Advances in ventilation – neurally adjusted ventilatory assist (NAVA) 317 1A03 1B04 2C04 3C00

A Skorko, D Hadfield, A Shah, P Hopkins

This review aims to introduce neurally-adjusted ventilatory assist (NAVA) to readers who do not have experience in using this form of ventilation. We will describe the basic principles and theoretical advantages of NAVA together with our experiences of introducing and using this mode in an intensive care unit.

Keywords: *mechanical ventilation; neurally adjusted ventilation assist; NAVA; synchrony; diaphragmatic EMG; weaning*

Introduction

Mechanical ventilation is a life-preserving intervention in a wide range of critical illnesses. Not only is it key to the resuscitation of patients with oxygenation or ventilatory failure from primary lung disease, it is also vital in the support of patients needing augmented oxygen delivery. In our institution, over the latest year analysed, 760 of 2,600 admissions (29%) were ventilated for longer than 48 hours, 379 (15%) for longer than 96 hours and 163 (6%) had tracheostomies performed (Medtrack data, Medical associated software house). Data published by ICNARC emphasises the significant contribution respiratory failure plays to critical illness in the UK.[1]

Controlled modes of ventilation, sometimes facilitated by pharmacological muscle relaxation, can be useful to completely replace the patient's respiratory effort during the initial stages of critical illness and resuscitation.[2] Post-resuscitation however, patient-triggered ventilatory support modes in conjunction with the ventilator care bundle are vital to expedite liberation of patients from mechanical ventilation.[3-5] Provided they are applied optimally, these modes can exercise the respiratory muscles and minimise iatrogenic muscular injury.[6,7] Several modes of spontaneous ventilatory support have been developed, aiming to strike the balance between beneficial activity and detrimental fatigue, including synchronised intermittent mandatory ventilation (SIMV), pressure support (PS) and proportional assist ventilation (PAV). Here, we describe the newest addition to the stable of support modes, neurally adjusted ventilatory assist (NAVA).

Basic principles and development of NAVA

The NAVA system was first described by Sinderby's group in 1999, as a way to detect diaphragmatic electrical activity via an adapted nasogastric (NG) tube (the NAVA catheter) and use it to drive a ventilator (**Figure 1**).[8]

There are two major differences between NAVA and conventional modes of ventilation. The first is that rather than using pneumatic/flow triggering (where the ventilator detects a pressure/flow change in the circuit from patient effort), NAVA uses the neural signal of diaphragmatic electrical activity (EAdi) to initiate the mechanical offloading of respiratory muscles, referred to as neural triggering.

Figure 1 Position of the NAVA catheter in relation to the diaphragm.

The second difference is that, once initiated, a breath is assisted with pressure support in proportion to the amplitude of the EAdi signal. The EAdi signal is sampled every 16 ms; such rapid sampling enables the ventilator to titrate support throughout the course of every breath as well as between breaths.

The commercial NAVA system is now available on the Servo-I (Maquet) ventilator platform.[9-11]

Potential advantages

Data from animal and small-scale human studies, together with individual institutional experience, suggests several potential advantages of NAVA over conventional modes of pressure support, principally through improved synchrony and proportionality of support.[12-14] However, evidence from randomised controlled trials showing the clinical superiority of NAVA is still lacking.

Figure 2 Screenshot from a Servo-I ventilator showing NAVA preview mode. The white pressure curve is the hypothetical pressure trace that would be achieved if NAVA mode were used at the specified level, superimposed over the current pressure trace.

EAdi as a monitoring tool

Measuring EAdi offers an insight into a patient's respiratory drive and neural demand for ventilatory support. So long as the NAVA catheter remains *in situ* and connected to a ventilator, EAdi can be continuously recorded, even in the absence of mechanical ventilation. This ability to constantly monitor EAdi, independent of NAVA's other role as a novel form of ventilatory support, has enhanced our basic understanding of respiratory physiology in health and disease.[9,15-20]

The use of NAVA as a monitor in conjunction with the ventilator's 'NAVA preview' screen (where a predicted NAVA pressure trace is superimposed on the current pressure trace) provides a useful means of introducing the NAVA concept to a naive ICU without committing the team to the mode as a means of ventilation (**Figure 2**).

The ventilator also has the facility to display data from the preceding 24 hours, so can be used to track the trend in EAdi. This has proved very informative when reviewing the impact of ventilatory manoeuvres on respiratory drive (**Figure 3**).

Neural monitoring may well prove to be invaluable in a variety of situations, from pre-empting deterioration on non-invasive ventilation (NIV) or predicting the need for re-intubation, through to tracking respiratory recovery and aiding prognostication in spinal cord trauma, as well as facilitating research into diaphragmatic function.[21] One possibility is to quantify the patient's ability to convert neural demand into tidal ventilation (via a neuro-ventilatory efficiency index) and see whether this can predict failure to wean.[22,23]

Monitoring neural demand may one day enable every patient to have a truly individualised weaning programme, tailored according to the relative impact that mobilisation, airway weaning and ventilatory weaning have on their EAdi.

Improved synchrony

Asynchrony occurs when there is uncoupling of the patient's neural demand to breathe from the ventilator's mechanically delivered breaths. It can be a profound barrier to ventilatory weaning, leading to more ventilator days, higher rates of

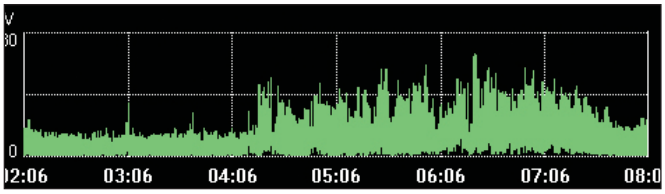

Figure 3 Screenshot from Servo-I ventilator of a six-hour trend in EAdi. This patient was initially on CPAP and at 4 am was put on a trache mask, with a rise in EAdi as neural demand increased.

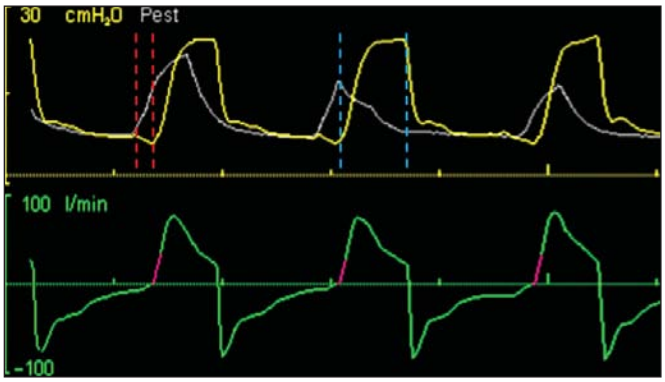

Figure 4 Screenshot from a Servo-I ventilator showing overlapping pressure curves; actual pressure curve in pressure support mode (yellow) and theoretical curve if patient were in NAVA mode (white). Inspiratory asynchrony (where neural inspiration begins before flow is triggered), is shown by lack of overlap of the red lines. Expiratory asynchrony (where neural demand starts to fall but the pressure trace shows that mechanical ventilation continues) is shown by lack of overlap of blue lines.

tracheostomy and a trend toward increased patient mortality.[24] Neural triggering has been shown to reduce patient-ventilator asynchrony.[12-15]

Asynchrony can occur during the inspiratory or expiratory phase.[13,23,25] Both types of asynchrony become more pronounced with increasing levels of pressure support but not with NAVA.[13,16,20]

Inspiratory asynchrony occurs during the triggering phase of a breath. It occurs as a result of trigger delay or failure (for example when a patient is weak, has low respiratory drive or is over-inflated) the result of which is that a patient-demanded breath is sensed too late or not at all (**Figure 4**). NAVA, by using neural triggering, overcomes this form of asynchrony and has the added benefit of a faster triggering time.[13]

Expiratory asynchrony occurs when 'cycling off' occurs inappropriately, either too early or too late. This results in either prolonged or prematurely discontinued mechanical inflation as compared to the neural respiratory cycle (**Figure 4**). This form of asynchrony has become more readily apparent as a result of EAdi monitoring and has proven to be an impediment to weaning.[9,13,26]

A third discrete form of asynchrony known as 'flow-assist asynchrony' refers to the discrepancy between the magnitude of neural demand and actual support delivered, which again has become more apparent since neural monitoring has become available.

In our experience 'over-ventilation' (often coupled with over-sedation) proved to be unexpectedly common once we

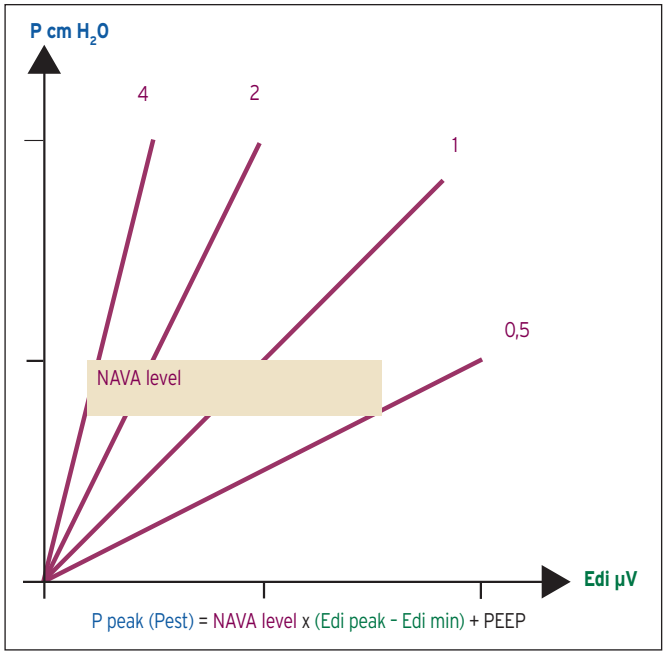

Figure 5 Graphical representation of relationship between NAVA level and actual pressure support delivered. As the NAVA level is increased by the operator the amount of pressure delivered per microvolt of EAdi is increased by the factor of the NAVA level.

began to monitor EAdi. We have found that initiating EAdi monitoring often leads to an accelerated reduction of support and an earlier ability to challenge patients with spontaneous breathing trials. In our ICU this has resulted in an increase in ventilator-free days in survivors.[27]

Proportionality of support

With conventional pressure support ventilation, the degree of assistance is user-defined and identical for every breath. NAVA support, on the other hand, is adjusted every 16 ms during each breath, which results in a more heterogeneous pressure-time curve. Studies suggest that greater breath-to-breath variability may improve oxygenation and lung mechanics and potentially increase the chance of successful extubation.[28-30]

The relationship between EAdi and pressure support can be augmented by the NAVA level. This offers a 'gain' in the following way:

Paw (cm H_2O) = EAdi (µV) × NAVA level (cm H_2O/µV).

The clinician can therefore amplify the amount of support offered by the factor of the NAVA level. For example if EAdi is 8 µV and NAVA level set at 2, the patient will receive 16 cm H_2O pressure support (**Figure 5**).

Protection against ventilator-induced lung injury (VILI)

As it is coupled to the respiratory centre's output, NAVA takes advantage of the various protective reflexes that exist within the respiratory system to reduce the risk of over-ventilation.[18] Studies in both animals and critically ill patients have demonstrated that even with the application of NAVA levels over and above those required to optimally off-load the respiratory muscles, subjects were able to down-titrate their EAdi to maintain tidal volumes (Vt) in the range of 6-9 mL/kg.[16,23,28,31] Brander *et al* also investigated biomarkers of biotrauma (IL-8 levels in plasma and lungs) and found them to be reduced in animal models of acute lung injury when comparing NAVA with PS at Vt of 6 mL/kg.[17]

Basic assumptions
The diaphragm is the primary respiratory muscle and so electrical activity of the diaphragm is equivalent to total neural demand
The neuro-ventilatory coupling circuit is intact: • Output from respiratory centre is present and appropriate • Phrenic nerve, diaphragm and the neuromuscular junctions are all intact and function appropriately • Patient is not sedated to the extent that respiratory drive is suppressed
Other noxious stimuli are not over-activating the respiratory centre and causing hyperventilation
Sensitivity of the feedback loop to the respiratory centre (eg via chemo and baroreceptors) is appropriate

Table 1

Absolute contra-indications to NAVA
Oesophageal, pharyngeal or maxilo-facial pathology or trauma preventing NG or OG tube insertion
Brainstem or high spinal cord injury (above C3)
Severe neuropathy (eg demyelination) affecting phrenic nerve signalling
Raised intra-cranial pressure
Analgesic/hypnotic dose causing total respiratory drive depression
Patients receiving muscle relaxants

Table 2

Other advantages

Numerous other benefits have been postulated with NAVA ventilation. Chief among these is improved quality of sleep, an important determinant of successful weaning.[32,33] In a cohort crossover study, patients ventilated with NAVA had a higher proportion of REM sleep and less fragmented sleep.[34]

Limitations of NAVA

In order to understand the limitations of NAVA it is important to be aware of the assumptions it makes (**Table 1**) and its contraindications (**Table 2**).[35]

Clinical experience shows that not all patients ventilate appropriately with NAVA; the causes for this are still to be fully understood.[36,37] In particular, patients with severe adult respiratory distress syndrome (ARDS) often become tachypnoeic and do not have safe tidal volumes despite offloading with high NAVA levels. It is postulated that in such instances, the respiratory centre is overwhelmed by inputs from a myriad of nociceptors, so that despite mechanically offloading the respiratory system there remains an excessive drive to breathe.[38] In such instances, it may be of benefit to disregard central respiratory output and to ventilate the patient with a mandatory mode until the noxious stimuli abate. An

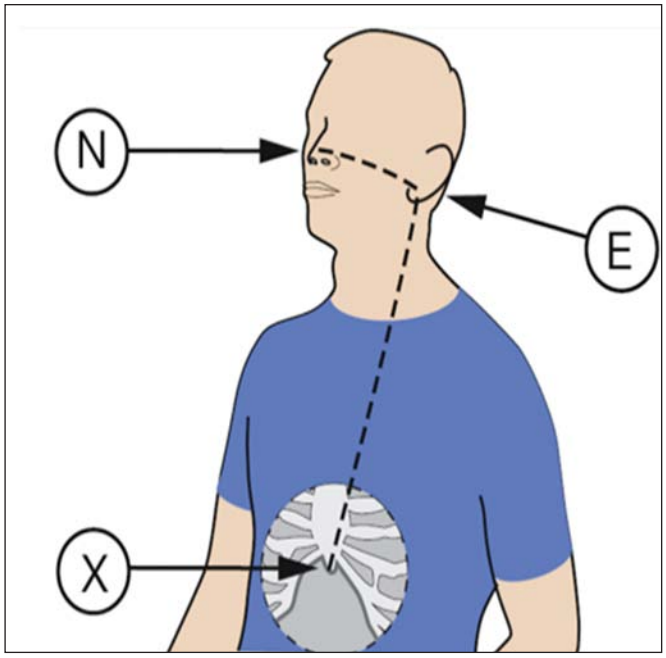

Figure 6 Calculating the nose-ear-xyphisternum (NEX) measurement.

alternative strategy may be to remove the noxious stimulus (eg, with extracorporeal CO_2 removal) while maintaining the patient with a spontaneous ventilatory mode. To this end, Karagiannidis *et al* investigated the use of NAVA with veno-venous extracorporeal membrane oxygenation (VV ECMO) in six patients and demonstrated that such a strategy is feasible.[39]

In our experience, ARDS is not an absolute contraindication to NAVA and we have successfully used the mode in early ARDS even with oxygenation indices in excess of 20. The optimal strategy seems to require 'opening the lung' and establishing adequate PEEP (using high frequency oscillation and/or muscle relaxants if necessary) and only once recruitment is adequate, making an attempt to acquire EAdi in conjunction with a sedation hold. Using such a strategy, we have had anecdotal success in using NAVA to wean patients with ARDS.

Practical aspects of NAVA ventilation

Patient selection

NAVA is a well-tolerated and extremely adaptable technology useful in a wide range of patients, from respiratory to neurological critical illness to those with very poor lung compliance.[23,39-43] Overall, it is postulated that NAVA will be of greatest benefit in patients with chronic heart and lung diseases in whom weaning is likely be prolonged or who have previously failed with alternative modes.

There are few absolute contraindications to NAVA (**Table 2**), provided a patient is capable of neurally triggering ventilation. 'Over-ventilation' with conventional ventilatory modes activates central reflexes which cause the respiratory centre to become quiescent and so it may be necessary to reduce support before an EAdi signal can be appreciated.[25]

Signal detection

The technique of NAVA catheter insertion is the same as that of

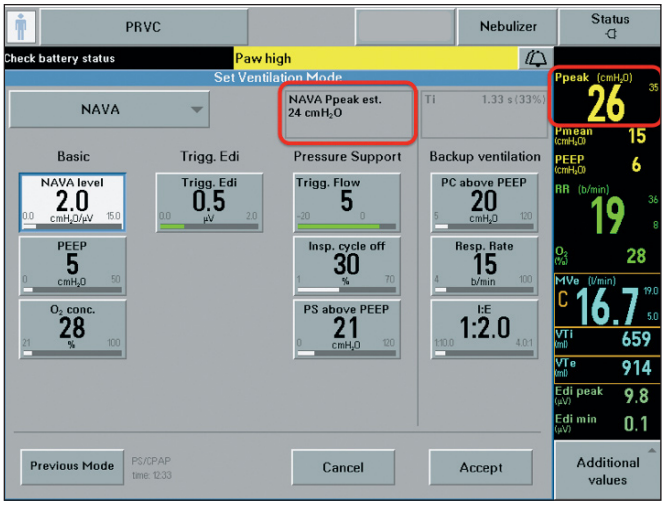

Figure 7 Screenshot from Servo-I to demonstrate NAVA level selection. The NAVA level is increased until the estimated NAVA Ppeak is equivalent to that in the current ventilatory mode.

an ordinary NG tube. However, in order to maximise EAdi pick-up, the position of the catheter tip is critical. To this end, two specific tools are used: the Nose-Ear-Xiphoid or 'NEX' measurement provides an estimated catheter insertion length[10] (**Figure 6**) and a 'catheter positioning tool' on the ventilator facilitates optimal placement to maximise EAdi pick-up. Once *in situ* the NAVA catheter can be used as a standard NG tube for feeding or gastric decompression.

Although NAVA has been used for extended periods, it is important to emphasise the manufacturer's recommendation of a maximum use period of seven days per catheter. After this, although there is signal fidelity, degradation of the detector array is often visible.

Setting the NAVA level

There are two main methods by which the initial NAVA level can be set. One method is to use the principle of 'equipotence' and choose a NAVA level that produces a Ppeak equivalent to that on conventional ventilation[16] (**Figure 7**). This method has the advantage of being easy to achieve so is useful where clinical pressure limits the time available for titration.

An alternative strategy is the titration procedure.[19,31,38] With this method, the NAVA level is set at a low level and increased in 0.1 µV increments every 20 seconds while trends in Vt, peak airway pressure (Paw) and EAdi are assessed. Escalating NAVA levels will cause the Vt and Paw to rise and the EAdi to fall as ventilatory support begins to meet neural demand. The Vt and Paw will initially rise steeply but then plateau at a point where the respiratory system is optimally offloaded. The optimal NAVA level is deemed to be at the point of transition to this plateau.[20,31] Further increasing NAVA beyond this plateau point will lead to a minimal rise in Vt and Paw at the expense of continually falling EAdi. It is important to note that in NAVA mode the EAdi signal will never be totally abolished, even with excessive NAVA levels, but instead the respiratory pattern may become chaotic.[16,25,31] This method of NAVA titration is used for research purposes to select precise NAVA levels, and although more accurate, is time-consuming and may be inappropriate in acutely unwell patients.

Triggering and cycling off

Breath triggering with NAVA occurs when EAdi increases by 0.5 µV above the patient's EAdi(min), this degree of change being higher than variability seen due to external noise.[25]

A breath may still be initiated by conventional pneumatic triggers, as triggering occurs on a 'first come, first served' basis. As with other ventilatory modes, the sensitivity of triggers can be altered but our experience shows that this rarely needs changing.

Cycling off is fixed and occurs when the EAdi falls to 70% of peak EAdi (**Figure 8**). Additional parameters may also lead to cycling off; if the upper pressure limit is achieved, if pressure rises by more than 3 cm H_2O above target inspired pressure or when maximum inspired time limit is exceeded (2.5 seconds for adults). The ventilator also has backup pressure support and pressure control modes (with adjustable defaults) should the EAdi signal be insufficient or apnoea occur.

NAVA and PEEP

With conventional modes of ventilation, patients who have high intrinsic PEEP need to expend significant effort to overcome it in order to trigger the ventilator, leading to a high number of ineffective efforts and increased work of breathing.[14] One approach to combating this is to set a high extrinsic level of PEEP on the ventilator, accepting the potential risks. With NAVA, patients do not have to expend effort overcoming intrinsic PEEP to trigger ventilation so extrinsic PEEP can be set at lower levels.

Evidence suggests that EAdi may be a useful adjunct for titrating PEEP. Specifically, it has been demonstrated that when extrinsic PEEP is inadequate, high levels of EAdi (min) are seen in a phenomenon called 'tonic EAdi.' It is postulated that this is a sign of inadequate PEEP, as it resolves with the application of extrinsic PEEP.[25,29,38]

Weaning NAVA

The optimal strategy for weaning NAVA has yet to be determined and there are several hypotheses. As with all forms of invasive ventilation, the ventilator care bundle remains a vital part of patient management. In particular, consideration of daily sedation holds and spontaneous breathing trials (SBTs) remain invaluable. One approach adopted by Roze *et al* used EAdi measurements during SBTs to titrate NAVA levels on a daily basis.[44] Alternatively, gradual 're-loading' of respiratory muscles over time by reducing the NAVA level, with an option to schedule periods of nocturnal rest (eg using a synchronised control mode) may also prove a reasonable approach.

EAdi monitoring can inform the weaning process in a number of ways. As recovery occurs, neuro-ventilatory coupling becomes more efficient and so the EAdi is lower with the same degree of support. In terms of weaning, reducing the NAVA level at this stage should lead to only a minimal drop in Vt and Paw and only a small rise in EAdi. Monitoring of neural demand has also shown potential as an adjunct to traditional predictors for extubation success such as the rapid shallow breathing index.[22]

Overall, it is likely that a protocolised weaning schedule will provide better outcomes than *ad hoc* weaning of NAVA levels, as has been shown in numerous ventilatory weaning studies.[45]

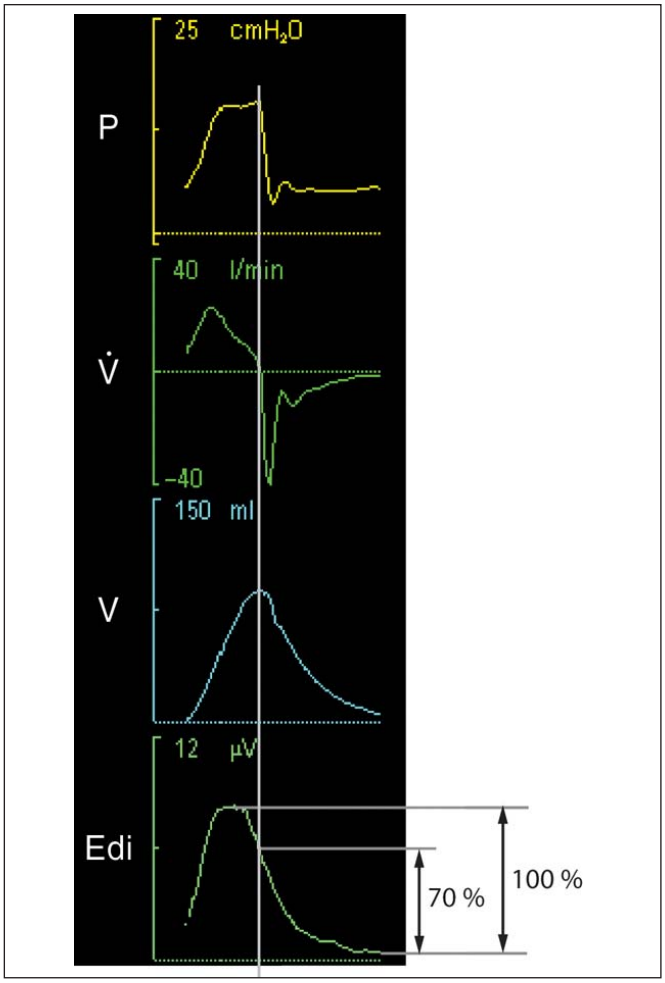

Figure 8 Cycling off occurs when EAdi falls to 70% of maximum EAdi.

Non-invasive ventilation (NIV)

Given that air leaks during NIV lead to profound patient-ventilator asynchrony, this seems a logical place for the use of NAVA.[46] The main limiting factors are the need for NG insertion and that NIV must be driven through a Servo-I ventilator. Several centres in Europe use this technique and have demonstrated improved synchrony.[47,48] However, there remains limited evidence for outcome benefits compared to alternate interfaces.[49,50]

Summary

Neurally-adjusted ventilation assist provides a novel way to enhance patient-ventilator synchrony. Critically, it is not dependent on the presence of an endotracheal tube and non-invasive systems are commercially available. Its method of signal detection is minimally invasive and is stable over time. Independent of the signal's ability to drive ventilatory support, the EAdi provides an invaluable monitor of neural demand that can be informative even post-extubation. Although it does not provide a ventilatory panacea, NAVA is effective in a wide number of clinical settings.

However, despite some key theoretical advantages over conventional modes, no randomised controlled trial data exist to substantiate these. Even more fundamentally, there is no

clear evidence base for either optimal initiation of NAVA support or best practice for weaning it. A recent roundtable report suggests that a consensus of how best to apply this technology is not far away.[38]

The introduction of NAVA to our own institution required a significant investment in research nurse and practice development nurse time. The formation of a super-user group to develop protocols, ensure the safe and effective use of this technology and perform parallel translational research has been critical. Overall, it is our belief that the time and effort we have invested in NAVA has been repaid. The system provides insight into pulmonary mechanics and physiology and enhances inter-professional use of ventilatory support. Finally, NAVA makes teleological sense, is intuitive to use and reinforces other ventilatory practices that do have a strong evidence base for saving lives and money.

Conflict of interest

Drs. Skoro, Hadfield and Hopkins have received sponsorship from Maquet to attend NAVA-related conferences.

No financial support was received for this work.

Aknowledgement

We are grateful to Maquet for supplying images 1, 5, 6 and 8 and for permission to publish these.

References

1. **Harrison D, Brady A, Rowan K**. Case mix, outcome and length of stay for admissions to adult general critical care units in England, Wales and Northern Ireland: the Intensive Care National Audit and Research Centre case mix programme database. *Crit Care* 2004;8:R99-R111.
2. **Papazian L, Forel JM, Gacouin A *et al***. Neuromuscular blockers in early acute respiratory distress syndrome. *N Engl J Med* 2010;363:1107-16.
3. **Ely E, Baker A, Dunagan D *et al***. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. *N Engl J Med* 1996;335:1864-69.
4. **Kress J, Pohlman A, O'Connor M, Hall J**. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med* 2000;342:1471-77.
5. **Girard T, Kress J, Fuchs B *et al***. Efficacy and safety of paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awake and Breathing Controlled trial): a randomised controlled trial. *Lancet* 2008;371:126-34.
6. **Vassilakopoulos T, Petrof B**. Ventilator-induced diaphragmatic dysfunction. *Am J Respir Crit Care Med* 2004;169:336-41.
7. **Hudson M, Smuder A, Nelson W**. Both high level pressure support ventilation and controlled mechanical ventilation induce diaphragmatic dysfunction and atrophy. *Crit Care Med* 2012;40:1254-60.
8. **Sinderby C, Navalesi P, Beck J *et al***. Neural control of mechanical ventilation in respiratory failure. *Nat Med* 1999;5:1433-36.
9. **Beck J, Gottfried S, Navalesi P *et al***. Electrical activity of the diaphragm during pressure support ventilation in acute respiratory failure. *Am J Respir Crit Care Med* 2001;164:419-24.
10. **Barwing J, Ambold M, Linden N *et al***. Evaluation of the catheter positioning for neurally adjusted ventilatory assist. *Intensive Care Med* 2009;35:1809-14.
11. **Barwing J, Pedroni C, Quintel M, Moerer O**. Influence of body position, PEEP and intra-abdominal pressure on the catheter positioning for neurally adjusted ventilatory assist. *Intensive Care Med* 2011;37:2041-45.
12. **Schmidt M, Demoule A, Cracco C *et al***. Neurally adjusted ventilatory assist increases respiratory variability and complexity in acute respiratory failure. *Anesthesiology* 2010;112:670-81.
13. **Spahija J, de Marchie M, Albert M *et al***. Patient-ventilator interaction during pressure support ventilation and neurally adjusted ventilation assist. *Crit Care Med* 2010;38:518-26.
14. **Piquilloud L, Vignaux L, Bialais E *et al***. Neurally adjusted ventilatory assist improves patient-ventilator interaction. *Intensive Care Med* 2011;37:263-71.
15. **Beck J, Campoccia F, Allo J *et al***. Improved synchrony and respiratory unloading by neurally adjusted ventilatory assist (NAVA) in lung-injured rabbits. *Pediatr Res* 2007;61:289-94.
16. **Colombo D, Cammarota G, Bergamaschi V *et al***. Physiologic response to varying levels of pressure support and neurally adjusted ventilatory assist in patients with acute respiratory failure. *Intensive Care Med* 2008;34: 2010-18.
17. **Brander L, Sinderby C, Lecomte F *et al***. Neurally adjusted ventilatory assist decreases ventilator-induced lung injury and non-pulmonary organ dysfunction in rabbits with acute lung injury. *Intensive Care Med* 2009;35:1979-89.
18. **Leiter J, Manning H**. The Hering-Breuer reflex, feedback control, and mechanical ventilation: the promise of neurally adjusted ventilatory assist. *Crit Care Med* 2010;38:1915-16.
19. **Passath C, Takala J, Tuchscherer D *et al***. Physiological responses to changing positive end-expiratory pressure during neurally-adjusted ventilatory assist in sedated, critically ill adults. *Chest* 2010;138:578-87.
20. **Terzi N, Pelieu I, Guittet L *et al***. Neurally adjusted ventilatory assist in patients recovering spontaneous breathing after acute respiratory distress syndrome: Physiological evaluation. *Crit Care Med* 2010;38:1830-37.
21. **Doorduin J, Sinderby C, Beck J *et al***. The calcium sensitizer levosimendan improves human diaphragm function. *Am J Respir Crit Care Med* 2012;185:90-95.
22. **Liu L, Liu H, Yang Y *et al***. Neuro-ventilatory efficiency and extubation readiness in critically ill patients. *Crit Care* 2012;16:R143.
23. **Tuchscherer D, Z'Graggen W, Passath C *et al***. Neurally adjusted ventilatory assist in patients with critical illness polyneuropathy. *Intensive Care Med* 2011;37:1951-61.
24. **Navalesi P, Colombo D, Della Forte F**. NAVA ventilation. *Minerva Anaesth* 2010;76:346-52.
25. **Sinderby C, Beck J**. Neurally adjusted ventilatory assist (NAVA): An update and summary of experiences. *Neth J Crit Care* 2007;11:243-52.
26. **Chiumello D, Polli F, Tallarini F *et al***. Effect of different cycling-off criteria and positive end-expiratory pressure during pressure support ventilation in patients with chronic obstructive pulmonary disease. *Crit Care Med* 2007; 35:2547-52.
27. **Hadfield D, Colorado L, Vercueil A, Hopkins P**. The introduction of neurally adjusted ventilatory assist (NAVA) into a central London teaching hospital and a comparison with conventional pressure support. *Intensive Care Med* 2010; 36:S108.
28. **Patroniti N, Bellani G, Saccavino E *et al***. Respiratory pattern during neurally adjusted ventilatory assist in acute respiratory failure patients. *Intensive Care Med* 2011;38:230-39.
29. **Allo J, Beck J, Brander L *et al***. Influence of neurally adjusted ventilatory assist and positive end-expiratory pressure on breathing pattern in rabbits with acute lung injury. *Crit Care Med* 2006;34:2997-3004.
30. **Coisel Y, Chanques G, Jung B *et al***. Neurally adjusted ventilatory assist in critically ill postoperative patients: a crossover randomized study. *Anesthesiology* 2010;113:925-35.
31. **Brander L, Leong-Poi H, Beck J *et al***. Titration and implementation of neurally adjusted ventilatory assist in critically ill patients. *Chest* 2009;135:695-703.
32. **Bosma K, Ferreyra G, Ambrogio C *et al***. Patient-ventilator interaction and sleep in mechanically ventilated patients: pressure support versus proportional assist ventilation. *Crit Care Med* 2007;35:1048-54.
33. **Cabello B, Thille A, Drouot X *et al***. Sleep quality in mechanically ventilated patients: comparison of three ventilatory modes. *Crit Care Med* 2008;36:1749-55.
34. **Delisle S, Ouellet P, Bellemare P *et al***. Sleep quality in mechanically ventilated patients: comparison between NAVA and PSV modes. *Ann Intensive Care* 2011;1:42-9.

35. **Laghi F**. NAVA; brain over machine? *Intensive Care Med* 2008;34:1966-68.
36. **Roze H, Richard JC, Mercat A, Brochard L**. Recording of possible diaphragm fatigue under neurally adjusted ventilatory assist. *Am J Resp Crit Care Med* 2011;184:1213-14.
37. **Brander L, Beck J, Sinderby C**. Interpreting success or failure of neurally adjusted ventilatory assist. *Am J Resp Crit Care Med* 2012;185:1248.
38. **Terzi N, Piquilloud L, Roze H *et al***. Clinical review: Update on neurally adjusted ventilatory assist – report of a round-table conference. *Crit Care* 2012;16:225 .
39. **Karagiannidis C, Lubnow M, Philipp A *et al***. Autoregulation of ventilation with neurally adjusted ventilatory assist on extracorporeal lung support. *Intensive Care Med* 2010;36:2038-44.
40. **Beck J, Weinberg J, Hamnegard C *et al***. Diaphragmatic function in advanced Duchenne muscle dystrophy. *Neuromus Disord* 2006;16:161-67.
41. **Roze H, Janvier G, Ouattara A**. Cystic fibrosis patient awaiting lung transplantation ventilated with neurally-adjusted ventilatory assist. *Br J Anaesth* 2010;105:97-98.
42. **Barwing J, Linden N, Ambold M *et al***. Neurally-adjusted ventilatory assist vs pressure support ventilation in critically ill patients: an observational study. *Acta Anaesthesiol Scand* 2011;55:1261-71.
43. **Mauri T, Bellani G, Foti G *et al***. Successful use of neurally-adjusted ventilatory assist in patients with extremely low respiratory system compliance undergoing ECMO. *Intensive Care Med* 2011;37:166-67.
44. **Rozé H, Lafrikh A, Perrier V *et al***. Daily titration of neurally adjusted ventilatory assist using the diaphragm electrical activity. *Intensive Care Med* 2011:37:1087-94.
45. **Blackwood B, Alderdice F, Burns K *et al***. Protocolized versus non-protocolized weaning for reducing the duration of mechanical ventilation in critically ill adult patients. *Cochrane Database Systematic Rev* 2010;5: CD006904.
46. **Beck J, Brander L, Slutsky A *et al***. Non-invasive neurally-adjusted ventilatory assist in rabbits with acute lung injury. *Intensive Care Med* 2008;34:316-23.
47. **Moerer O, Beck J, Brander L *et al***. Subject-ventilator synchrony during neural versus pneumatically triggered non-invasive helmet ventilation. *Intensive Care Med* 2008;34:1615-23.
48. **Cammarota G, Olivieri C, Costa R *et al***. Noninvasive ventilation through a helmet in postextubation hypoxemic patients: physiologic comparison between neurally adjusted ventilatory assist and pressure support ventilation. *Intensive Care Med* 2011;37:1943-50.
49. **Bertrand P, Futier E, Coisel Y *et al***. Neurally adjusted ventilatory assist versus pressure support ventilation for non-invasive ventilation during acute respiratory failure: a cross-over physiological study. *Chest* 2013; 143:30-36.
50. **Schmidt M, Dres M, Raux M *et al***. Neurally-adjusted ventilatory assist improves patient-ventilator interaction during post-extubation prophylactic non-invasive ventilation. *Crit Care Med* 2012;40:1738-44.

Agnieszka Skorko Clinical Research Fellow in Intensive Care, King's College Hospital, London

Daniel Hadfield BRC Fellow, King's College Hospital, London

Anand Shah Foundation Year 1, The Whittington Hospital

Philip Hopkins Consultant in Intensive Care, King's College Hospital, London
p.hopkins@nhs.net