Noninvasive Neurally Adjusted Ventilatory Assist (NIV-NAVA) in Children and Adults

15

Jennifer Beck, Yun Liu, and Christer Sinderby

Contents

J. Beck, PhD (✉)
Department of Pediatrics, University of Toronto, Toronto, ON, Canada

Keenan Research Centre for Biomedical Science, St. Michael's Hospital,
Toronto, ON, Canada
e-mail: jennifer.beck@rogers.com

Y. Liu, MD
Department of Critical Care Medicine, Jiangsu Province Hospital,
Nanjing Medical University, Nanjing, Jiangsu Province, China
e-mail: lyjz.2007@163.com

C. Sinderby, PhD
Keenan Research Centre for Biomedical Science, St. Michael's Hospital,
Toronto, ON, Canada

Department of Critical Care Medicine, St. Michael's Hospital, Toronto, ON, Canada
e-mail: sinderby@rogers.com

A.M. Esquinas (ed.), *Noninvasive Mechanical Ventilation: Theory, Equipment, and Clinical Applications*, DOI 10.1007/978-3-319-21653-9_15

Abbreviations

Edi	Electrical activity of the diaphragm
FRC	Functional residual capacity
NAVA	Neurally Adjusted Ventilatory Assist
NIV-NAVA	Noninvasive Neurally Adjusted Ventilatory Assist
PEEP	Positive end-expiratory pressure

15.1 Introduction

Neurally Adjusted Ventilatory Assist (NAVA) is a mode of ventilation controlled by the electrical activity of the diaphragm (Edi) and can be delivered invasively (NAVA) or noninvasively with different interfaces (NIV-NAVA). NAVA was US Food and Drug Administration approved and has been commercially available since 2007. More than 28 peer-reviewed studies in adults and infants ($n=376$ patients) have demonstrated unequivocally that, compared with conventional (pneumatically controlled) modes of ventilation, patient-ventilator interaction – both in terms of timing and proportionality – is much improved with NAVA and NIV-NAVA. For those studies ($n=261$ patients) reporting an Asynchrony Index (AI), NAVA has a significantly lower AI (4.7 %) compared with pneumatically controlled mechanical ventilation (25.6 %).

The improvement in synchrony observed with NAVA and NIV-NAVA is achieved by the use of a neural signal (the Edi), which is independent of pneumatics for the purpose of controlling the ventilator. Often neglected, but equally important in the evaluation of respiratory effort and respiratory metrics, is the additional benefit of using the Edi signal as a monitoring tool. The Edi signal represents the final output of the respiratory centers, after receiving multiple afferent inputs about lung stretch, diaphragm force, arterial blood gases, and voluntary influences (Fig. 15.1). Furthermore, the natural coordination of the upper airway (dilator) muscles with the neural activation of the diaphragm allows efficient delivery of assist during NIV-NAVA, without opposition from the upper airway constrictor muscles. The interested reader is referred to several detailed descriptions about NAVA, NIV-NAVA, and the Edi signal [1–3]. This chapter provides an update of the clinical and experimental findings of the use of NIV-NAVA since the 2013 Minerva publication [2].

15.2 Discussion and Analysis of NIV-NAVA

15.2.1 Equipment and Theory

The most important feature when using NIV-NAVA pertains to the Edi catheter (a routinely used naso- or orogastric feeding tube with miniaturized sensors embedded to record Edi), available in sizes suitable for adults and children (Fig. 15.2). The

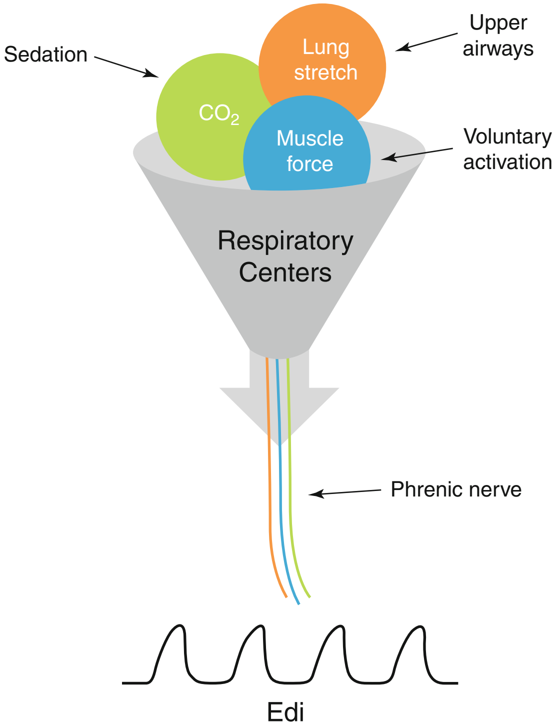


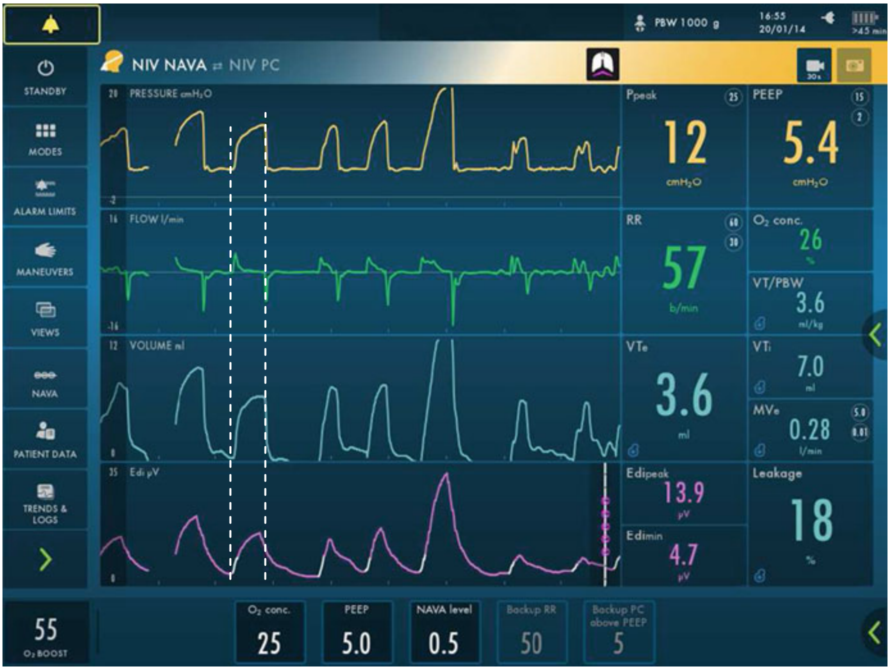
Fig. 15.1 Multiple afferent signals continuously meet and integrate in the respiratory centers. The electrical activity of the diaphragm (Edi) is the final neural output from the respiratory centers (efferent stimulation of the diaphragm) but contains the afferent information about lung stretch, $PaCO_2$, and muscle force

Edi catheter is connected to a SERVO-i or SERVO-U or SERVO-n ventilator (Maquet Critical Care, AB, Solna, Sweden). The catheter is well tolerated and easy to place, as described in the literature. During NIV-NAVA, any interface can be used (e.g., face mask, helmet, nasal prongs) with maintained synchrony, because the control of the ventilator is not affected by leaks.

15.2.2 Ventilator Control

To initiate a ventilator breath, the Edi signal triggers inspiration once a threshold change in Edi has been exceeded. The pressure delivered after triggering increases during inspiration in proportion to the Edi, until neural exhalation begins, and the ventilator cycles off (70 % of the peak Edi). The NIV-NAVA level determines the proportionality between the Edi and the ventilator pressure. After cycling off, the assist returns to a user-defined positive end-expiratory pressure (PEEP) level. In this fashion, the patient is in control of their own ventilator rate and level of assist, which can vary on a breath-by-breath basis. Figure 15.3 demonstrates Edi and ventilator pressure tracings for an infant patient breathing on NIV-NAVA, and demonstrates the synchrony between the Edi (patient) and airway pressure (ventilator), both in terms of timing and proportionality. As in any another mode of mechanical

Fig. 15.2 Example of an Edi catheter (8 F size shown), used for feeding and measuring of diaphragm electrical activity (Maquet, Solna, Sweden)



PBW 1000 g
16:55
20/01/14

Ppeak 12 cmH$_2$O (25)
PEEP 5.4 cmH$_2$O (15) (2)
RR 57 b/min (60) (30)
O$_2$ conc. 26 %
VT/PBW 3.6 ml/kg
VTe 3.6 ml
VTi 7.0 ml
MVe 0.28 l/min (5.0) (0.01)
Edipeak 13.9 µV
Edimin 4.7 µV
Leakage 18 %

55 O$_2$ BOOST
O$_2$ conc. 25
PEEP 5.0
NAVA level 0.5
Backup RR 50
Backup PC above PEEP 5

Fig. 15.3 Example of time tracings for ventilator pressure (*top*, *yellow*), flow (*green*), volume (*blue*), and Edi (*bottom*, *magenta*). Note the synchrony and proportionality between Edi and ventilator pressure, despite a leak (18 %)

ventilation, upper pressure limits can be set. Backup ventilation is provided in the case of apnea or accidental catheter removal.

15.2.3 Neural Integration with Respiratory Reflexes

The neural drive to breathe during NIV-NAVA is controlled by multiple afferent inputs originating in the lungs (stretch receptors), the central and peripheral chemoreceptors (CO_2 and pH sensitive), the respiratory muscles (muscle tension receptors), and the upper airway muscles (chemical and pressure receptors). Depending on clinical practice, a further influence on respiratory drive is sedation and analgesia. These multiple afferent inputs are continuously being "centralized" and "integrated" in the respiratory centers of the brainstem, with the resultant package of respiratory-related information being sent out via the phrenic nerves to electrically activate the diaphragm (i.e., the Edi) and other respiratory muscles (Fig. 15.1). Therefore, the physiological responses driving the patient's diaphragm are also simultaneously driving the ventilator throughout each breath during NIV-NAVA.

15.2.4 Recent Publications About NIV-NAVA

A total of 21 papers appear on PUBMED with the topic of NIV-NAVA since its release in 2008. Since the update in Minerva in 2013 [3], five clinical NIV-NAVA studies and one experimental study have been published [4–9]. Three of these articles were accompanied by editorials [10–12].

In 12 adult patients with COPD, Doorduin et al. [4] performed automated patient-ventilator interaction analysis during NIV-pressure support ventilation (PSV) (delivered with two separate ventilators, Maquet's SERVO-i and Respironics' Vision) and NIV-NAVA. Synchrony was superior (the Neurosync index was low, 5 %) during NIV-NAVA compared with NIV-PSV (24 % Vision, 21 % SERVO-i). The improvement in synchrony was mainly due to reduced triggering and cycling-off delays. The authors also found that there was a progressive number of wasted efforts as the triggering and cycling-off delays got worse.

In pediatrics, three studies have all shown feasibility and tolerance of NIV-NAVA, as well as insertion of the Edi catheter [5–8].

Vignaux et al. [5] demonstrated in six children (interquartile range 5–27 months) requiring NIV for respiratory failure after surgery, that NIV-NAVA improved patient-ventilator interaction (asynchrony index 2.3 %) compared to NIV-PSV (asynchrony index 40 %), even with optimization of expiratory trigger setting in PSV with Edi feedback. The improvement in synchrony was mainly due to reduced trigger delays and a reduction in ineffective efforts.

In younger children receiving NIV for respiratory support following cardiac surgery, Houtekie et al. [6] performed a cross-over study by randomizing babies (age range 1–22 weeks and weight <5 kg) to either nasal continuous positive airway pressure (CPAP) or NIV-NAVA immediately after extubation. The peak Edi values during NIV-NAVA were significantly lower, indicating more diaphragm unloading compared with nasal CPAP. Synchrony analysis was reported for NIV-NAVA and showed (despite average leakage of 70 %) 99 % neural triggering (compared with 95 % in the Vignaux et al. [5] study), with a low inspiratory trigger delay.

More recently, in another physiological cross-over study, NIV-NAVA was compared with conventional NIV in 13 children admitted to the pediatric intensive care unit for respiratory failure (interquartile age range 2–109 months), 8 of whom had pneumonia or bronchiolitis [7]. The authors found that during conventional NIV, patients spent between 27 and 32 % of the time in asynchrony, whereas it was only 8 % of the time in NIV-NAVA. This was mainly a result of reduced trigger delay, cycling-off delay, and ineffective efforts. These same authors also described the clinical importance of monitoring the Edi signal during all NIV modes after extubation in a recent review [13].

In 11 children with viral bronchiolitis who were failing nasal CPAP (aged on average 35 days), Baudin et al. [8] studied patient-ventilator interaction during nasal pressure assist control (settings determined clinically) versus NIV-NAVA (2 h each). With matching peak pressures in both modes, breath-by-breath analysis revealed a lower asynchrony index during NIV-NAVA, mainly due to less trigger delays. Ineffective efforts were extremely prevalent during nasal pressure assist control (~22 events per minute), and did not occur during NIV-NAVA. The number of auto-triggering events was higher in assist control (8 per minute) compared with NIV-NAVA. The neural respiratory rate and ventilator rate were comparable for NIV-NAVA; however, in pressure assist control, neural respiratory rate was higher than the ventilator rate.

In animals with early experimental injury, Mirabella et al. [9] examined lung injury markers after 6 h of volume control ventilation with a lung protective strategy (6 ml/kg with PEEP), compared with 6 h of NIV-NAVA and spontaneous breathing and no PEEP, and found a lower lung injury score and plasma interleukin (IL)-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 (FRC).

Conclusion

NAVA is a promising technique for NIV because it is able to provide synchronized and proportional assist, even in the presence of large leakage. In light of studies demonstrating the role of asynchrony on intensive care unit length of stay, duration of mechanical ventilation, and mortality [14], it would seem that improving synchrony should be a priority. NIV-NAVA allows the patient the freedom to choose their own breathing pattern, and to recruit the lung when needed with large inspirations (sighs) or maintenance of FRC with tonic activation of the diaphragm. The upper airway dilator muscles are coordinated with the onset of diaphragm activation, and therefore, the risk of gastric insufflation may be reduced with NIV-NAVA. We acknowledge that, in the presence of large leaks, pressure delivery may be underestimated, and it is possible that the NAVA level should be increased to compensate. The Edi signal offers the tool for this evaluation, as increasing the NAVA level – if resulting in unloading of the diaphragm – could be monitored. In addition, if respiratory rate is an important clinical metric, the neural frequency (which is unaffected by leaks) offers a reliable measurement, restoring confidence in decision support.

Key Major Recommendations

- Use NIV-NAVA to improve synchrony.
- Use Edi during NIV to obtain a reliable measure of neural respiratory drive.
- Use Edi during NIV to obtain a reliable measure of respiratory rate.

Disclosure Drs. Beck and Sinderby have made inventions related to neural control of mechanical ventilation that are patented. The patents are assigned to the academic institution(s) where the inventions were made. The license for these patents belongs to Maquet Critical Care. Future commercial uses of this technology may provide financial benefit to Drs. Beck and Sinderby through royalties. Dr. Beck and Dr. Sinderby each own 50 % of Neurovent Research Inc. (NVR). NVR is a research and development company that builds the equipment and catheters for research studies. NVR has a consulting agreement with Maquet Critical Care.

References

1. Sinderby C, Beck J. Neurally adjusted ventilatory assist. In: Tobin MJ, editor. Principles and practice of mechanical ventilation. 3rd ed. New York: McGraw Hill; 2012.
2. Sinderby C, Beck J. Neurally adjusted ventilatory assist in non-invasive ventilation. Minerva Anestesiol. 2013;79(8):915–25.
3. Oppersma E, Doorduin J, van der Heijden EH, et al. Noninvasive ventilation and the upper airway: should we pay more attention? Crit Care. 2013;17(6):245.
4. Doorduin J, Sinderby CA, Beck J, et al. Automated patient-ventilator interaction analysis during neurally adjusted non-invasive ventilation and pressure support ventilation in chronic obstructive pulmonary disease. Crit Care. 2014;18(5):550.
5. Vignaux L, Grazioli S, Piquilloud L, et al. Patient-ventilator asynchrony during noninvasive pressure support ventilation and neurally adjusted ventilatory assist in infants and children. Pediatr Crit Care Med. 2013;14(8):e357–64.
6. Houtekie L, Moerman D, Bourleau A, et al. Feasibility study on neurally adjusted ventilatory assist in noninvasive ventilation after cardiac surgery in infants. Respir Care. 2015;60(7):1007–14.
7. Ducharme-Crevier L, Beck J, Essouri S, et al. Neurally adjusted ventilatory assist (NAVA) allows patient-ventilator synchrony during pediatric noninvasive ventilation: a crossover physiological study. Crit Care. 2015;19:44.
8. Baudin F, Pouyau R, Cour-Andlauer F, et al. Neurally adjusted ventilator assist (NAVA) reduces asynchrony during non-invasive ventilation for severe bronchiolitis. Pediatr Pulmonol. 2014. doi:10.1002/ppul.23139.
9. Mirabella L, Grasselli G, Haitsma JJ, et al. Lung protection during non-invasive synchronized assist versus volume control in rabbits. Crit Care. 2014;18(1):R22.
10. Quintel M, Moerer O. Another brick in the wall of needs for invasive ventilation? Crit Care. 2014;18(2):122.
11. Ramet J, De Dooy J. Patient-ventilator asynchrony during noninvasive pressure support ventilation and neurally adjusted ventilatory assist in infants and children. Pediatr Crit Care Med. 2013;14(7):728–9.

12. Nava S, Pisani L. Neurally adjusted non-invasive ventilation in patients with chronic obstructive pulmonary disease: does patient-ventilator synchrony matter? Crit Care. 2014;18(6):670.
13. Ducharme-Crevier L, Du Pont-Thibodeau G, Emeriaud G. Interest of monitoring diaphragmatic electrical activity in the pediatric intensive care unit. Crit Care Res Pract. 2013;2013: 384210.
14. Blanch L, Villagra A, Sales B, et al. Asynchronies during mechanical ventilation are associated with mortality. Intensive Care Med. 2015;41(4):633–41.