Reference values for diaphragm electrical activity (Edi) in newborn infants

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Abstract

Background: Neurally adjusted ventilatory assist (NAVA) is an emerging mode of respiratory support that uses the electrical activity of the diaphragm (Edi) to provide synchronised inspiratory pressure support, proportional to an infant's changing inspiratory effort. Data on Edi reference values for neonates are limited. The objective of this study was to establish reference Edi values for preterm and term neonates. Methods: This was a prospective observational study of newborn infants breathing spontaneously in room air. The Edi signal was monitored by a specialised intragastric feeding tube with embedded electrodes positioned at the level of the diaphragm. Edi minimums and peaks were recorded continuously for four hours. Results: 24 newborn infants (16 preterm [<37 weeks' gestation]; 8 term) were studied. All infants were breathing comfortably in room air at the time of study. Edi data were successfully captured in all infants. The mean (±SD) Edi minimum was 3.02 (±0.94) µV and the mean Edi peak was 10.13 (±3.50) µV. In preterm infants the mean (±SD) Edi minimum was 3.05 (±0.91) µV and the mean Edi peak was 9.36 (±2.13) µV. In term infants the mean (±SD) Edi minimum was 2.97 (±1.05) µV and the mean Edi peak was 11.66 (±5.14) µV. Conclusion: Reference Edi values were established for both preterm and term neonates. These values can be used as a guide when using diaphragm-triggered modes on respiratory support in newborn infants.

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Original Research Article

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Neonatal Edi Reference Values

ABSTRACT

Background

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Methods

This was a prospective observational study of newborn infants breathing spontaneously in room air. The Edi signal was monitored by a specialised intragastric feeding tube with embedded electrodes positioned at the level of the diaphragm. Edi minimums and peaks were recorded continuously for four hours.

Results

24 newborn infants (16 preterm [<37 weeks' gestation]; 8 term) were studied. All infants were breathing comfortably in room air at the time of study. Edi data were successfully captured in all infants. The mean (±SD) Edi minimum was 3.02 (±0.94) µV and the mean Edi peak was 10.13 (±3.50) µV. In preterm infants the mean (±SD) Edi minimum was 3.05 (±0.91) µV and the mean Edi peak was 9.36 (±2.13) µV. In term infants the mean (±SD) Edi minimum was 2.97 (±1.05) µV and the mean Edi peak was 11.66 (±5.14) µV.

Conclusion

Reference Edi values were established for both preterm and term neonates. These values can be used as a guide when using diaphragm-triggered modes on respiratory support in newborn infants.

INTRODUCTION

The initiation of a spontaneous breath by the respiratory centre of the brain results in the electrical excitation of the diaphragm via the phrenic nerve and subsequent diaphragmatic contraction to facilitate an inflow of air. Recently, new technology has become available that can measure diaphragmatic excitation and associated electrical activity of the diaphragm (Edi)[1]. This is achieved using an Edi catheter, which is a specialised intragastric tube that has electrodes embedded at the level of the gastro-oesophageal junction. The catheter assesses neural respiratory control by measuring the total action potentials of the motor units in the diaphragmatic crura[1], representative of phrenic nerve activity and global diaphragm activation[2]. There are two key measures from this diaphragmatic electromyography: (1) Edi minimum (the baseline electrical activity of the diaphragm between breaths); and (2) Edi peak (the amplitude of electrical activity associated with inspiratory effort)[3].

These Edi signals can be filtered, processed and relayed to a ventilator, which can then provide synchronised inspiratory pressure support that is proportional to inspiratory effort. This modality, referred to as neurally adjusted ventilatory assist (NAVA), is an emerging mode of respiratory support that can be utilised either non-invasively via nasal prongs or mask, or invasively[4]. Over 100 clinical and experimental studies have demonstrated the benefit of neural monitoring and ventilator assist control compared to conventional modes of ventilation, during both non-invasive and invasive ventilation. These studies have shown that NAVA improves patient-ventilator interaction, offering equivalent or improved physiological outcomes and favourable ventilator parameters (lower peak inspiratory pressures and down-regulation of Edi to limit over-assist)[5].

Although several studies have evaluated the clinical use of NAVA in newborn infants, reference Edi data in healthy neonates have previously only been collected in two studies, involving 20 infants[3,6]. However, data pertaining to healthy preterm and term infants not requiring respiratory support is limited. Establishing reference values for this population is important for the clinical utility of this technology. Excessive respiratory support can suppress an infant's natural respiratory drive while under supporting breathing is also detrimental[7]. The potential morbidity and mortality associated with incorrect support is well established[8].

This observational study of preterm and term newborn infants aimed to establish reference Edi values. We also sought to determine how these values vary according to sleeping states, feeding and skin-to-skin care.

MATERIALS AND METHODS

Patient Selection

Newborn infants born at 29-42 weeks' gestation who were admitted to the Neonatal Intensive Care Unit (NICU) at the Royal Hospital for Women were opportunistically recruited for this prospective observational study. Inclusion criteria required that neonates were on room air with no current respiratory issues, free of respiratory support for at least one week and with an intragastric feeding tube in situ. Exclusion criteria included any congenital anomalies, major neurological conditions and brain anomalies, neuromuscular diseases and conditions affecting innervation of the diaphragm.

Study Procedure

Edi catheter was inserted when the infant's conventional intragastric feeding tube was due to be changed as per unit policy. The Edi catheter was positioned at the level of the diaphragm and the correct position confirmed by analysis using Servo-n software (Getinge AB Gothenburg, Sweden). The Edi signal was recorded continuously for the duration of the study. It was adjusted so that in the "catheter positioning screen", the Edi signal, superimposed as a pink signal, was noted to occur on the middle 2 out of 4 retro-cardiac ECG tracing. Data output included Edi peak, Edi min and respiratory rate, all of which were stored in one-minute increments.

Infants were observed for a continuous four-hour period, resulting in 240 data points for each variable observed. Heart rate and oxygen saturation (SpO2) were also recorded from telemetry monitors every 15 minutes throughout the study. An observer recorded sleep, awake and feeding states, as well as timing skin-to-skin care (defined as continuous skin-to-skin contact in a vertical position on the parent's chest). Feeding states for comparison were defined as one-hour pre- and post-prandial. During the study period, normal activity was not interrupted. On completion of the observation period, the Edi catheter was left in situ for use as a regular nasogastric tube. All infants were studied for a single four period only.

Statistical analyses

Basic descriptive statistics were performed to calculate population means and standard deviations. Paired sample t-tests were used to compare means between sleep states, feeding and skin-to-skin care. Statistical significance was defined as $p<0.05$.

Ethics

This study was performed following the Declaration of Helsinki and approved by the Human Research Ethics Committee of South Eastern Sydney Local Health District (Reference Number: 17/083). All parents or legal guardians provided written informed consent for infants to participate in the study.

RESULTS

Patient Inclusion

A total of 24 infants (16 preterm; 8 term) were enrolled in the study (**Table 1**). Birth weights ranged from 1270g to 3490g and postnatal age ranged from day 2 to 34. All infants were breathing comfortably in room air at the time of enrolment. Infants were studied for 240 minutes and all infants completed the study. For feeding state comparisons, at least 45 minutes of data was analysed per subject both pre- and post-prandially. Feeding state comparisons could not be conducted for one infant (not feeding at the time of the study).

Average Edi peak, Edi min, respiratory rate, heart rate and oxygen saturation across all 24 infants are presented in **Table 2** . Heart rate, respiratory rate and oxygen saturations were all within the normal range for gestational age. The mean (±SD) Edi minimum was 3.02 (±0.94) µV and the mean (±SD) Edi peak was 10.13 (±3.50) µV. Averaged data for the preterm and term infants are also presented. There was no significant difference in Edi minimum (p=0.844) or Edi peak (p=0.259) between preterm and term infants. Based on data from the entire cohort, the reference ranges (defined as mean ±2 SD) for Edi minimum and Edi peak would be 1-5 µV and 3-17 µV, respectively.

Edi minimum and Edi peak were compared during various states (**Table 3**). There were no differences observed with feeding (pre- vs post-prandial). Edi minimum was significantly higher when infants were awake (4.07 [±1.45] µV vs 2.69 [±0.82] µV; $p<0.001$). Similarly, Edi peak was significantly higher when infants were awake (13.43 [±4.49] µV vs 9.11 [±2.92] µV; $p<0.001$]. During skin-to-skin care, Edi peaks were significantly lower (7.01 [±0.50] µV vs 10.14 [±3.53] µV; p=0.013). Differences between Edi minimums did not reach statistical significance.

DISCUSSION

The observational data in this study represent Edi signals from a large cohort of healthy preterm and term newborn infants, which we have used to define reference values for Edi minimum (1-5 µV) and Edi peak (3-17 µV). These values can be used as a reference in clinical practice to define a goal for electrical activity in infants requiring respiratory support. This is particularly relevant in infants being supported with NAVA as breathing support is always proportional to the infant's Edi activity. There was no significant difference found between the preterm and term population in the study suggesting that diaphragm electrical activity is similar in infants that are spontaneously breathing without support. This supports the use of these reference values in both preterm and term infants.

We noted that diaphragm electrical activity was significantly higher when infants were awake. This is an expected finding as the sleep stage is characterised by slower, more regular respiration rates[9]. It is also consistent with previous studies, which demonstrated that peak Edi activity was 60% higher in the awake state[3]. Peak Edi was also significantly lower during skin-to-skin contact. This has not previously been reported but is not surprising given the known positive effects of skin-skin care on cardiorespiratory stability and sleep quality[10,11].

We found that Edi signals were significantly higher after feeds. This is likely to be an effect of an increase in diaphragm activity associated with increased intragastric pressure[12]. Previous studies have shown a post-prandial decrease in peak Edi, however, this was in a small population of term infants who were suck feeding[3]. The majority of infants in this study were predominantly fed with an intragastric tube, which potentially explains this discrepancy.

There were some important limitations to acknowledge with respect to this study. Although these data represent the largest reported cohort of spontaneously breathing preterm and term infants, the sample size does not allow for a true reference range based on gestation. We found that the electrical diaphragm activity is similar in preterm infants and term infants but these were all infants who did not require respiratory support. This reflects an increasingly small percentage of the population as gestation decreases. Consequently, we were not able to recruit infants less than 29 weeks gestation where differences in diaphragm activity may be more apparent. We also acknowledge that the inclusion of infants admitted to a special care nursery may not represent a true healthy newborn population. Further to this, some infants were admitted and subsequently diagnosed with transient tachypnoea of the newborn. Although infants were subjectively breathing comfortably at the time of enrolment, some residual subclinical respiratory disease cannot be ruled out. We are reassured that our findings are similar to previous published data[3,6].

In summary, reference Edi minimum and peak values were established for both preterm and term neonates. These values can be used as a guide for clinicians when using diaphragm-triggered modes on respiratory support in newborn infants to ensure an optimal level of respiratory support.

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CONFLICT OF INTERESTS

The specialised nasogastric feeding tubes required for this study were provided at no cost by the manufacturer (Getinge AB, Gothenburg, Sweden). The manufacturer had no involvement in study concept, design, conduct, analyses or manuscript preparation.

AUTHOR CONTRIBUTIONS

SB conceived the study. SB, VG, TS, JS and KL designed the study. VG coordinated the implementation of the study and was responsible for data acquisition and subsequent analysis. ST drafted the manuscript. All authors (SB, VG, TS, JS, KL and ST) reviewed and revised the manuscript, providing important intellectual content, and approved the final version.

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