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Original Article

The longitudinal effects of persistent periodic breathing on cerebral oxygenation in preterm infants

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ABSTRACT

Objectives: Periodic breathing is common in preterm infants, but is thought to be benign. The aim of our study was to assess the incidence and impact of periodic breathing on heart rate (HR), oxygen saturation (SpO_2), and brain tissue oxygenation index (TOI) over the first six months after term-equivalent age.
Study design: Twenty-four preterm infants (27–36 weeks gestational age) were studied with daytime polysomnography in quiet sleep (QS) and active sleep (AS) and in both the prone and supine positions at 2–4 weeks, 2–3 months, and 5–6 months post-term corrected age. HR, SpO_2, and TOI (NIRO-200 spectrophotometer) were recorded. Periodic breathing episodes were defined as greater than or equal to three sequential apneas each lasting ≥3 s.
Results: A total 164 individual episodes of periodic breathing were recorded in 19 infants at 2–4 weeks, 62 in 12 infants at 2–3 months, and 35 in 10 infants at 5–6 months. There was no effect of gestational age on periodic breathing frequency or duration. Falls in HR (−21.9 ± 2.7%) and TOI (−13.1 ± 1.5%) were significantly greater at 2–3 months of age compared to 2–4 weeks of age.
Conclusions: The majority of preterm infants discharged home without clinical respiratory problems had persistent periodic breathing. Although in most infants periodic breathing was not associated with significant falls in SpO_2 or TOI, several infants had significant desaturations and reduced cerebral oxygenation especially during AS. The clinical significance of this on neurodevelopmental outcome is unknown and warrants further investigations.

1. Introduction

Worldwide, around 10% of all infants are born preterm and figures indicate that numbers have increased by 36% over the last 25 years (www.marchofdimes.com). Respiratory instability during sleep is very common in infants born preterm and is thought to be due to immaturity of the central and peripheral mechanisms that control breathing [1]. Short periods of apnea not associated with decrements in oxygenation are not problematic; however, if they are associated with significant desaturation, they can have adverse consequences [2,3].

Apneas can occur in isolation or in a repetitive pattern termed "periodic breathing" [4]. Periodic breathing is common in term-born infants in the first 2 weeks of life and significantly decreases with age [5]; however, the frequency is low, making up <1% of total sleep time (TST) [5,6]. Periodic breathing is significantly more prevalent in ex-preterm infants compared to term-born infants at term-equivalent age [7]. However, to date, few studies have followed ex-preterm infants after term-equivalent age. One early study reported an increased incidence of periodic breathing at 52 weeks post-conceptional age (ie, three months post-term corrected age, CA) but a similar incidence at 64 weeks postconceptional age (ie, six months post-term CA) compared to term-born infants [7]. Because of its high prevalence, and the fact that it is thought not to be associated with significant hypoxia or bradycardia, the traditional view of periodic breathing is that it is simply due to immaturity of respiratory control and is benign [8].

The limited number of studies which have assessed the impact of periodic breathing have however found that repetitive apneas can be associated with falls in both peripheral oxygen saturation and cerebral oxygenation. A study of one preterm infant born at 27 weeks of gestation and studied at 37 weeks postconceptional age with near-infrared spectroscopy (NIRS) showed that significant cyclical changes in cerebral blood volume were recorded during periods of periodic breathing [9]. A later study in 10 term-born infants studied at 6–8 weeks postnatal age also demonstrated that cyclical desaturation

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and reoxygenation occurred during episodes of periodic breathing [10]. To date, studies have not examined the effects of periodic breathing on the cerebral circulation longitudinally in preterm infants after term-equivalent age, nor have they assessed the influences of sleep state and sleeping position. Thus, the aim of this study was to evaluate longitudinally the incidence of periodic breathing during sleep across the six months after term-equivalent age and to assess the impact of periodic breathing on heart rate (HR), arterial oxygen saturation, and cerebral oxygenation in both active sleep (AS) and quiet sleep (QS) and in both the prone and supine positions.

2. Methods

The Monash Medical Centre and Monash University Human Research Ethics Committees granted ethical approval for this project. This project arose as a number of preterm infants participating in a larger study of infant sleeping position on cerebral oxygenation [11] were identified to have persistent periodic breathing well past term-equivalent age.

2.1. Subjects

In the larger study, 35 healthy preterm infants were recruited from Monash Newborn, Monash Medical Centre, and the Special Care Nursery at Jessie Macpherson Private Hospital, Melbourne, Australia. For the current study, as we were investigating the longitudinal effects of periodic breathing, only data from the 24 infants (13 M/11 F) who completed all three studies at 2–4 weeks CA, 2–3 months CA, and 5–6 months CA were analyzed. Before the study, written informed consent was obtained from parents and no monetary incentive was provided for participation.

2.2. Polysomnographic recordings

Infants were studied using daytime polysomnography at the Melbourne Children's Sleep Centre, Monash Medical Centre. All electrodes and measuring devices for polysomnography were attached during the infant's morning feed. Infants were then allowed to sleep naturally in a pram in a darkened room at constant temperature. Infants were visually monitored continuously via an infrared camera placed above the pram and behavioral changes, such as body movements and crying, were recorded. Infants were put to sleep in both the prone and supine sleeping positions, with the initial starting position randomized. The sleeping position was changed between morning and afternoon sleep periods that were interrupted by a midday feed. Sleep state was assessed as QS, AS, or indeterminate sleep using electroencephalogram (EEG), behavioral, HR, and breathing pattern criteria [12].

Polysomnographic recordings included continuous monitoring of EEG (C4/A1; O2/A1), electrooculogram, submental electromyogram, electrocardiogram (ECG), thoracic and abdominal breathing movements (Resp-ez Piezo-electric sensor, EPM Systems, Midlothian, VA, USA), airflow from the nose and mouth (Breathsensor, Thermal Airflow Sensor, Mortara Instruments Australia, Sydney, NSW, Australia), arterial blood oxygen saturation (SpO_2) with a 2-s averaging time (Masimo Radical Oximeter, Masimo Corporation, Irvine, CA, USA), and abdominal skin temperature (ADInstruments, Sydney, NSW, Australia). In addition to the standard polysomnogram (PSG) leads, we also measured cerebral oxygenation using a NIRO-200 (NIRO-200 spectrophotometer, Hamamatsu Photonics KK, Tokyo, Japan) with optodes positioned 4 cm apart on the frontal region as previously described [13]. NIRS depends on the relative transparency of biological tissue to light in the near-infrared region of the spectrum. NIRS enables the noninvasive measurement of cerebral tissue oxygenation index (TOI). All physiological data were recorded at a sampling frequency of 512 Hz using a Compumedics E-Series Sleep Recording system with ProFusion PSG 2 software (Compumedics Limited, Abbotsford, VIC, Australia). At the completion of the study, data were exported via the European Data Format to analysis software (Chart 7.0, ADInstruments, Sydney, NSW, Australia).

2.3. Data analysis

Sleep state was scored independently of periodic breathing episodes. As few epochs of indeterminate sleep were scored, these were included in AS. Periodic breathing episodes were defined as three or more sequential apneas lasting >3 s separated by no more than 20 s of normal breathing [14]. An example of periodic breathing is presented in Fig. 1. The duration of each periodic breathing episode was measured from the beginning of the first apnea until the end of the last apnea. The frequency of periodic breathing was determined for each infant as the total number of episodes recorded and also the amount of TST spent in periodic breathing. Changes in HR,

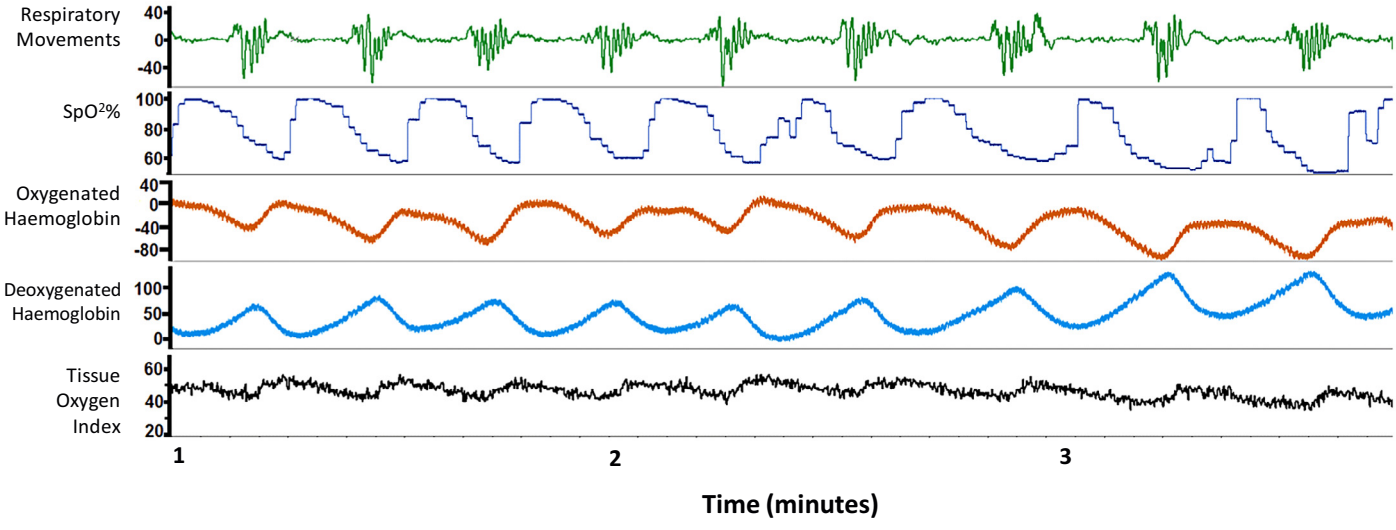

Fig. 1. An example of the effects of periodic breathing on cerebral oxygenation and peripheral arterial oxygen saturation (SpO_2) in a preterm infant at 2–4 weeks post-term corrected age.