Respiratory Physiology & Neurobiology 258 (2018) 1–4

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

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

Rapid respiratory transition at birth as evaluated by electrical activity of the diaphragm in very preterm infants supported by nasal CPAP

Arata Oda[a,*], Vilhelmiina Parikka[a,b], Liisa Lehtonen[a,b], Hanna Soukka[a,b]

[a] Department of Pediatrics and Adolescent Medicine, Turku University Hospital, Turku, Finland
[b] University of Turku, Turku, Finland

A R T I C L E I N F O

Keywords:
Newborn
Resuscitation
Neonatal pulmonary transition
Neurally adjusted ventilatory assist
Continuous positive airway pressure

A B S T R A C T

Objective: To investigate breathing patterns during respiratory adaptation in preterm infants using the electrical activity of the diaphragm (EAdi) signal.
Patients: Infants born between 28 + 0 and 31 + 6 gestational weeks and supported by early nasal continuous positive airway pressure (nCPAP) were studied. The EAdi signal was recorded for 120 min after birth.
Results: Eight preterm infants were evaluated. The median EAdi peak value of 19.2 μV (lower quartile 13.1; upper quartile 22.2) at 20 min after birth decreased to 11.4 μV (9.5–14.7) at 55 min of age. The median EAdi minimum value of 4.5 μV (2.2–5.5) at 25 min after birth decreased to 1.6 μV (1.2–2.7) at 85 min of age.
Conclusion: EAdi was high right after birth. This indicates that preterm infants are capable of generating sufficient respiratory drive and diaphragm tone during expiration to establish and maintain functional residual capacity. Diaphragm activity decreased within the first 90 min, suggesting that early adaptation was accomplished by 90 min of age.

1. Introduction

Major changes occur during the respiratory transition from fetal to neonatal life. When an infant takes the first breaths, lung liquid is cleared and the lungs fill with air. The first breaths are triggered by strong inspiratory effort produced by the diaphragm tone, which is generated against both the inward force of spontaneous chest recoil and the surface tension in the alveoli. The first breaths are characterized by large tidal volumes, high peak inspiratory flows, low peak expiratory flows, large inspirations and prolonged expirations, known as expiratory braking (te Pas et al., 2009; Hooper et al., 2016, 2013; van Vonderen et al., 2014; van Vonderen and te Pas, 2015). This breathing pattern helps to establish and maintain functional residual capacity (FRC). If failure to establish FRC occurs, it may lead to a need for invasive ventilation.

In preterm infants, the adaptation phase might be challenging due to weak or absent respiratory drive, weak chest muscles, flexible ribs, surfactant insufficiency and impaired lung liquid clearance (te Pas et al., 2009). Therefore, most infants born at less than 32 gestational weeks require some respiratory support after birth to enhance pulmonary adaptation. The respiratory support should guarantee sufficient oxygenation and ventilation, while overtreatment should be carefully avoided so as not to harm the fragile lungs and brain (Isayama et al., 2016). Successful early adaption can be supported by the provision of early nasal continuous positive airway pressure (nCPAP), which enhances the aeration of the lung, decreases work of breathing, prevents the collapse of alveoli and facilitates the establishment of FRC (Siew et al., 2009a), and eventually, may prevent the need for intubation (Isayama et al., 2016).

The early use of nCPAP in the delivery unit has been shown to be preferable when compared to endotracheal intubation and mechanical ventilation in preterm infants in terms of decreasing bronchopulmonary dysplasia and death (Subramaniam et al., 2016). Therefore, early nCPAP therapy is widely used in delivery units (Huberts et al., 2018; Siew et al., 2015).

The electrical activity of the diaphragm (EAdi) is the sum of all motor unit action potentials of the diaphragm muscle steered by the respiratory center. The signal can be measured reliably and objectively with the EAdi catheter, which contains electrodes at the level of diaphragm (Beck et al., 2011; Iyer et al., 2017; Stein et al., 2012). For each breath, this signal gives the peak value, representing neural inspiratory effort, and the minimum value, representing the tonic activity of the diaphragm at the end expiration. Previously, the EAdi signal has been used successfully to study the effect of caffeine citrate, skin-to-skin care and extubation on breathing patterns and diaphragm activation in preterm infants (Iyer et al., 2017; Parikka et al., 2015; Soukka et al.,

* Corresponding author at: Arata Oda Kiinamyllynkatu 4-8, 20500, Turku, Finland.
E-mail address: arata-oda@nkodomo-hsp.jp (A. Oda).

https://doi.org/10.1016/j.resp.2018.09.009
Received 5 May 2018; Received in revised form 6 September 2018; Accepted 25 September 2018
Available online 28 September 2018

2014). Furthermore, it has been used to compare nCPAP to high flow nasal cannulae during weaning from respiratory support (Nasef et al., 2015).

The EAdi signal is an easily available and noninvasive tool, which can also be used to assess diaphragm activity in high-risk infants. Until now, no studies have reported the EAdi signal during early adaptation. Therefore, normal pattern of EAdi values during this period is not known. In this prospective observational study, we recorded and analysed the EAdi signal in preterm infants who were successfully treated with early nCPAP immediately after birth. We chose to study preterm infants born between 28 + 0 and 31 + 6 gestational weeks, since respiratory adaptation is challenging in this subset of infants and the infants may either adapt well or fail early nCPAP and require invasive ventilation and surfactant. We hypothesized that both EAdi peak and minimum values would be high immediately after delivery and then decrease gradually during the successful 2-h adaptation period. Patients and methods

We performed a prospective observational study in preterm infants born between 28 + 0 to 31 + 6 gestational weeks and routinely treated with early nCPAP immediately after birth. Infants with major congenital anomalies or prenatally diagnosed diseases were excluded. The study was conducted in the delivery unit and in the neonatal intensive care unit of the Turku University Hospital (level III NICU) between August 2016 and December 2017. The recordings were performed when the study ventilator (Servo-n) and research personnel were available. The study was approved by the Ethics Committee, Hospital District of Southwest Finland as well as by the scientific research committee of the Paediatric Department of the Turku University Hospital, Finland. A written informed consent was obtained from both parents or guardians according to the guidelines of the Research and Ethics Board before the delivery.

Our early respiratory support strategy for preterm infants born between 28 and 32 weeks of gestation is to begin early nCPAP in the delivery unit if the infant has spontaneous breathing or starts to breathe regularly after a short positive pressure ventilation with bag and mask. The infant is then transferred to the NICU while on early nCPAP. For the infants participating the study, the care providers followed similar routines with early nCPAP, which was provided using a Servo-n ventilator (Maquet, Solna, Sweden) and EasyFlow CPAP interface (Stephan, Gackenbach, Germany). The initial nCPAP settings were 6 cm H_2O pressure and 30% supplemental oxygen. The nCPAP pressure was kept constant and the target saturation was 90–95% during the study period. The EAdi catheter, containing eight bipolar electrodes (Maquet, Solna, Sweden), was inserted by caregivers as soon as possible, and the EAdi signal recording was started in the delivery ward and continued during the 2-h adaptation period. The EAdi catheter was placed in the esophagus at the level of the crural diaphragm and its position was determined along the electrode array with the help of the positioning tool provided by the ventilator. The catheter was placed nasally, fixed properly and no readjustments were needed during the study period. In case of twins, only the first one was included in our study due to unavailability of equipment for both.

Data were exported from the ventilator log data which gives the value for EAdi peak and EAdi minimum for each minute. Oxygen saturation (SpO_2) and heart rate were simultaneously and continuously recorded using the Radical or Radical7 pulse oximeters (Masimo Irvine, US). Data from the first 120 min were analysed.

The following background data were collected: the use of prenatal steroids, gestational age at birth, birth weight, sex, mode of delivery, pH and Apgar score.

The primary outcomes were both the EAdi peak and the EAdi minimum during the first two hours after birth. The secondary outcomes were neural respiratory rate, heart rate and FiO_2.

All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University; http://www.jichi.ac.jp/saitama-sct/SaitamaHP.files/statmedEN.html; Kanda 2012), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria, version 2.13.0). The data is presented as median (range) or median (IQR) to take into account the intersubject variability between the patients. Statistical analysis of the parameters measured at different time points were performed using the Friedman test and the Bonferroni adjustment method. A p-value < 0.05 was considered to indicate a statistically significant difference.

Table 1
Demographic and clinical characteristics of the study infants, n = 8.

Gestational age, week	30 + 1 (28 + 0–31 + 6)
Birth weight, g	1377 (700–1850)
Twin, number (%)	2 (25%)
C-section, number (%)	5 (63%)
Antenatal betamethasone	8 (100%)
Full course	2 (25%)
Partial course	6 (75%)
Premature rupture of membranes	3 (38%)
Umbilical cord pH	7.30 (7.23–7.37)
Apgar at 1 min	7 (4–9)
Apgar at 5 min	9 (7–9)
Manual ventilation at birth	3 (38%)

Data are expressed as median (range) or number (%).

2. Results

Eight preterm infants were recruited during the study period. The median gestational age was 30 + 1 (28 + 0–31 + 6) weeks and the median birthweight was 1377 g (700–1850 g) (Table 1). Five infants were born by Caesarean section. All mothers received antenatal betamethasone, but the course was completed in only two cases. Three of eight infants needed positive pressure ventilation for a few minutes immediately after birth. The median umbilical pH was 7.30 (7.23–7.37) and the median Apgar score was 7 at 1 min and 9 at 5 min of age. All infants had their EAdi catheter inserted between 3–6 min of life so that at 5 min, the Edi data recording was on-going for four infants. We did not face any clinical difficulties in inserting or positioning the catheter via the nasal route. The position of the catheter was checked repeatedly using the positioning tool. We found the signal to be easy to interpret and there were no data deletions due to artefacts.

The EAdi peak values were high, 19.2 μV (13.1–22.2 μV) during the first 20 min after birth, and thereafter the values gradually decreased over the study period. At 55 min of age, the EAdi peak values had decreased significantly to 11.4 μV (9.5–14.7 μV) compared to the first 20 min (Fig. 1A). Similarly, the EAdi minimum values were high, 4.5 μV (2.2–5.5 μV) during the first 25 min after birth, and thereafter the values decreased, being significantly lower, 1.6 μV (1.2–2.7 μV) at 85 min of age (Fig. 1B).

The neural respiratory rate (nRR) increased during the first 40 min. At 10 min of age, the nRR was 24 per minute (21–34), and at 60 min of age, the nRR was 39 per minute (34–57) (Fig. 1C). The median SpO_2 was around 75% during the first 5 min. After 20 min of age, all infants had stable saturation above 95% without supplemental oxygen. Heart rate was stable in all infants during the recording at an average level of 150 beats per minutes (Fig. 2).

3. Discussion

The main finding of this study with preterm infants on early nCPAP was that the EAdi peak and minimum values were high immediately after birth, reflecting strong respiratory effort and expiratory braking. Both values decreased gradually over 60–90 min towards stable levels, indicating successful respiratory adaptation during this time period.

The entry of air into the lungs during early adaptation is dependent on the generation of a transpulmonary pressure created by inspiratory effort, mainly in the form of contraction of the diaphragm (te Pas et al.,