

CASE REPORT

Elimination of central sleep apnoea by mitral valvuloplasty: the role of feedback delay in periodic breathing

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Central sleep apnoea is a form of periodic breathing which resembles Cheyne-Stokes respiration but occurs only during sleep. One mechanism in the pathogenesis is a delay in chemical feedback from the lungs to the medullary respiratory centre. We explored the relationship between circulatory feedback delay in a patient with central sleep apnoea and Cheyne-Stokes respiration before and after mitral valve repair. Preoperatively the patient had severe central sleep apnoea and an increased circulation time. Following mitral valvuloplasty the circulation time was decreased with resolution of central sleep apnoea. This case demonstrates the role of feedback delay in central sleep apnoea and suggests that similar haemodynamic mechanisms may lead to central sleep apnoea and Cheyne-Stokes respiration.

Periodic breathing was first associated with severe heart failure by Stokes in the early 19th century.¹ Subsequent investigators suggested that a delay in chemical feedback to the medullary respiratory centre was a major cause for the pattern of periodic breathing now known as Cheyne-Stokes respiration.^{2,3} Central sleep apnoea is characterised by respiration that starts and stops abruptly without significant variability in its frequency and depth,⁴ while Cheyne-Stokes respiration is characterised by a sinusoidal pattern in the frequency and depth of respiration.⁵ The mechanism of central sleep apnoea may be similar to that of Cheyne-Stokes respiration and be caused by a delay in chemical feedback to the medullary respiratory centre.⁴ This report describes a patient with central sleep apnoea, mitral regurgitation with reduced cardiac index, and a markedly prolonged arm to tongue circulation time that was corrected by mitral valvuloplasty.

CASE REPORT

A 64 year old man in whom a heart murmur had been noted since the age of 19 remained well until the age of 63 when he complained of progressive dyspnoea on exertion, fatigue, sleepiness, and weight loss. On physical examination the patient's height was 175 cm and his weight was 63 kg. His blood pressure was 160/80 mm Hg with an irregular pulse of 84 per minute and regular respirations of 18 per minute. A precordial heave was noted and a grade 3/6 systolic murmur was heard at the apex with radiation to the axilla.

Laboratory data included an electrocardiogram which demonstrated atrial fibrillation and left ventricular hypertrophy. Cardiomegaly was evident on chest radiography. Two dimensional echocardiography revealed a thickened mitral valve (0.8 cm) and a flail anterior mitral leaflet. The left atrium was markedly enlarged with a diameter of 7 cm. The left ventricle was thick (1.5 cm) and moderately dilated (6.5 cm) with rapid early diastolic filling and a fractional shortening of 32–47%. Cardiac catheterisation showed

normal coronary arteries and confirmed gross mitral regurgitation with reflux of dye into the pulmonary veins and increased pulmonary capillary wedge pressure (V waves = 40 mm Hg, mean PA pressure = 20 mm Hg). A sleep study was performed using standard techniques as previously described.⁶ The patient had recurrent apnoea and hypopnoeas (apnoea/hypopnoea index (AHI)) at a rate of 54 per hour with a mean event duration of 30 (9) seconds (table 1); 61% of the events were central, 29% were mixed, and 10% were obstructive (fig 1). Mean baseline oxyhaemoglobin saturation was 98% and fell to a mean low of 93% during events. A second full night sleep study was performed with oxygen supplementation at a flow rate of 4 l/min via nasal cannulae. Central and mixed disordered breathing events were seen with a 45% reduction in AHI and a slight increase in event duration (table 1). The circulation time from the arm to the tongue was determined by injection into the right antecubital vein of 400 mg magnesium sulfate diluted to 100 mg/ml as described by Friedberg.⁷ The patient's mean (SD) arm to tongue circulation time was 50.9 (3.7) seconds which was much longer than the arm to tongue circulation time of 19.3 (1.9) seconds measured in two healthy subjects.

After mitral valvuloplasty the patient noted marked improvement in his sleep, daytime hypersomnolence, dyspnoea and fatigue, and a weight gain of 10 kg. An echocardiogram showed normal mitral valve motion and a low normal left ventricular ejection fraction (45–50%). The cardiac index by thermodilution improved from 1.4 l/min/m² immediately before the operation to 2.4 l/min/m² immediately afterwards. The mean (SD) arm to tongue circulation time decreased to 29.2 (1.7) seconds. Two months after the operation a sleep study showed complete resolution of the previously documented sleep apnoea (table 1).

DISCUSSION

This case highlights the relationship between circulation time and central sleep apnoea. Our patient had central sleep apnoea in association with increased circulation time, both of which improved after mitral valvuloplasty. The patient's response suggests that circulation time plays a major role in the pathogenesis of central sleep apnoea.

In biological systems, periodic breathing may be produced by either altered chemosensitivity of the respiratory centre (controller gain), decreased oxygen stores, or by delayed chemical feedback (CO₂ and O₂) from the blood in the lungs to the respiratory centres in the central nervous system (feedback delay).³ The circulation time is a function of both cardiac output and blood volume: circulation time = blood volume/cardiac output.⁷ With the development of mitral regurgitation in our patient, a prolonged circulation time could have been caused by both increased blood volume from atrial enlargement and reduced forward cardiac output.

Previous studies have linked periodic breathing (Cheyne-Stokes respiration) with increased circulation time in

Table 1 Sleep parameters

	Total sleep time (min)	Apnoea/hypopnoea index (AHI) (apnoeas + hypopnoeas/h sleep)*			Apnoea duration (s)	Baseline SaO ₂ (%)†	Mean low SaO ₂ (%)‡
		Central	Mixed	Obstructed			
Study 1: baseline	228	34	15	5	30 (9)	98 (1.6)	93 (1.8)
Study 2: breathing O ₂	157	8	15	7	34 (9)	98 (1.0)	96 (1.9)
Study 3: after mitral valvuloplasty	273	0	0	0	–	96	

*Non-REM sleep.

†Initial baseline value only.

‡Minimum SaO₂ in the absence of apnoea.

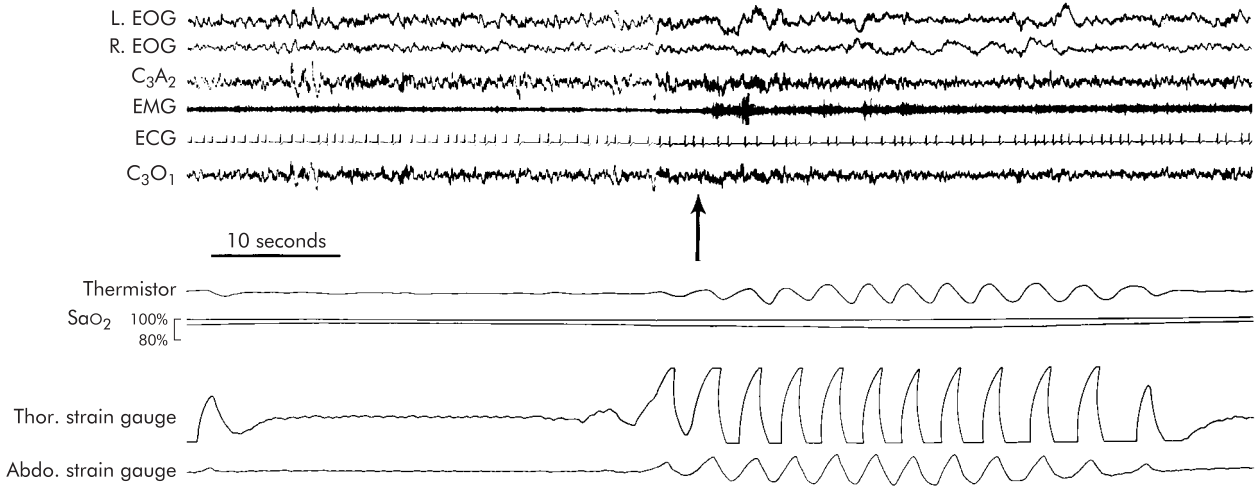


Figure 1 A 35 second central apnoea followed by an arousal (arrow) and a 37 second ventilatory phase. The prolonged circulation time is reflected in the fall in oxyhaemoglobin saturation persisting long after the onset of breathing. The artefact in the thoracic tracing is caused by the patient's hyperdynamic precordium.

patients with congestive heart failure.^{2, 8} In fact, clinical data have indicated similar prolongation of circulation time (30–54 seconds) in patients with congestive heart failure and Cheyne-Stokes respiration to that observed in our patient preoperatively. Periodic breathing can be induced by lengthening the circulation time in animals.³ In patients with congestive heart failure and Cheyne-Stokes respiration, cycle lengths were observed that were twice the lung to brain circulation time.⁸ Our patient had a similar 2:1 ratio with a cycle length of 70 seconds and a lung to artery circulation time of approximately 36 seconds (estimating a vein to lung time of 15 seconds in severe congestive heart failure from the data of Pryor² and of Lange and Hecht⁸). Following correction of our patient's severe mitral regurgitation, the circulation time decreased markedly and periodic breathing during sleep resolved completely.

In addition to feedback delay, periodic breathing may also be caused by altered respiratory centre chemosensitivity (controller gain). For a given circulation time, an increase in the chemosensitivity of the respiratory control centres results in an increase in the tendency for breathing to oscillate.⁵ Although we did not measure oxygen chemosensitivity, previous studies have shown that supplemental oxygen decreases central sleep apnoea by decreasing the controller gain of the respiratory centre.^{9–11} Our finding that the apnoea/hypopnoea index decreased markedly on oxygen is consistent with the notion that a concomitant increase in controller gain also has a role in the pathogenesis of periodic breathing. Nevertheless, improvement in hypoxia while the circulation time remained prolonged did not eliminate sleep apnoea, which suggests that a prolonged circulation time

played a major role in the pathogenesis of sleep apnoea in our patient.

This case report demonstrates the elimination of central sleep apnoea by a reduction in circulation time from markedly prolonged levels to near normal levels following surgical correction of severe mitral regurgitation. It highlights the similarity between the mechanism of central sleep apnoea and that of Cheyne-Stokes respiration. Our findings suggest that central sleep apnoea may be responsible for the sleep complaints in patients with congestive heart failure, including paroxysmal nocturnal dyspnoea.¹²

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