0
4	281	221	29	0	37	8	0
5	318	248	54	0	14	9	0
6	312	226	62	0	1	9	0
Chronic bronchitis and emphysema							
1	279	213	48	0	8	14	2
2	388	276	43	0	36	29	5
3	310	252	76	0	78	37	5
4	181	136	17	0	15	21	1
5	494	320	124	1	5	27	7
6	395	278	76	0	11	47	5

*Total sleep time: total time spent in EEG sleep 1,2,3, and 4; non-rapid eye-movement (non-REM) sleep: EEG sleep stages 2,3,and 4.
†Fall in SaO_2 10% from immediately preceding stable baseline SaO_2 during sleep.

apnoeic episodes. Hypopnoea occurred much more frequently than apnoea, and accounted for over 98% of the total number of episodes of irregular breathing in each patient. Only five apnoeic episodes were recorded in the whole study, and these were all of central type.

In the 12 patients the SaO_2 averaged 83% when they were awake and was not significantly different in the two groups. Hypoxaemia occurred much less often when they were asleep and was much less

severe in the patients with shunts. We have defined a significant hypoxaemic episode as a fall in SaO_2 greater than 10% from the immediately preceding stable baseline SaO_2 during sleep.² No such episodes were seen in the patients with shunts, whereas hypoxaemic episodes occurred in all six bronchitic patients, from once to seven times a night ($p < 0.05$; fig 1). The lowest SaO_2 during sleep was 85–65% (mean 76%) in the patients with shunts, compared with 75–30% (mean 53%) in the bronchitic patients

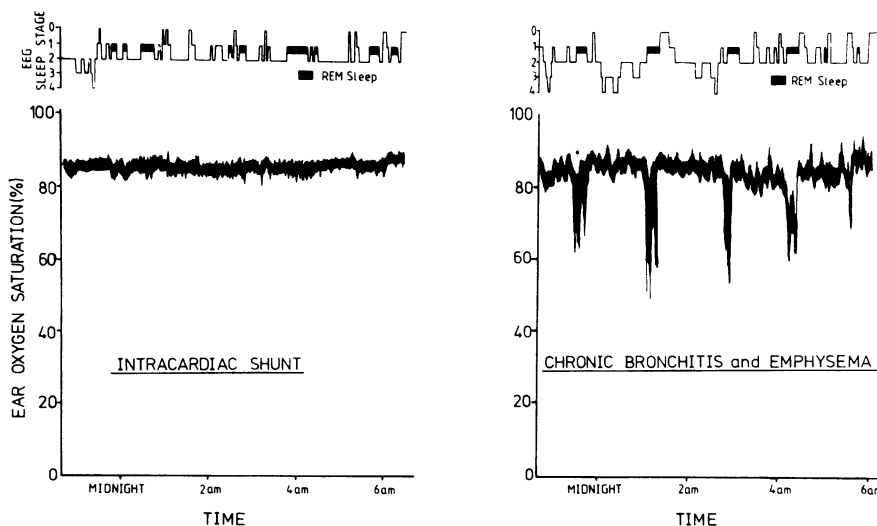


Fig 1 Oxygen saturation (SaO_2 ; earoximeter) and EEG sleep stage throughout the night in a 52-year-old man with chronic bronchitis and emphysema (right) whose SaO_2 when awake was 85% and in a 50-year-old man with right-to-left cardiac shunt (left) whose SaO_2 when awake was 87%.

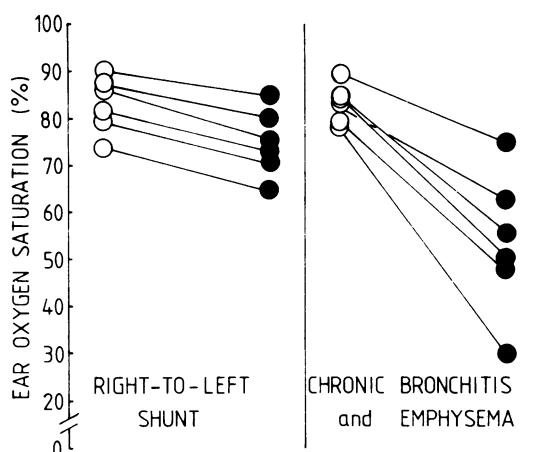


Fig 2 Oxygen saturation (ear oximeter) before sleep (○) and lowest during sleep (●) in six patients with chronic bronchitis and emphysema and six patients with right-to-left shunts.

($p < 0.02$). In the former the mean fall in SaO_2 from the "awake" level to the lowest level during sleep was 8% (5–10%), much less than the mean fall of 29% (14–47%) in the bronchitic patients ($p < 0.01$, fig 2).

Of the 27 hypoxaemic episodes in the bronchitic patients, 24 occurred in REM sleep and three during EEG sleep stage 2. Chest wall movement was reduced in all 27 episodes, and hypopnoea (as defined above) occurred in 24 of these 27 hypoxaemic episodes.

Discussion

We have found that patients with daytime hypoxaemia due to right-to-left cardiovascular shunts maintain a higher level of arterial oxygenation during sleep than do patients with chronic bronchitis and emphysema, despite similar degrees of daytime hypoxaemia. Thus the arterial oxygen tension during wakefulness is not the only factor which determines the severity of any nocturnal hypoxaemia.^{4 14}

None of the patients had a sleep apnoea syndrome as defined by Guilleminault.¹⁹ Hypoxaemia may occur during sleep in patients who do not have sleep apnoea, and although the exact mechanism is still debated hypoventilation seems to be the major factor.¹⁴ Such hypoventilation usually occurs repeatedly during REM sleep and is also seen in healthy people.^{14 20 21} In 24 (89%) of the 27 hypoxaemic episodes in the bronchitic patients the breathing pattern met our strict criteria for hypopnoea. The patients with shunts, although younger than the

bronchitics,²¹ showed hypopnoea of similar duration and severity. The breathing patterns in the two groups were indistinguishable, but the effect on alveolar ventilation could be quantitatively different in the two groups because of their different ventilatory mechanics; and indeed the patients with shunts showed little fall in oxygen saturation during the periods of hypopnoea. This probably arose because only part of the right ventricular output in patients with right-to-left shunts is exposed to alveolar gas, and any change in alveolar oxygen tension (which would fall in hypoventilation) affects only that blood which passes through the pulmonary capillaries. Furthermore, the blood which does leave the pulmonary capillary bed in these patients is normally well oxygenated and therefore lies on the flat part of the oxyhaemoglobin dissociation curve, where any change in oxygen tension produces only a small change in the oxygen content of the blood. Thus in patients with right-to-left shunts nocturnal hypoventilation will have relatively little effect on the oxygen content or saturation of systemic arterial blood. In patients with chronic bronchitis and emphysema, on the other hand, daytime hypoxia is due to impaired gas exchange, different alveoli having a wide range of \dot{V}/\dot{Q} ratios. Nocturnal hypoventilation in these patients causes a fall in arterial oxygen tension which is similar to that seen in normal subjects¹⁴ but their fall in oxygen saturation during REM sleep is much greater than in normal people because many of the alveoli start the night on the steeper part of the oxyhaemoglobin dissociation curve.

The age difference between the two groups has to be considered as a possible cause for the differences in nocturnal oxygenation.²¹ This is unlikely to be a major factor, however, as the duration of irregular breathing during sleep was the same in both groups.

It has been suggested that nocturnal hypoxaemia may provide a stimulus to development of secondary polycythaemia and pulmonary hypertension.^{2 12 13} We have, however, observed greater nocturnal hypoxaemia in patients with chronic bronchitis and emphysema, who may have less secondary polycythaemia than patients with shunts,²² although this latter suggestion has been challenged.²³ Our results do not suggest a major effect resulting from nocturnal hypoxaemia as in our study the packed cell volumes of the patients with shunts were not significantly different from those of the patients with bronchitis.

Non-invasive studies of oxygenation and breathing during sleep are being used increasingly for the assessment of patients being considered for domiciliary oxygen treatment and for those who pose diagnostic problems. This study suggests that the level of oxygenation while a patient is asleep

cannot be predicted from the oxygen tension when he is awake unless the cause of the arterial hypoxaemia is known. Furthermore, although sleep studies are not recommended as a diagnostic test for right-to-left shunts, we suggest that if a patient who is appreciably hypoxic when awake fails to show further desaturation during sleep then possibly a right-to-left cardiac or intrapulmonary shunt should be borne in mind.

We thank Dr D de Bono and Dr HC Miller for allowing us to study patients under their care. We also thank Mrs C Hoy and Mrs M Miller for their technical assistance.

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