REVIEW

Impact of heart failure on quality of sleep

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Chronic heart failure is an important health problem associated with a high mortality and morbidity. Appropriate treatment reduces mortality and leads to improved exercise tolerance but many patients report poor quality of sleep. Sleep studies of patients with heart failure suggest that sleep disordered breathing is experienced in 50% of patients and is a powerful predictor of poor prognosis. Sleep disordered breathing broadly comprises obstructive sleep apnoea, when upper airway instability causes mechanical obstruction to breathing; and central sleep apnoea, characterised by an absence of ventilatory effort. Sleep disordered breathing occurring in patients with heart failure is in most part attributable to central sleep apnoea and reflects uncompensated instability of the ventilatory feedback mechanism.

Chronic heart failure is an important health problem. Its crude overall prevalence is 0.3%–2%¹ but in the over 65s it increases considerably to 3%–13%.² The associated high mortality and morbidity³ creates a considerable socioeconomic burden.

Clinical trials have established that pharmacological interventions can reduce symptoms, improve prognosis, and improve quality of life.^{4–5}

Prognosis has been shown to be dependent upon a range of factors including haemodynamic variables such as cardiac output and pulmonary vascular resistance,⁶ neurohumoral activity,^{7,8} and electrophysiological parameters such as spontaneous ventricular tachycardia.

Drug treatment often leads to improved exercise tolerance and reduction in fatigue and breathlessness but many patients report poor quality of sleep. Sleep studies of patients with heart failure showed that changes in either respiratory periodicity or frequency, or both, were common, being observed in about one in two patients with impairment in left ventricular function.^{9–10} Sleep disordered breathing may be reported by an observant spouse, who may be woken by a partner's reduced tidal volume or recurrent episodes of apnoea.⁹ Such abnormal breathing patterns are particularly powerful predictors of poor prognosis.^{11–12}

PATHOPHYSIOLOGY OF HEART FAILURE AND ITS RELATION WITH SLEEP

Heart failure is characterised by a decrease in cardiac output attributable to impaired cardiac function; this results in symptoms of exertional and paroxysmal nocturnal dyspnoea, fatigue, orthopnoea, and peripheral oedema.

Blood flow to any region of the body depends on perfusion pressure and resistance to flow, which is controlled by sympathetic nervous system.¹³ Short term regulation of flow is controlled by arterial baroreceptor and chemoreceptor reflexes while long term regulation depends on an interaction between various hormones and the sympathetic system.

Baroreceptors are located in the walls of the carotid sinus and aortic arch and are the terminals of afferent fibres that run in the glossopharyngeal and vagal nerves. These respond to vessel wall distension and signal changes in arterial pressure over a wide range, from about 50 mm Hg to 150 mm Hg.^{14–15}

Highly specialised chemoreceptors located in the carotid and aortic bodies are stimulated primarily by a decrease in the partial pressure of oxygen in arterial blood. The afferent arm of the reflex runs in the glossopharyngeal and vagus nerves and evokes both an increase in ventilation and sympathetically mediated vasoconstriction in various vascular beds other than the brain and the heart.

Both baroreceptor and chemoreceptor primary afferent fibres terminate in the nucleus tractus solitarius in the brain stem.

Neurally mediated increases in heart and ventilatory rate at the onset of exercise also occur as a consequence of a central command initiated from the cortex.

In long term regulation, a key element is a change in salt retention resulting in a reciprocal change in the level of circulating angiotensin 2, which, if sustained will result in a sustained change in sympathetic activity. This mechanism could be an important factor contributing to the increase in sympathetic nerve activity in conditions such as heart failure where the renin-angiotensin system is activated. Increased efferent sympathetic activity may have several adverse effects,¹⁶ including de-sensitisation and down regulation of cardiac baroreceptors.¹⁷

CONTROL OF BREATHING

Ventilatory control maintains the partial pressure of arterial oxygen (Pao₂) and carbon dioxide (Paco₂) within a narrow range, despite fluctuations in oxygen consumption, carbon dioxide production, and changes in basal metabolic rate. Such exquisite control relies on three components—sensors, a central controller, and effectors (fig 1).¹⁸

Abbreviations: OSA, obstructive sleep apnoea; CSA, central sleep apnoea; REM, rapid eye movement; NREM, non-rapid eye movement; PSG, polysomnography; CPAP, continuous positive airway pressure

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Figure 1 Control of respiration. Reprinted with permission from Waravdekar and Zwillich.¹⁸

The primary sensors comprise carotid body chemoreceptors that sense PaO_2 and hydrogen ion concentration and medullary based chemoreceptors that sense PaCO_2 and hydrogen ions. The central controller, the respiratory centre located in the brain stem, sends efferent impulses to effectors, the respiratory musculature of the diaphragm, intercostals, and abdominal muscles.

Normal respiration maintains blood gas and acid-base homeostasis within strict levels with minimal expenditure of mechanical energy. Breathing is under the control of a negative feedback system. Inputs from higher cortical centres are superimposed on this. In healthy wakeful subjects at rest, a neural feedback loop modifies the respiratory generator to produce a rhythmic ventilatory pattern termed eupnoea. Peripheral arterial chemoreceptors are sensitive to changes in arterial oxygen, carbon dioxide, and hydrogen ion concentrations, while a central chemoreceptor on the ventral surface of the medulla oblongata, in direct contact with cerebrospinal fluid, senses changes in hydrogen ion and carbon dioxide concentrations, both of which are in a buffered equilibrium with the serum.

Hypercapnia, hypoxaemia, and acidaemia stimulate ventilation in humans.

- Ventilation increases in a linear fashion with increasing carbon dioxide concentration. The apnoeic threshold is the value of PaCO_2 below which ventilation will cease at a given PaO_2 .
- Hypoxaemia has a non-linear relation because of the sigmoid shape of the oxy-haemoglobin dissociation curve,

which will permit oxygen saturation to remain well in excess of 90% until PaO_2 decreases below this.

- Acidification of the serum brings about an increase in ventilation, mediated acutely via peripheral arterial chemoreceptors.

WHAT HAPPENS IN SLEEP?

“Normal” sleep comprises two phases, non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. Several cycles of NREM and REM occur, each cycle lasting about 90 minutes¹⁹ and containing a greater proportion of REM sleep than that preceding it.

During REM sleep, the rate and variability of breathing is increased and most or all skeletal muscle tone is suppressed²⁰ because of hyper-polarisation of motor neurons²¹; this prevents muscular contraction, even though brain stem motor systems are intensely active. Arousal to respiratory stimuli, such as hypercapnia or the less potent hypoxia, is delayed in REM sleep. During non-REM sleep, however, breathing patterns are extremely regular and slow, with in particular prolonged inspiratory times. This has profound implications for clinical aspects of sleep, including sleep disordered breathing.

Periods of ventilatory instability are common during the onset of sleep even in normal subjects because the control of breathing becomes critically dependent on the chemical/metabolic control system, the result of the abolition of the waking neural drive to breathing and behavioural control systems during NREM sleep. As the subject flips from sleep to wakefulness, a ventilation surge occurs that is large enough to drive the PaCO_2 below the apnoeic threshold.²² Any disease process that exaggerates these parameters will sustain periodic breathing during sleep.

WHAT IS ABNORMAL?

Sleep disordered breathing broadly comprises obstructive sleep apnoea (OSA), when upper airway instability causes mechanical obstruction to breathing; and central sleep apnoea (CSA), characterised by an absence of ventilatory effort.

In OSA, apnoeic episodes are associated with continued respiratory effort, resulting in hypoxaemia and hypercapnia. Arousal from sleep is purposeful in so much as it leads to removal of mechanical obstruction to breathing and is disruptive to sleep architecture.

Two forms of CSA are recognised.²³ In the hypercapnic form, respiratory drive is chronically depressed with hypercapnia during wakefulness and sleep.²⁴ In the more prevalent hypocapnic form, nocturnal breathing is periodic, characterised by a regular, crescendo-decrescendo oscillation of tidal volume probably caused by dysfunction of central respiratory control. As central respiratory drive slowly fades, ventilation temporarily ceases, then resumes again; this results in an oscillation between hyperventilation²⁵ and central hypopnoea (a 50% reduction in the sum of thoraco-abdominal movements lasting 10 seconds or more followed by a decrease of >4% in peripheral oxygen saturation) or central apnoea (a reduction of more than 90% in thoraco-abdominal movement or complete cessation of ventilatory effort).

Intervals of hyperventilation separated by periods of hypopnoea are described as periodic breathing. In heart failure, disturbances in the chemical control mechanisms involved with the maintenance of blood gas and acid-base homeostasis lead to a characteristic respiratory pattern called Cheyne-Stokes respiration, when both hypopnoea and apnoea are present.¹⁰

DIAGNOSING SLEEP DISTURBED BREATHING PATTERNS

Polysomnography (PSG) is a long established method for diagnosing sleep disordered breathing and the standard Rechtschaffen and Kales (1968) criteria have proved to be a reproducible and robust tool for identification and characterisation of sleep state.

Nocturnal PSG, however, is expensive, unobtainable in a timely fashion for many patients, and labour intensive for both patient and investigator.

The US Department of Health and Human Services reported that there was “no standard for diagnosing sleep disorders” and recommended that PSG “be compared with alternative low technology approaches such as questionnaires, home monitoring...for making the initial diagnosis”.²⁶

Since then, home based monitoring systems, ranging from simple oximetry^{27 28} to limited channel portable polysomnography and “smart” continuous positive airway pressure (or CPAP) machines²⁹ with unattended monitors, an adhesive finger oximeter, and chest belts with mercury switch to indicate body position³⁰ have been shown to acceptable, albeit less sensitive, measures of sleep disordered breathing.

LIMITATIONS

When performing ambulatory sleep monitoring outside the laboratory setting, quality and integrity of data are particularly important. Scoring these “unattended” studies is made more difficult as electrode artefacts arise from oximeter disturbances caused by patient movement and unit malfunction.³¹

PREFERRED MEASUREMENT INDICES

Sleep disordered breathing, particularly OSA, has traditionally been defined according to the apnoea-hypopnoea index, calculated as the sum of apnoeic and hypopneic episodes per hour of sleep.

There is only one widely used definition of apnoea—cessation of airflow for more than 10 seconds—but the definition of hypopnoea varies widely and includes various degrees of reduction in airflow and/or thoraco-abdominal movement with an associated oxygen desaturation. This is particularly relevant when comparing studies from different centres.

PREVALENCE OF SLEEP DISTURBED BREATHING

Obstructive sleep apnoea occurs in 4% of men and 2% of women in the general population, between the ages of 30 to 60 years³² but sleep disordered breathing is much more common in patients with heart failure—40%–50% of those with chronic^{9 33} and up to 80% in acute heart failure.³⁴

PATHOGENESIS

Sleep disordered breathing occurring in patients with heart failure is in the most part attributable to central sleep apnoea^{9 12 35} and reflects uncompensated instability of the ventilatory feedback mechanism.²³ In general, feedback controls de-stabilise if their damping capacity is overridden (see below). This can occur if the information transfer is delayed or controller gain is changed.³⁶

INCREASED CONTROLLER GAIN

Increased sensitivity of the respiratory centre to carbon dioxide leads to an oscillating hypocapnia³⁷ induced by hyperventilation during sleep, with ventilation ceasing when P_{aCO_2} decreases below the apnoea threshold. The endogenous catecholamines norepinephrine (noradrenaline) and adrenaline (epinephrine) can change chemoreceptor sensitivity.³⁸

Levels of both hormones are raised in patients with heart failure, probably as a compensation for cardiac pump failure. Increased circulating concentrations of these catecholamines might increase the responsiveness of respiratory controller to carbon dioxide, leading to hyperventilation.⁴⁰

UNDER-DAMPING

The ratio of the volume of stored gas in the body to change in gas tension in the blood is known as the dampening ratio.^{22 36 41} Larger stores of carbon dioxide allow for better buffering and thus stability of arterial blood gas tensions during transient changes in ventilation. In patients with heart failure, the functional residual capacity is reduced because of pulmonary vascular congestion and thus pulmonary gas volume is decreased. As a result, total body stores of carbon dioxide and oxygen are both decreased and the respiratory system becomes much more unstable.⁴²

PROLONGED CIRCULATION TIME

In heart failure, a circulatory time delay can occur between the gas exchange occurring at the alveolar capillary membrane of the lungs and carotid body chemoreceptors.^{36 41 43} This results in delayed feedback to the medulla, causing instability of gas homeostasis and to periodic respirations.

PROGNOSIS

There is an increased incidence of hypertension,³⁰ arrhythmia, myocardial infarction,⁴⁴ and stroke,⁴⁵ so obstructive sleep apnoea is not a benign condition.^{46–48}

The development of sleep disordered breathing occurring in patients with heart failure has serious implications. The prognosis of patients is worse if congestive heart failure is associated with a sleep apnoea syndrome.⁴⁹ The prevalence of cardiac arrhythmias is higher than in patients with the same degree of heart failure who do not experience periodic breathing.^{12 33} Patients with periodic breathing are more limited and develop dyspnoea at lower workload. A survey of patients in chronic congestive heart failure with and without Cheyne-Stokes respiration showed that patients with disordered breathing had significantly worse cumulative survival and transplant free rate.¹¹

The typical symptoms of sleep disordered breathing include daytime hypersomnolence and fatigue. Repetitive arousals cause sleep fragmentation with a reduction in the amount of slow wave and REM sleep, the most refreshing sleep stages.^{50 51} It is also responsible for impaired psychomotor performance in patients with heart failure.⁵²

CHANGING THE NATURAL HISTORY

Improvement of cardiac function can improve Cheyne-Stokes respiration associated with heart failure.⁴² It is important to optimise the medical treatment of the underlying heart disease before considering specific treatment for periodic breathing,⁵³ which includes drug treatment, supplemental oxygenation, and ventilation.

Theophylline,⁵⁴ morphine derivatives, and supplementation of inhaled oxygen with 3% carbon dioxide⁵⁵ have been successfully applied under experimental conditions in small studies. Supplementing oxygen overnight with flow rates of two to three litres per minute can reduce Cheyne-Stokes respiration by half and can improve sleep architecture⁵⁶; exercise performance and cognitive function may improve although daytime symptoms may not.^{57 58} Nocturnal, non-invasive ventilation using continuous positive pressure ventilation (CPAP) for a period of one month can significantly reduce the frequency of apnoeas and hypopnoeas, increase oxygen saturation and P_{CO_2} , and normalise tidal volume during sleep.⁵⁹

CONCLUSION

Sleep disordered breathing occurs commonly in patients with heart failure but is often unrecognised, perhaps because its associated symptoms, fatigue, impaired physical performance, dismal quality of life, and cognitive impairment are attributed to heart failure. Current therapeutic approaches have focused on correction of the abnormal breathing pattern, the most readily available and most successful being CPAP and supplemental oxygen. There are no conclusive studies on long term outcome of any treatment in sleep disordered breathing.

Although pharmacological interventions have improved the outlook for millions of patients with heart failure, the prognosis for those with periodic breathing remains poor.

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