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Review

Non-invasive ventilation with neurally adjusted ventilatory assist in newborns

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SUMMARY

Neurally adjusted ventilatory assist (NAVA) is a mode of ventilation in which both the timing and degree of ventilatory assist are controlled by the patient. Since NAVA uses the diaphragm electrical activity (Edi) as the controller signal, it is possible to deliver synchronized non-invasive NAVA (NIV-NAVA) regardless of leaks and to monitor continuously patient respiratory pattern and drive. Advantages of NIV-NAVA over conventional modes include improved patient–ventilator interaction, reliable respiratory monitoring and self-regulation of respiratory support. In theory, these characteristics make NIV-NAVA an ideal mode to provide effective, appropriate non-invasive support to newborns with respiratory insufficiency. NIV-NAVA has been successfully used clinically in neonates as a mode of ventilation to prevent intubation, to allow early extubation, and as a novel way to deliver nasal continuous positive airway pressure. The use of NAVA in neonates is described with an emphasis on studies and clinical experience with NIV-NAVA.

1. Introduction

Mechanical ventilation can be a life-saving therapy for neonates with respiratory failure. There is consensus today that invasive mechanical ventilation via an endotracheal tube should be minimized or avoided completely to reduce the risk of ventilator-induced lung injury. This can often be achieved by non-invasive respiratory support delivered via a mask or nasal prongs. Support can be provided by applying nasal continuous positive airway pressure (nCPAP) or nasal intermittent positive pressure ventilation (NIPPV). A recent Cochrane review assessing NIPPV versus nCPAP in preterm infants after extubation showed that NIPPV may be more effective than nCPAP in reducing short-term extubation failure [1].

The goal of NIPPV, like invasive ventilation, is to provide respiratory muscle unloading and adequate ventilation while maintaining lung volume through the application of positive end expiratory pressure (PEEP). This method of non-invasive support has been embraced by many neonatologists and recent data from the more than 900 neonatal intensive care units (NICUs) in the Vermont Oxford Network showed that 28–31% of very low birth weight neonates received support with NIPPV at some point during their hospitalization. However, failure occurs frequently and ~30% of these infants require reintubation [1].

Although often effective without it, synchronization may be important in delivering effective NIPPV. Unsynchronized NIPPV is usually time-cycled and pressure-targeted, with total disregard for the patient's spontaneous breathing pattern. Alternatively, synchronized NIPPV has been delivered using pneumatic signals such as pressure or flow. However, in the presence of leaks, rapid respiratory rates and small tidal volumes, achieving good interaction between the patient and the ventilator remains challenging. Although abdominal movements have been used to trigger the ventilator in NIPPV, the issue of appropriate cycling-off has yet to be resolved. In addition, most conventional NIPPV modes are pressure-targeted, and provide no room for the variable respiratory demand observed in preterm newborns [2]. Asynchronous delivery

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of assist can lead to upper airway constrictor muscle activation [3,4], and diversion of ventilator breaths into the stomach [5]. Often neglected, during NIPPV, monitoring the patient's respiration is problematic as the parameters used to evaluate respiratory metrics are also affected by leaks.

One newer method of delivering assisted ventilation has the potential to overcome these challenges. Neurally adjusted ventilatory assist (NAVA) is a mode of ventilation in which both the timing and amount of ventilatory assist are controlled by the patient [6,7]. Since NAVA uses the diaphragm electrical activity (Edi, or EAdi) as the controller signal, it is possible to deliver synchronized non-invasive NAVA (NIV-NAVA) regardless of leaks and to continuously monitor patient respiratory pattern and drive. In theory, these characteristics may make NIV-NAVA an ideal mode to provide effective, appropriate non-invasive respiratory support to newborns with respiratory insufficiency.

2. NAVA: what is it and how does it work?

NAVA is a mode of mechanical ventilation intended for use in spontaneously breathing patients. The patient's own Edi waveform is used to trigger-on and cycle-off each assisted breath, also controling the pressure delivered, thus providing truly synchronized and proportional assist. The Edi waveform is recorded with an “Edi catheter”, a standard-sized naso- or orogastric feeding tube with miniaturized sensors embedded within. When correctly placed at the level of the gastroesophageal junction, the Edi signals are detected from the crural portion of the diaphragm. The Edi catheter is connected to a Servo ventilator (Maquet Critical Care, AB, Solna, Sweden) that is equipped to provide NAVA to a patient. The catheter is well tolerated and easy to place. The act of feeding through the catheter does not interfere with signal quality (electrode function), and stable Edi waveforms have been observed over several days, regardless of baby's movements or handling [8].

2.1. Physiological rationale for using the Edi waveform

The Edi waveform is a measure of the baby's neural respiratory drive, and, being electrical, is pneumatically independent. The respiratory centers in the brainstem continuously receive afferent information about lung stretch, lung de-recruitment, arterial blood gases, respiratory muscle loading, and other inputs. The output of the respiratory centers – representing all respiratory reflexes and responses – travels down the phrenic nerves and electrically activates the diaphragm motor units. The Edi waveform is a representation of this neural activation (motor unit recruitment and firing rate). Hence, during NIV-NAVA, the same physiological responses driving the patient's diaphragm are also simultaneously driving the ventilator throughout each breath.

Compared to adult patients, the Edi waveform in infants is highly variable (Fig. 1); it can be quantified breath-by-breath for its peak (Edi_{peak}, representing tidal inspiratory effort) or its minimum (Edi_{min}, representing the effort to prevent de-recruitment) values. Sighs (neural recruitment maneuvers and central apneas) can be detected, and other respiratory metrics, such as the neural respiratory rate, can be quantified, even in the presence of leaks.

2.2. NIV-NAVA and ventilator control

Figure 2 demonstrates ventilator waveforms for a newborn breathing on NIV-NAVA, showing synchrony between the Edi (patient) and airway pressure (ventilator), in terms of timing and proportionality. During NIV-NAVA, the Edi signal triggers inspiration and targets pressure delivery throughout inspiration. The level of pressure targeted can be adjusted by changing the NIV-NAVA level. The ventilator cycles-off once the Edi has decreased by 30% from its peak, and then returns to a user-defined PEEP level. In this fashion, patients are in control of their own ventilator rate and level of assist, which can vary breath to breath. As described in Section 6, upper pressure limits can be set, and backup ventilation is provided in the case of apnea or accidental catheter removal.

3. Pre-clinical/laboratory studies testing of NIV-NAVA

NIV-NAVA was first shown to be feasible and to improve patient–ventilator synchrony in an animal model of hypoxemic failure using a prototype Edi-controller on the Servo-300 platform [9]. In 3 kg rabbits with experimental lung injury, ventilation via a single nasal prong (75% leak) resulted in failure to trigger conventional NIV with pressure support. Activation of NIV-NAVA showed that synchronized and proportional assist could be delivered, with more favorable ventilation. In fact there was no significant difference in trigger delays, nor in cycling-off delays, between intubated (leak-free NAVA) and NIV-NAVA. It should be pointed out that despite the extreme leak (75%) and the 50% reduction in lung compliance, these lung-injured animals could be effectively ventilated without complications or gastric distension even when peak inspiratory (nasal prong) pressures reached 40 cmH_2O [9].

In the same animal model, Mirabella et al. [10] examined lung injury markers after 6 h of volume control ventilation with a lung-protective strategy (6 mL/kg with PEEP), compared to 6 h of NIV-NAVA and spontaneous breathing and no PEEP, and found a lower lung injury score and plasma interleukin-8 for the NIV-NAVA group. Interestingly, despite no PEEP being applied during NIV-NAVA, the upper airways were able to aid in the maintenance of functional residual capacity.

A challenge during non-invasive ventilation is to avoid insufflation of gas into the esophagus and stomach. Recently, in spontaneously breathing, awake newborn lambs, the group of Praud et al. [3] demonstrated activation of the thyroarytenoid (a glottal constrictor) at high levels of non-invasive pressure support, which was not observed in any of the lambs during NIV-NAVA [4]. The neural co-ordination of upper airway dilation and neural inspiration likely explain the favorable results during NIV-NAVA.

Using the same prototype as in the animal work, Beck et al. [11] showed in a small pilot study ($n = 7$) of low birth weight newborns that NIV-NAVA was feasible, and was not affected by leaks, in terms of patient–ventilator interaction.

4. Relevant clinical studies with invasive NAVA in neonates

The literature on NAVA has expanded considerably over the last decade. In all, 235 peer-reviewed manuscripts have been published. Fifty-four of these pertain to children (age 0–18 years including premature infants), ~25% of the publications. Most of the publications relate to the use of invasively delivered NAVA. Readers are referred to the latest systematic review on the topic of NAVA in infants for a summary of all the studies [12].

Regarding the literature related exclusively to premature infants, there are six studies ($n = 106$ babies) related to invasive NAVA (average lowest gestational age (GA) at birth 24 weeks, average birth weight 728 g, when reported) and two studies ($n = 17$ babies) with NIV-NAVA (very similar characteristics, average lowest GA 24 weeks, birth weight 812 g).

A summary of the relevant studies on invasively delivered NAVA is provided below.