Respiration during sleep in kyphoscoliosis

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ABSTRACT Eleven subjects with non-paralytic and 10 with paralytic kyphoscoliosis and nine normal control subjects were studied during sleep. The Cobb angle of those with kyphoscoliosis varied from 60° to 140° (median 100°) and the vital capacity varied from 17% to 56% (median 28%) of the value predicted on the basis of span. Recordings made during sleep included expired carbon dioxide tension at the nose, gas flow at the mouth, arterial oxygen saturation, chest wall movement, and the electroencephalogram, electro-oculogram, and electrocardiogram. In three subjects transcutaneous carbon dioxide tension was measured simultaneously. Patients with kyphoscoliosis hypoventilated during sleep, particularly in rapid eye movement sleep, resulting in a rise in end tidal and transcutaneous carbon dioxide tension, and a reduction in oxygen saturation to a degree not observed in normal subjects. Reduced chest wall movement was the major cause of these episodes, which were more frequent and occupied a greater proportion of sleep time in those with kyphoscoliosis than in normal subjects. Serious cardiac arrhythmias were rarely associated. It is concluded that disturbances of respiration during sleep occur in patients with kyphoscoliosis and that these may be important in the pathogenesis of cardiorespiratory failure.

Severe kyphoscoliosis may lead to cardiorespiratory failure and premature death.¹ Factors contributing to the onset of respiratory failure are thought to include reduced surface area for diffusion, ventilation-perfusion inequality, alveolar hypoventilation, increased respiratory work, and an abnormal increase in pulmonary artery pressure during exercise.^{2,3} Recent work by Mezon *et al*⁴ and Guilleminault *et al*⁵ has suggested that sleep related disturbances of respiration may also contribute. Discrepancies between their findings, which were based on only a few subjects, prompted this larger study to identify the major abnormality and mechanism of disturbances of respiration during sleep in patients with kyphoscoliosis, to distinguish any differences between non-paralysed and paralysed subjects, and to try to assess the importance of these abnormalities in the pathogenesis of cor pulmonale.

Methods

Patients with thoracic kyphoscoliosis were selected if they had a forced vital capacity (FVC) less than 30% predicted on the basis of span, or gave a history of

sleep disturbance or early morning headache for which no non-respiratory cause could be found. None had had an episode of illness of any type during the preceding month. Control subjects were within five years of age of at least one patient of the same sex, although there were no controls for the patients below 20 years of age. None had a history of chest disease, sleep disturbance, recent upper respiratory tract infection, or rhinitis, but those with a history of occasional snoring were accepted. Ethical approval was obtained from the ethics committee of Brompton Hospital and verbal agreement to participate was obtained from each subject after the nature of the study had been explained.

A full history was taken and physical examination carried out on those with scoliosis. Clinical details are presented in table 1. Only treatment with bronchodilators or diuretics was continued during the study, nebulised salbutamol (2.5-5 mg) being substituted for any other inhaled aerosol in those using a bronchodilator. The mechanical nocturnal respiratory support (negative pressure ventilation with a cuirass) used by three patients was discontinued during the two nights of the study.

The Cobb angle⁶ and angle of kyphosis⁷ were measured from the most recent spinal radiographs. FEV₁ and FVC were measured in all patients with a dry rolling seal spirometer, and measurements were re-

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Table 1 *Anthropometric and clinical details of subjects studied*

Group	Sex (F:M)	Age (y, median (range))	Weight (kg, median (range))	Aetiology of curve	Age when curve first noticed (y, median)	Cobb angle (degrees, median (range))	Smoking history
Control	6:3	37 (30-53)	60.5 (52.7-79)				3 never 4 ex 2 current
Non-paralytic kyphoscoliosis	8:3	36 (11-57)	47.5 (16.3-60)	Congenital 4 Idiopathic 6 Other 1	0 7 6	91 (72-134)	7 never 3 ex 1 current
Paralytic kyphoscoliosis	5:5	36 (12-50)	36 (20.5-49)	Poliomyelitis 9 Myopathy 1	6-9 0	100 (60-140)	7 never 2 ex 1 current

peated after inhalation of up to 5 mg salbutamol in those with evidence of airflow limitation. Predicted values were calculated from regression equations,⁸ span being used as an estimate of height. The haemoglobin concentration and ear lobe arterialised blood gas tensions were measured with the subject at rest and seated. In the control subjects measurements were made of haemoglobin concentration, arterialised ear lobe blood gas tensions at rest, and spirometric volumes.

Studies during sleep were carried out in a quiet darkened cubicle on two successive nights but recordings were made only on the second night; an eight channel Seimens Mingograph pen recorder was used, with a paper speed of 1 cm/s. A skilled observer was present throughout. The electroencephalogram (EEG) and electro-oculogram (EOG) were recorded and sleep was staged over minute epochs on the basis of the EEG and EOG criteria of Rechtschaffen and Kales.⁹ Sleep was divided into non-rapid eye movement (NREM), comprising stages 2-4, and rapid eye movement (REM) sleep.

The arterial oxygen saturation (Sao_2) was recorded with a Hewlett Packard 47201A ear oximeter. Nasal expired gas was sampled with a probe in the centre of the stream and end tidal carbon dioxide tension was measured with a mass spectrometer (200 MGA, TC Centronic Ltd). The validity of this measurement and its use as an independent index of gas flow have been reported elsewhere.^{10,11} Simultaneous measurements of transcutaneous carbon dioxide tensions were made in one control and in one subject with non-paralytic and one with paralytic kyphoscoliosis with a Hewlett Packard 47210A capnometer and skin piece. Gas flow at the mouth was recorded with a bead thermistor.

Chest wall motion was recorded with two pairs of magnetometers to obtain anteroposterior diameters with one pair placed at the level of the nipples and the second pair above the umbilicus in the midline.¹² The positions were varied slightly in individual kyphoscoliotic subjects to record maximal movement. The

heart rate and rhythm were recorded by means of standard bipolar leads.

DATA ANALYSIS

The Sao_2 was read from the continuous record as instantaneous values at minute intervals throughout the night; minimum values reached during waking and NREM, and REM sleep were noted. A mean value for oxygen saturation with the subject awake was calculated for a minimum of 10 minutes before the onset of stage 1 sleep, the subject having been lying supine for at least one hour. Mean values of Sao_2 were also calculated for all periods of NREM and REM sleep.

Values of end tidal carbon dioxide tension (PetCO_2) were selected over one minute periods every 15 minutes throughout the night except during REM sleep, when the record was sampled at five minute intervals. All breaths during the period were noted, provided that the expired trace reached a plateau lasting 0.5 seconds or more during nasal breathing. Breaths in which such a plateau could not be identified were excluded from analysis. The peak expired carbon dioxide tension was considered to be the end tidal value, and the mean of all breaths over the minute period was recorded. Values of transcutaneous carbon dioxide tension (PrCCO_2) were read from the trace at minute intervals.

All records were examined for respiratory irregularities (apnoea or hypopnoea) and for episodes of desaturation of 4% or more during non-REM and REM sleep. A period of apnoea was defined as cessation of gas flow at nose or mouth for 10 seconds or more, and its character, either central or obstructive,¹³ was noted. Episodes of hypopnoea were defined as a reduction in gas flow at the nose and mouth. Hypopnoea without evidence of upper airway obstruction was associated with a 50% or greater reduction in movement of either pair of magnetometers with a coincident reduction of 25% or more from the other pair, the preceding baseline having been established during a minimum of 10 seconds. The duration

Table 2 Respiratory function and sleep time of subjects (values are medians with ranges in parentheses)

Group	FVC (ml)	FVC (% predicted)	Pao ₂ (kPa)	Paco ₂ (kPa)	TST (min)	REM time/TST (%)
Control	4590 (3430–5890)	115 (97–123)	13.7 (10.8–14.6)	4.6 (4.1–5.1)	264 (154–348)	21 (5–24)
Non-paralytic kyphoscoliosis	910 (530–1620)	28 (20–45)	9.9 (7.9–12.9)	5.2 (4.7–6.7)	293 (205–402)	23 (15–29)
Paralytic kyphoscoliosis	770 (440–1610)	27 (17–56)	9.4 (7.0–12.9)	6.0 (4.5–8.4)	209 (107–370)	22 (0–30)

FVC—forced vital capacity; Pao₂—arterial oxygen tension; Paco₂—arterial carbon dioxide tension; TST—total sleep time.

of each episode was noted, as was the degree of desaturation produced. The frequency of episodes of hypopnoea during total sleep time and the total time thus occupied, expressed as a percentage of sleep time, were calculated.

Statistical differences were determined by the Wilcoxon signed rank test; the Kruskal-Wallis one way analysis of variance by ranks, which was used to compare data between the three groups; and the Mann-Witney U test to determine differences between two independent groups. Correlations were tested with the Spearman rank correlation test.

Results

We studied 30 subjects—nine controls and 11 with non-paralytic and 10 with paralytic kyphoscoliosis. Clinical, anthropometric, and lung function data are shown in tables 1 and 2. Two normal subjects exceeded the ideal weight for height,¹⁴ and the weight of one asthenic subject was not recorded.

With span as an estimate of height, all but two patients with non-paralytic kyphoscoliosis were below the standard weight for height.¹⁴ The FEV₁/FVC ratio was reduced in two with mild asthma and in one who smoked; all had a demonstrable response to salbutamol inhalation. All the patients with paralytic kyphoscoliosis were below the ideal weight for height based on span. Two subjects had a reduced FEV₁/FVC ratio, but only one had ever smoked, and neither showed a response to 5 mg inhaled salbutamol.

There were no significant differences in age or haemoglobin concentration between the three groups. There were significant differences between the two kyphoscoliotic groups and the controls with regard to lung function and resting arterial blood gas tensions, but no difference in these variables between the two groups of patients.

SLEEP

Total sleep time and the proportion of REM sleep time were similar in the three groups (table 2). EEG and EOG recordings could not be carried out on one

non-paralytic and three paralytic subjects, and sleep was therefore staged by observation of behavioural patterns. The onset of NREM sleep was recorded when the patient appeared to be sleeping, with no eye movements and regular respiration. REM sleep was recorded when sleep continued but rapid eye movements occurred and breathing became irregular. Since the results of these patients were similar to those of the rest of the group, their data have been included.

ARTERIAL OXYGEN SATURATION

The mean arterial oxygen saturation was lower in kyphoscoliotic than in control subjects during wakefulness. There was little change during sleep in the control group, except in one man who snored; whereas mean saturation fell in kyphoscoliotic subjects during each stage of sleep (fig 1). More strikingly, minimum arterial oxygen saturation fell in the two groups of patients, particularly during REM sleep, to a median value of 71%, and to 50% or less in four patients.

The degree of nocturnal desaturation was related to the waking saturation in both groups of patients, with correlation coefficients between mean nocturnal and waking saturation of 0.80 for the non-paralytic and 0.733 for the paralytic group. There was no relationship between the severity of the nocturnal disturbances and the Cobb angle in either group of patients; but desaturation during sleep was more prominent in the older non-paralytic patients ($r_s = 0.743$), and in those paralytic patients who had the greatest reduction in vital capacity ($r_s = 0.813$).

END TIDAL CARBON DIOXIDE TENSION

The mean end tidal carbon dioxide during wakefulness was higher in those with paralytic kyphoscoliosis than in controls. It rose significantly from waking to NREM sleep, and the increment was similar in all three groups. A further increase in mean PetCO₂ was seen during REM sleep in kyphoscoliotic subjects only (fig 2) with no difference between the two groups of patients. Similar changes were observed in maximum PetCO₂. Figures recorded in REM sleep were related to waking values in both groups of

Fig 1 Mean arterial oxygen saturation with subjects awake and during non-REM (NREM) and REM sleep (*p* values refer to differences from control subjects).

patients ($r_s = 0.738$, $p < 0.025$; $r_s = 0.670$, $p < 0.05$).

RESPIRATORY PATTERN

The frequencies of periods of apnoea, hypopnoea and desaturation are shown in figure 3. Episodes of apnoea were uncommon, brief (not exceeding 16 seconds), and central in character in all but one male control subject, in whom they were obstructive. There were no significant differences between the three groups.

Episodes of hypopnoea occurred in all subjects, but were more common among the patients. In all but one control subject, in whom hypopnoea due to partial obstruction of the upper airway was predominant, all

were due exclusively to reduced chest wall movement. The two youngest patients with kyphoscoliosis had the lowest frequencies of episodes of hypopnoea.

The total duration of all episodes of hypopnoea expressed as a proportion of time spent in each sleep stage (fig 4), was greater in REM than NREM sleep.

In both groups of patients episodes of desaturation were caused primarily by periods of hypopnoea. The other episodes were generally associated with a reduction or change in chest wall movement that did not meet the criteria for hypopnoea. No more than three episodes of desaturation a night in three patients with non-paralytic kyphoscoliosis could not be accounted for by any of these mechanisms.

Fig 2 Mean end tidal carbon dioxide tension recorded with subjects awake and during non-REM (NREM) and REM sleep.

Fig 3 Number of episodes of apnoea, hypopnoea and desaturation per hour of sleep.

In two patients with previous poliomyelitis the surface EMG of the sternomastoid muscle was recorded.

Cyclical activity of this muscle related to inspiration occurred during waking. The electrical activity was reduced during sleep but the reduction was greatest during periods of reduced chest wall movement, particularly in REM sleep (fig 5).

CARDIAC ARRHYTHMIAS

The only serious arrhythmia occurred in one patient who had brief episodes of second degree heart block related to falls in Sao_2 to 66% and 44% in both NREM and REM sleep. Periods of relative bradycardia and tachycardia related to hypopnoea and desaturation occurred, but were no more striking in patients with the most severe hypopnoea and desaturation. Similar variations in heart rate were often induced by movement during sleep.

Discussion

Some of the results of the present study are similar to those of Mezon *et al*⁴ and Guilleminault *et al*⁵ in that oxygen saturation fell in patients with kyphoscoliosis during sleep. The magnitude of the fall in our study was related to waking oxygen saturation, as observed in patients with chronic airflow limitation.¹⁵

Contrary to the report by Guilleminault *et al*,⁵ however, we found no evidence of obstructive or mixed apnoea. This could be because the patients reported by Guilleminault *et al*⁵ were heavier (57–71 kg), a considerable number had systemic

Fig 4 Proportions of time occupied by episodes of hypopnoea, expressed as a percentage of non-REM (NREM) and REM sleep time in three groups of subjects (p values refer to differences between REM and non-REM sleep).

Fig 5 Polygraphic record of an episode of hypopnoea during REM sleep in a patient with paralytic kyphoscoliosis, showing simultaneous reduction in surface electromyographic (EMG) activity of the sternomastoid muscle. ECG—electrocardiogram, EOG—electro-oculogram.

hypertension, and obstructive sleep apnoea had been suspected in one patient because his physical deterioration was thought to be disproportionate to the thoracic deformity. Obesity and systemic hypertension are known to be associated with disordered breathing during sleep.^{16 17} The body weight of the patients reported here was much lower. The ideal weight for height in patients with kyphoscoliosis is difficult to determine. On the basis of true height ideal weight

would tend to be underestimated, while on the basis of span it would probably be overestimated. So far as could be ascertained, however, the kyphoscoliotic subjects reported here were not overweight.

A few patients had evidence of airflow limitation although in most cases this was very mild, and they were studied after treatment with inhaled bronchodilator to achieve maximal improvement. Airflow limitation is therefore unlikely to have influenced the

Fig 6 Recording of transcutaneous and end tidal carbon dioxide tension (PCO_2) and arterial oxygen saturation (SaO_2) during sleep in a subject with non-paralytic kyphoscoliosis. W—waking; N—non-REM; R—REM.

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findings during sleep. Changes in arterial carbon dioxide tension are difficult to record non-invasively. Respiration is irregular during REM sleep and a steady state is not achieved, making measurement of end tidal carbon dioxide tension less accurate than usual. In the absence of intrinsic pulmonary disease, however, changes in end tidal carbon dioxide tension during sleep follow those in arterial carbon dioxide tension,¹⁰ and are also reflected in transcutaneous carbon dioxide tension when the two methods are used simultaneously (fig 6). In some cases it was impossible to measure end tidal carbon dioxide tension because with a rapid respiratory rate or low tidal volume a true end tidal plateau was not observed.

Both subjectively and objectively, sleep times were short. Sleep time in the three groups was, however, reduced to a similar degree and, as most subjects had some non-REM and some REM sleep, the findings are probably representative of the usual sleep patterns; but they may underestimate the severity of the abnormalities.

Hypoventilation, manifest particularly by episodic hypopnoea in REM sleep, was the most important abnormality occurring during sleep in our patients. Among the normal subjects there were significant increases in both maximum and mean end tidal carbon dioxide tension between waking and non-REM sleep, with no further increase in REM sleep. The increase in mean P_{etCO_2} between waking and non-REM sleep was similar in the three groups, suggesting that the reduction in ventilation induced by the onset of sleep in the patients was no greater than normal. This contrasts with the findings in REM sleep, where a further increase in P_{etCO_2} was seen only in those with kyphoscoliosis.

A reduction in inspiratory muscle activity, particularly in relation to phasic REM sleep, is the most likely explanation for the episodes of hypopnoea and was demonstrated in two patients by recording the sternomastoid surface EMG. The diaphragm is at a considerable mechanical disadvantage in kyphoscoliosis and in the paralytic patients it may also be weak. They are therefore likely to be more than usually dependent on accessory muscle activity to maintain ventilation and these muscles are less active in REM sleep.¹⁸ Similar observations have been made on accessory muscle function during sleep in patients with chronic airflow limitation.¹⁹

Lopes *et al*,²⁰ measuring transdiaphragmatic pressure during sleep in normal adults and recording surface EMG, showed that diaphragm activity in REM sleep was increased to maintain the same transdiaphragmatic pressure, because of the impaired efficiency of the muscle when intercostal activity is substantially reduced. In kyphoscoliosis it may not be possible to generate an increase in diaphragm activity

under these circumstances, perhaps because of fatigue or weakness. This too would lead to hypoventilation.

Episodic hypopnoea during sleep will have two consequences: hypoxaemia and hypercapnia—and, possibly, changes in ventilation-perfusion ($\dot{V}/\dot{Q}$) matching caused by small airway closure, leading to an even greater fall in arterial oxygen tension. Hypoxaemia and hypercapnia increase pulmonary arterial pressure and, by analogy with patients with chronic airflow limitation or sleep apnoea syndromes,^{21 22} could contribute to the development of pulmonary hypertension in kyphoscoliosis. Both hypoxia and hypercapnia also impair respiratory muscle function.^{23 24} Thus nocturnal hypoventilation could reduce muscle strength and increase fatiguability, so perpetuating the abnormalities throughout the day.

Hypercapnia during sleep in these patients has important therapeutic implications. Correction of hypoxaemia with oxygen treatment alone could increase the magnitude of the rise in carbon dioxide tension, and this would need to be assessed by nocturnal recording of oxygen saturation and transcutaneous carbon dioxide tensions. Patients with a substantial increase in transcutaneous carbon dioxide during sleep are more appropriately treated with nocturnal mechanical ventilation, because this overcomes the primary defect of hypoventilation.²⁵

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