International Journal of Cardiology 206 (2016) S4–S7

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Review

Epidemiology of central sleep apnoea in heart failure

Matthew T. Naughton

General Respiratory & Sleep Medicine, The Alfred Hospital & Monash University, Melbourne, Victoria, Australia

ARTICLE INFO

Article history:
Received 15 November 2015
Received in revised form 27 January 2016
Accepted 21 February 2016
Available online 26 February 2016

Keywords:
Central and obstructive sleep apnoea

ABSTRACT

Central sleep apnoea occurs in about a third of patients with reduced systolic heart failure and is a marker of increased mortality. Such patients usually are older males with advanced heart failure (i.e., high pulmonary wedge pressure), often in atrial fibrillation, with evidence of hyperventilation (i.e., low $PaCO_2$) in the absence of hypoxemia. Characteristically, ventilation waxes and wanes in a sinusoidal pattern, with mild hypoxemia, occurring in the lighter levels of sleep usually when supine. Snoring may also occur in central sleep apnoea, often at the peak of hyperventilation, sometimes contributing to the confusion or overlap with obstructive sleep apnoea. Central sleep apnoea is associated with orthopnoea, paroxysmal nocturnal dyspnoea and an oscillatory respiratory pattern with an incremental cardiopulmonary exercise study. Importantly, heart failure therapies (e.g., afterload reduction, diuresis, pacemakers, transplantation) attenuate central sleep apnoea. Night to night variability in severity of central sleep apnoea may occur with changes in patients' posture during sleep (less severe when sleeping on-side or upright).

Contents

1. Introduction . . . S4
2. Clinical features . . . S4
3. Pathogenesis . . . S5
4. Differentiation from other breathing disorders during sleep . . . S5
5. Definition . . . S5
6. Epidemiology . . . S5
7. Mortality . . . S6
8. Compensatory theory . . . S6
9. Recognition . . . S6
10. Conclusion . . . S7
Conflict of interest . . . S7
References . . . S7

1. Introduction

Whilst dyspnoea has long been known to be a cardinal feature in the heart failure (HF) syndrome, it has only been in recent times that the patterns of breathing have been studied in depth. One particular type of dyspnoea results in an oscillatory or periodic breathing pattern during sleep, and is referred to as central sleep apnoea with Cheyne Stokes respiration (CSA-CSR). Occasionally in patients with CSA-CSR, a similar periodic breathing pattern (without apnoeas) occurs during an incremental exercise study and is referred to as exertional oscillatory ventilation (EOV).

2. Clinical features

Central sleep apnoea with Cheyne Stokes respiration is often associated with advanced heart failure as indicated by a reduced LVEF and exercise capacity (VO_2 max and 6 min walk distance) and an elevated PCWP, BNP and sympathetic nerve activity (SNA) [1]. In such patients with CSA-CSR, an elevated VE/VCO_2 slope during exercise and central and peripheral ventilatory chemoreceptor activity with hyperventilation are also observed.

During sleep, CSA-CSR is associated with a prevailing hyperventilation and hypocapnia, triggered by an arousal or state change. The oscillatory pattern continues for at least 3 cycles and periods of greater than 10 min [2]. Characteristically it is observed during the transition from wake to nonREM sleep stages 1 and 2, worse when supine and alleviated when non-supine [3] or when the head of the bed is raised [4].

E-mail address: m.naughton@alfred.org.au.

http://dx.doi.org/10.1016/j.ijcard.2016.02.125
0167-5273/

The ventilation pattern in patients with CSA-CSR usually normalizes during slow wave sleep and REM sleep.

Patients with CSA-CSR complain of fatigue, insomnia and occasionally orthopnoea with paroxysmal nocturnal dyspnoea. The bed partner often observes apnoeas during their partner's sleep, sometimes with snoring during the peak of hyperventilation. The risk factors which should alert clinicians to the possibility of CSA-CSR are age ≥60 years, male gender, atrial fibrillation and low $PaCO_2$ [5] in patients with unstable HF. CSA-CSR is relieved by improving the underlying cardiac function (pump, rhythm and valves) through medications, devices (pacemakers, left ventricular assist device), surgery (valve repair & transplantation) or correction of co-existent medical problems such as anaemia or OSA.

3. Pathogenesis

Studies into the pathogenesis of CSA-CSR have suggested the following mechanisms: an elevated respiratory drive (due to increased SNA or increase pulmonary vagal afferent activity) [6,7], reduced lung function (i.e., reduced volume and impaired diffusing capacity [8,9]) and a delay in the chemical signal ($PaCO_2$) required to stimulate ventilation reaching the brain from the heart (i.e., due to low cardiac output). The periodic breathing pattern relates to the prevailing $PaCO_2$ level oscillating above and below the apnoea threshold [6].

The mean SNA (plasma and urine norepinephrine) is higher in the CSA-CSR patient group than in groups with HF and no sleep apnoea [10]. Initially, it was thought that recurring arousals and hypoxemia due to CSA-CSR were responsible for the elevated SNA. However, detailed multivariate analyses indicate that the severity of HF is a more important factor responsible for the elevated SNA than is the severity of CSA (i.e., the AHI) [11]. In addition, CSA-CSR is not always associated with hypoxemia, a potent stimulus for elevated SNA. Moreover, patients without CSA-CSR frequently have arousals (due to periodic limb movements) without necessarily having high SNA. Of note beta blockers do not appear to have altered the prevalence of CSA-CSR [12,13]. Although increased vagal activity is an additional proposed mechanism supported by the elevated PCWP [14], vagally denervated patients (due to lung transplantation) still have CSA-CSR [15].

4. Differentiation from other breathing disorders during sleep

The CSA-CSR breathing disturbance should be distinguished from two other common breathing disorders during sleep. The first breathing disorder is snoring with obstructive sleep apnoea which is thought to contribute to difficult to control hypertension [16] and heart failure [17] via large negative intrathoracic pressures, swings in oxygenation and associated surges in systemic and pulmonary pressures during the supposedly "restful" and recuperative period of sleep. Upper airway collapse at the base of the tongue occurs often in the setting of obesity or craniofacial abnormalities. The second breathing disorder is central apnoea with hypoventilation and elevated $PaCO_2$ due to conditions such as kyphoscoliosis, motor neurone disease or morbid obesity.

5. Definition

CSA-CSR is defined by a frequency of apnoeas or hypopnoeas (complete or partial reductions in tidal volume) per hour sleep occurring in a cyclic nature for >3 cycles and >10 min duration, from which the apnoea hypopnoea index (AHI) is derived [1]. A less commonly used metric of CSA-CSR is the % of sleep time in which CSA-CSR occurs [1]. A third metric, recently found to be indicative of treatment response is loop gain, defined as a ratio of the response (apnoea) to the trigger (hyperpnoea) [18]. Typically the apnoea and hyperpnoea cycle length is 45–75 s in patients with advanced HF. If a shorter (<45 s) cycle length is observed, non-HF causes for CSA should be considered such as atrial fibrillation with otherwise normal cardiac function [19], stroke [20], narcotic ingestion [21], premature infancy [22] and high altitude [23].

Although the "AHI" definition of CSA-CSR that is commonly used in research papers and epidemiological studies appears straight forward, it is open to some parochial interpretation and variation for several reasons.

First is that the threshold of significant CSA-CSR used by various investigators varies from ≥5 to ≥30 events per hour.

Second, the AHI is a ratio of the numbers of apnoeas and hyopnoeas per hour sleep, where the denominator of the AHI should be the number of hours sleep. Sleep duration is measured by using polysomnography (monitoring of sleep [EEG, EOG and EMG], ventilation and ECG) in either an attended or unattended environment. However several research groups use polygraphy (monitoring of ventilation and ECG, i.e., not sleep) and use "recording time" as the denominator. Given that the average sleep efficiency (sleep time/recording time) of patients with HF is ~70% [6], the AHI based upon recoding time may underestimate the AHI based upon sleep time by ~25%.

Third, although in the research studies that recorded sleep duration, it is well recognised that patients with HF have poor quality sleep characterised by fragmentation with brief (<15 s) periods of sleep, making precise sleep scoring for quality and duration with standard measures [24] difficult resulting in potential variation from one centre to another. The R + K criteria were based upon normal subjects in 1960s.

Fourth, the definition of apnoea or hypopnoea is also dependent upon the method of assessing ventilation (pressure, temperature or pneumotachograph) and whether this measurement is of the nasal, oral or oronasal flow. Measurements of pressure and temperature change, as markers of ventilation are non-linear measurements of flow. Accordingly, a 25% reduction in either nasal pressure or oronasal thermistor does not translate to a 25% reduction in ventilation. By convention, an apnoea is when ventilation is <10% and hypopnoeas <50% of preceding normal airflow flow lasting >10 s and associated with either an arousal or a drop in SpO_2 of ≥3%. Nasal ventilation may cease or be overwhelmed by oral flow in cases of nasal obstruction or hyperventilation. The effect of using only nasal pressure as the single monitoring signal of ventilation may over estimate obstructive sleep apnoea. The oximeter averaging time and storage capacity can also influence the sensitivity of SpO_2 readings.

Fifth, the exact categorization into "obstructive" (where there is complete or partial reduction in ventilation with incremental respiratory effort) or "central" apnoea groups can be difficult to measure without accurate measures of respiratory effort (e.g., intrathoracic pressure) and total flow (i.e., with an oronasal pneumotachograph). Moreover, the type of apnoea may vary across the night from obstructive to central [25] and alter with changes in body position (rotation, head elevation and neck flexion).

Finally, the severity (AHI) and type of apnoea (Obstructive vs CSA-CSR) may vary from night to night depending upon HF control, nasal resistance and various factors that can alter respiratory control (blood glucose level, thyroid status, medications [progesterone, aminophylline, narcotics] and social drugs [alcohol, cigarettes]).

6. Epidemiology

The Sleep Heart Health Study was a longitudinal study of 6441 community dwellers, aged >40 years in USA who had an unattended home polysomnogram in 1994 along with general and cardiovascular assessment [26]. The polysomnogram was repeated in a subgroup 4 to 8 years later with data censored in 2006 and again in 2011. The SHHS indicated that OSA occurred in about 1 in 5 subjects (46% had AHI ≥ 5; 18% had AHI ≥ 15 and 6% had AHI ≥ 30 events per hour) whereas CSA-CSR was exceptionally rare (<1%).

Two large epidemiological studies of HF populations assessing apnoea prevalence have been published in 1999 [5] and 2007 [27]. In the