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CME article

Cardio-respiratory control during sleep in infancy

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EDUCATIONAL AIMS

- To discuss the development of cardio-respiratory control in infants over the first year of life.
- To help the reader appreciate that sleep state has marked effects on cardio-respiratory parameters and control.
- To understand the implications of immature cardio-respiratory control during infancy.

ARTICLE INFO

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SUMMARY

During the first year of life and particularly the first 6 months autonomic control of the cardio-respiratory system is still undergoing maturation and infants are at risk of cardio-respiratory instability. These instabilities are most marked during sleep, which is important as infants spend the majority of each 24 hours in sleep. Sleep state has a marked effect on the cardio-respiratory system with instabilities being more common in active sleep compared to quiet sleep. Responses to hypoxia are also immature during infancy and may make young infants more vulnerable to cardio-respiratory instability. It has been proposed that an inability to respond appropriately to a life threatening event underpins the Sudden Infant Death Syndrome (SIDS). The major risk factors for SIDS, prone sleeping and maternal smoking, both impair cardio-respiratory control in normal healthy term infants.

INTRODUCTION

Infancy sees the convergence of marked maturational changes in the cardiovascular system and its control by the autonomic nervous system, together with a considerable maturation of the respiratory system. Given the underlying immaturity and the rapid reorganisation of these critical body systems, it is perhaps not surprising that infants are at increased risk for cardio-respiratory disturbances and hypoxaemia. The risks of these instabilities are most marked during sleep, as sleep has a marked influence on cardio-respiratory control.[1] This is of particular importance as term infants spend up to 70% of each 24 hours asleep, with preterm infants spending an even greater proportion of time asleep.

The maturation of sleep is one of the most important physiological processes occurring during the first year of life and is particularly rapid during the first 6 months after birth.[1] Sleep states and sleep architecture in infants are quite different to those in adults. In infants, sleep states are defined as active sleep (AS) and quiet sleep (QS), which are the precursors of adult rapid eye movement sleep (REM sleep) and non rapid eye movement sleep (NREM sleep), respectively. QS is characterised by high voltage low amplitude electroencephalograph activity, the absence of eye movements and regular heart rate and respiration. In contrast, AS is characterised by low amplitude high frequency electroencephalograph activity, eye movements, and irregular heart rate and respiration (Figure 1). At birth infants spend about equal amounts of time in each sleep state, with the two states alternating throughout each sleep period. The proportion of QS increases with age, while the amount of AS decreases. Cardio-respiratory disturbances occur predominantly in AS or REM sleep, so the predominance of AS in early infancy may increase the risk of cardio-respiratory disturbances during this period.

CARDIOVASCULAR CONTROL DURING SLEEP

In human infants any measurement of autonomic nervous system (ANS) function needs to be non-invasive and able to be carried out during sleep. Heart rate (HR) and heart rate patterning or variability (HRV) are closely dependent on ANS control and are a direct result of ANS functioning, with short term or high frequency (HF) variability related to parasympathetic vagal activity and long term of low frequency (LF) variability depending on both

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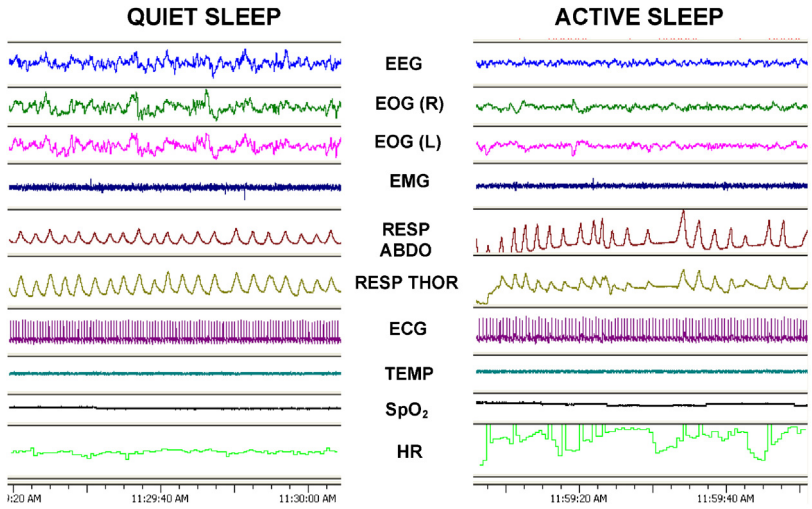

Figure 1. Cardio-respiratory parameters in Quiet and Active sleep in an infant. EEG electroencephalograph; EOG electrooculograph; EMG electromyograph; RESP ABDO abdominal respiratory effort; RESP THOR thoracic respiratory effort; ECG electrocardiograph, TEMP abdominal temperature; SpO_2 oxygen saturation; HR heart rate. Note regular breathing and heart rate in quiet sleep compared to active sleep.

sympathetic and parasympathetic branches of the ANS. Thus, studies of HR and HRV have been used as a measure of central nervous system integrity.[2] The vagal and sympathetic activities constantly interact, however under resting conditions vagal tone dominates. Vagal afferent stimulation leads to reflex excitation of vagal efferent activity and inhibition of sympathetic efferent activity resulting in a decrease in HR and blood pressure (BP). The opposite reflex effects are mediated by the stimulation of sympathetic afferent activity. Analysis of the changes in HR pattern has been used to infer the state and function of the central oscillators, sympathetic and parasympathetic vagal activity, humoral factors and the sinus node.[2] Traditionally, HRV has been analysed using two methods: time domain and frequency domain. Time domain analysis usually calculates the standard deviation of the variability between successive heart beats. The standard deviation of the change in R-R interval from one beat to the next (SDR-R) which relates to the variance of the R-R histogram data projected on the x-axis and the standard deviation of the difference between R-R intervals (SDΔR-R) which relates the variance of the R-R interval histogram data points parallel to the line of identity can be calculated.[3] Computerised spectral analysis of HRV shows that these rhythmical oscillations are concentrated in two main frequency ranges.[2] The long term or LF component (in adults 0.04-0.15 Hz) reflects vasomotor activity associated with baroreceptor activity.[2] The short term HF peak occurring above 0.15–0.4 Hz corresponds to the respiratory frequency.[2] These adult values are not appropriate for infants because of their higher respiratory rates which may range between 30 and 90 breaths per minute, similar to 0.5 and 1.5 Hz respectively and HRs which may range between 100 and 200 beats per minute similar to 1.7 and 3.3 Hz respectively.[4] In the past, neonatal studies have used different spectral divisions for defining LF and HF components to account for these heart and respiratory rate differences from adults and the different band widths used may explain some of the differences in findings of these studies. Based on previous studies and taking into account the ranges of neonatal heart and respiratory rates it has been proposed that the spectral divisions for neonates be 0.04–0.15 Hz for LF and 0.4–1.5 Hz for HF.[4]

There have been far fewer studies in infants of blood pressure variability (BPV), primarily because of the difficulty of measuring BP continuously and non-invasively. Use of a photoplethysmographic cuff designed for an adult finger placed around the wrist of an infant has been validated as an accurate method of continuously measuring BP.[5] The LF component of BPV is thought to reflect sympathetic vasomotor modulation.[6] The HF component, while influenced by the mechanical effects of respiration acting directly on intrathoracic elements of the cardiovascular system, is also influenced via changes in stroke volume and R-R interval that are affected by parasympathetic activity.[6] The ratio of low to high spectral power (LF/HF) of both HRV and BPV has been used to reflect sympathovagal balance.[2,6]

Effects of sleep state on cardiovascular control

There are marked differences in cardiovascular control between different sleep states in infants (Table 1). As in adults, HR has been shown to be higher by 3–6 beats/min in AS compared to QS as early as 2–3 weeks in term infants.[7–11] In addition, HRV has also been shown to be higher in AS compared to QS, associated with a predominance of sympathetic activity in AS.[10–12] A longitudinal study of HRV and BPV assessed from both spectral analysis of baseline measurements and during changes in BP and HR induced by a head up tilt found that overall for HRV, LF power, the LF/HF ratio and total power averaged higher in AS than QS, at 2–4 weeks and 2–3 months. In contrast, HF power was not different between sleep states at 2–4 weeks or 2–3 months, but was lower in AS than QS at 5–6 months.[13] Similarly, BPV spectral indices were generally higher in AS than QS for all indices at all ages studied. Similar results were obtained for both HRV and BPV measured during head up tilts.[13]

In addition to sleep state dependant changes, marked effects of postnatal age on cardiovascular control have also been shown.

Table 1
Effects of sleep state on cardio-respiratory variables

Cardio-respiratory Variable	Active Sleep	Quiet Sleep
Heart rate	increased	decreased
Blood pressure	increased	decreased
Heart rate variability	elevated	decreased
Blood pressure variability		
Respiratory rate	increased	decreased
Respiratory variability	increased	decreased
Hypoxic ventilatory response	immature	immature
Hypoxic arousal response	arousal elicited	Both arousal and non arousal responses