Spring 2021

Neurally Adjusted Ventilatory Assist: Summation of the Safety Proofs and Benefits

Landry Carneal
The University of Akron, lrc46@uakron.edu

Neurally Adjusted Ventilatory Assist: Summation of the Safety Proofs and Benefits

Landry Carneal

Department of Respiratory Therapy

Honors Research Project

The Williams Honors College, The University of Akron

April 23, 2021

Abstract.

Neurally Adjusted Ventilatory Assist (NAVA) is a mode of ventilation that is triggered by neither flow nor pressure but by the electrical activity of the diaphragm (Stein & Firestone, 2018, p. 227). NAVA puts ventilatory control into the hands of the patient and is often used in neonates who are more challenging to ventilate. Medical practitioners, however, are skeptical to put this mode of ventilation into practice with fear that neonates are neither strong enough nor capable to manage their own respiratory efforts without hypoventilation or damage to the lungs (Lubarsky et al., 2020, p. 3). Research shows that despite these apprehensions, neonates are able manage their own breathing safely and effectively (Lubarsky et al., 2020; Stein & Firestone, 2018). NAVA also offers some benefits in comparison to other traditional modes of ventilation such as quicker weaning, better patient-ventilator synchrony, and decreased work of breathing (Stein & Firestone, 2018, p. 228, 232; Matlock et al., 2020; Schmidt et al., 2012). The NAVA technology does not simply stop at ventilation alone; it is an additional asset that can provide CPAP with backup ventilation in cases of Apnea of Prematurity and can aid in detecting CCHS, a hypoventilation syndrome (Hussain et al., 2020; Rauf et al., 2019). NAVA is of great value to the neonatal intensive care unit and beyond.

Introduction.

Mechanical ventilation is used in patients when they are unable to control and maintain their respiratory efforts. This is to ensure a patient receives adequate oxygenation and ventilation delivery while they recover from the predisposing issue causing their failure to be able to breathe completely on their own (Verbrugghe & Jorens, 2011, p. 328). Within mechanical ventilation, there are several different modes of ventilation such as Volume Control, Pressure Control, Pressure Regulated Volume Control, etcetera. Each of these modes of ventilation delivers a breath uniquely and is used for different circumstances, but gets the job done nonetheless. All assisted modes of mechanical ventilation can be triggered by the patient spontaneously when they want a breath. This means the ventilator delivers a breath when it senses an inspiratory effort by either flow or pressure. A flow-triggered mode will deliver a breath when the patient inhales a certain amount of flow which is measured in liters per minute, while a pressure-triggered mode will deliver a breath when a drop in pressure is detected within the circuit (p. 328). Then, there is a new mode of ventilation called Neurally Adjusted Ventilatory Assist (NAVA). NAVA is triggered by neither flow nor pressure, but by the electrical signal of the diaphragm (Stein & Firestone, 2018, p. 227).

The electrical signal from the diaphragm is referred to as Edi and is detected by a specialized nasogastric tube which is placed at the level of the diaphragm in the patient (Stein & Firestone, 2018, p. 227). The diaphragm contracts by demand of the central nervous system and the phrenic nerve in order to initiate a breath, so to have inspiratory effort detection at the level of the diaphragm is of benefit (Verbrugghe & Jorens, 2011, p. 329). Once the ventilator senses the electrical impulse from the diaphragm, the machine will deliver an amount of flow that is proportional to the amount of electrical activity that was sensed (Stein & Firestone, 2018, p.

227). NAVA puts much of the control of ventilation into the hands of the patient and allows for several advantages to be seen through this newer mode of ventilation and patient triggering.

NAVA is used in neonates and pediatric patients primarily because they are much more difficult to effectively ventilate due to asynchrony, air leaking around the endotracheal tube used to deliver breaths, their higher respiratory rates, and because children often are not as sedated as an adult patient would be (Firestone, K., personal communication, November 25, 2020). Additionally, other modes of ventilation triggered by flow or pressure are harder to be precise in neonates due to their tiny nature; a pressure or flow difference in a neonate is minuscule compared to that of an adult. NAVA is still rather new to the healthcare field as its debut occurred only eleven years ago, and there are many health care practitioners who already have all the means to do so, but do not implement this new mode of ventilation in their NICUs and PICUs. Many are apprehensive to allow a neonate or a pediatric patient to have so much control over their own breathing (Lubarsky et al., 2020, p. 3). However, there is adequate evidence to convince a neonatologist who already has the equipment, to implement NAVA in their NICUs and PICUs.

In order to implement NAVA, the hospital must already have, or be willing to purchase the necessary equipment and software. The Neurally Adjusted Ventilatory Assist mode is only offered on the Getinge-Maquet Servo ventilators but can be delivered both invasively and noninvasively (Verbrugghe & Jorens, 2011, p. 331). Invasive deliverance is through the endotracheal tube, while noninvasive deliverance could be through a mask or a RAM cannula similar to normal noninvasive ventilation (p. 333). The only other additional item the medical practitioner needs to deliver NAVA would be the special nasogastric tube to be able to place at the level of the diaphragm and detect the Edi (p. 331).

Research.

Some doctors and healthcare professionals are skeptical to believe that a neonate can control their own respiratory efforts. This means that they are afraid that the neonate may take too large of breaths causing barotrauma due to the large amount of pressure delivered to their tiny lungs (Lubarsky et al., 2020, p. 3). Another worry is that they will take too few, tiny breaths leading to inadequate ventilation and oxygenation (p. 3). However, ample evidence is present to prove that a neonate can indeed tell us what is best for them.

A study on the changes of the electrical activity of the diaphragm in response to painful stimuli was conducted to seek and answer these very concerns. Because NAVA "delivers inspiratory pressure in proportion to the electrical activity of the diaphragm, and because NAVA allows self-regulation of [peak inspiratory pressure], there is apprehension that painful stimulus may increase respiratory drive and result in excessive [peak inspiratory pressure]" (Lubarsky et al., 2020, p. 3). This study was conducted on fourteen neonates less than 32 weeks of age on NAVA and NIV NAVA, and the painful stimulus was a heel stick which was already ordered for a necessary blood sample on the patient (p. 3). The results of this study proved that "although premature neonates respond to pain with increases in their respiratory drive, these increases do not trigger sustained, excessive PIPs" (Lubarsky et al., 2020, p. 8). This study adds to the literature in proving that while there may be a slight increase for the neonate's respiratory drive momentarily, it is still within normal limits. It is imperative that the healthcare professionals simply set appropriate limits so that the staff is aware when more dangerous pressures are being reached.

An additional built-in safeguard to prevent the over ventilation and increased pressures worried upon by healthcare professionals would be that of the Hering-Breur reflex. The

Hering-Breuer reflex is a lung protective mechanism evident in both neonates and adults. It works “as the lung inflation progresses, vagally mediated stretch receptors in the lungs sense an adequate level of lung distension and turn off inspiration, so the ventilator will be cycled off when neural exhalation begins” (Stein & Firestone, 2018, p. 228). This lung protective strategy may be an explanation to the results seen in research conducted by changing the NAVA levels in premature neonates to see its effect on the peak inspiratory pressure. This was done by increasing the NAVA level by 0.5 cm H_2O μV^{-1} every 3 minutes, starting at 0.5 and ending at 4.0 cm H_2O μV^{-1} (Firestone et al., 2015, p. 1). The outcome of this study revealed that as the NAVA level was initially increased, the peak inspiratory pressures and amount of respiratory support also increased. However, as the NAVA level continued to rise, a breakpoint (BrP) was reached (p. 3). This breakpoint is where the PIP seemed to plateau based on a safe level delivered to the neonate, which suggested that an adequate amount of ventilatory support was reached without over distending the lungs. As the NAVA level passed the breakpoint, the pressure did not increase further; simply more muscle unloading was present, which gave most of the control to the ventilator rather than the patient (p. 3). This study adds to the evidence that even as the NAVA level is increased, neonates still have the reflective responses to signal when enough pressure has been delivered to their lungs to protect from over-distention.

Benefits.

Neurally adjusted ventilatory assist has also proved to provide better patient-ventilator synchrony. A study done to compare NIV NAVA versus NAVA concluded that NIV NAVA “produces marked improvement in patient-ventilator synchrony compared with NIV” (Matlock et al., 2020, p. 952). This study was conducted with fifteen subjects who were randomly placed on NIV NAVA or NIV and monitored using respiratory inductance plethysmography, then switched to the other method and monitored once more (p. 950). The study concluded that NAVA decreased patient-ventilator asynchrony, but their methods did not seem to find conclusive results for a decreased work of breathing (WOB) which seems to be apparent in different literature (p. 950).

This decrease in work of breathing is something that is continually being studied after a study on piglet lungs concluded a true decrease in work of breathing in NIV NAVA mode (Jones et al., 2015, p. 1478). Twelve healthy neonatal piglets were randomly started on either regular NIV or NIV NAVA and then measured later on the alternate mode. The piglet was then measured in both modes with injured lungs, which was mimicked by a saline solution washout. The lungs were considered injured when their compliance was 50-70% of the baseline (p. 1480). The work of breathing was measured based on pressure waveforms for the pressure-time-product (PTP) (p. 1481). The first pressure-time-product was the area of the pressure curve with respect to time from the initiation of the breath to the beginning of the ventilator pressurization, and this represented the patient's work of breathing required to trigger a breath (p. 1481). The results showed a significant difference in the PTP work of breathing area under the curve between NIV NAVA and regular NIV (p. 1482). It proved that work of breathing was decreased in both healthy and unhealthy lungs in NIV NAVA compared to NIV. This is likely because NIV NAVA allows the patient to control their own breathing efforts and take an additional sigh breath when necessary, which would increase recruitment within the lungs and increase lung compliance (p. 1483). It is likely that similar findings have not been found in neonates because of the lack of a control group, which the piglet study had. The piglet study was able to view the work of breathing both before and after lung injury on NAVA, which simply is not doable in a neonate study.

NAVA can also be of benefit to patients post-cardiac surgery because of the lower average airway pressures. As intrathoracic pressures increase with positive pressure ventilation, this reduces the venous return of the heart and the afterload of the right ventricle (Crulli et al., 2018, p. 208). In patients post-cardiac surgery, it is imperative to minimize the ventilatory pressure (p. 208). Research was conducted for this reason to see if the pressures delivered by way of NAVA were less than the pressures delivered by conventional ventilation and if NAVA was of beneficial use in post-cardiac surgery patients (p. 208). This study used NAVA in 33 of their cardiac surgery patients, and compared the pressures to the other 525 patients who were ventilated conventionally post-cardiac surgery (p. 210). The overall results showed that not only were the average peak inspiratory pressures lower in NAVA mode, the average airway resistance was also reduced (p. 211). And while this research lacks a control group, the research is still beneficial in addressing the use of NAVA in post-cardiac surgical patients. An additional use of NAVA in this particular research was during weaning, and its success was seen in 71% of their patients without the need for reintubation (p. 210). This information is of value once again to add to the knowledge that NAVA can be used to facilitate spontaneous breathing much quicker to aid in sooner extubation.

An added bonus to the NAVA technology is that it allows the neonate to strengthen naturally and wean themselves from the support. While in the NAVA mode, the neonate is able to strengthen their main respiratory muscle, the diaphragm. As their lung compliance increases, meaning their lungs are able to stretch and expand and work better, their respiratory drive and demand will decrease, which is proportional to the Edi detected by the catheter (Stein & Firestone, 2018, p. 232). As the Edi decreases, the peak inspiratory pressures and tidal volumes delivered by the ventilator will also decrease (p. 232). This means that the neonate is progressively doing their own work while the ventilator is still there to assist if necessary. (Stein & Firestone, 2018, p. 232).

Additional Uses.

The NAVA technology does not stop being useful when it comes to invasive and noninvasive ventilation in neonates. There are additional uses that are also of benefit to the purchasing hospital and the health care practitioners involved in implementing the technology. The first of these benefits still lies within the pediatric field but is even more useful than for ventilation alone. There is new research being conducted to use NAVA on a level of zero for CPAP. Apnea of Prematurity is a common condition in neonates where they become apneic, or stop breathing for more than 20 seconds (Hussain et al., 2020). If a neonate were placed on a NAVA with a level of zero, this simply means that they would be receiving simple positive pressure ventilation without any additional support just like if they received bubble CPAP or something similar. The advantage with this is that if the neonate does slip into apnea, and the ventilator set up with NAVA senses that there is no Edi signal, it will automatically switch into backup ventilation. This is beneficial to ensure that the patient is constantly and adequately receiving appropriate ventilation and oxygenation rather than simply hoping the neonate will be just fine. The neonate will be placed on NAVA level zero so that they can try to become strong and breathe sufficiently on their own until outside intervention is absolutely necessary. This NAVA level of zero as CPAP "may offer a safe and effective option to avoid non-invasive ventilation or intubation due to premature neonates failing CPAP due to frequent CSEs from [Apnea of Prematurity]" (Hussain et al., 2020; Firestone et al., 2020).

This alternative to prolong or avoid intubation altogether is tremendous in the respiratory field. Studies have continuously proven that once mechanical ventilation is initiated, mortality, morbidity, and infection rates increase. This is because “endotracheal intubation bypasses the natural upper and lower respiratory tract defense mechanisms, increasing the risk of lung invasion by harmful microorganisms" (Weber, 2016, p. 178). Intubation, prolonged ventilation, and ventilatory acquired pneumonias are costly to both the hospital and the families, avoiding them altogether is beneficial. It is because of these intubation hazards that prolonged mechanical ventilation is also something that should be avoided if possible and why removal of the tube as soon as possible is preferred.

A case of NAVA being used to supplementally diagnose congenital central hypoventilation syndrome (CCHS) has also been reported. CCHS is “a disease characterized by shallow breathing during sleep due to negligible ventilatory sensitivity to hypercarbia and hypoxemia” (Rauf et al., 2019, p. 536). The diagnosis of this syndrome is often determined by a genetic test for PHOX2B mutation, which is not always easily available. However, NAVA has been used to suspect this in order to begin the process to seek the proper testing (p. 536). This happened when a patient had episodes of apnea at three and four months of life, brought to the hospital, placed on the ventilator, and went apneic in CPAP. The patient was then placed on NAVA to monitor the neural respiratory drive using the Edi. NAVA showed that Edi was virtually absent during sleep which meant that respiratory drive was poor during sleep. After a normal nerve conduction velocity test of the phrenic nerve ruled out neuropathy as a cause of the poor Edi signal, proper testing to confirm the presence of CCHS was then conducted (p. 537). NAVA was able to be used in this scenario to monitor the electrical activity of the diaphragm in correspondence with the breathing pattern in order to help determine the cause of the apneas.

Future Areas of Study.

More research needs to be conducted to determine the long-term effects of ventilating a neonate in the NAVA mode of ventilation. It is not known if NAVA actually causes additional pulmonary trauma, however, it is predicted that this is not the case due to the smaller peak pressures delivered in the NAVA mode. This hypothesis is one that needs to be researched and perhaps to find out if there are actually a decreased amount of chronic lung diseases post NAVA ventilation. It is also not known how NAVA may affect certain disease processes long term.

References

Crulli, B., Khebir, M., Toledano, B., Vobecky, S., Poirier, N., & Emeriuad, G. (2018). Neurally adjusted ventilatory assist after pediatric cardiac surgery: clinical experience and impact on ventilation pressures. *Respiratory Care,* 63(2), 208-214. Retrieved March 28, 2021 from CINAHL. doi:10.4187/respcare.05625

Firestone, K., Horany, B., Leon-Belden, L., & Stein, H. (2020). Nasal continuous positive airway pressure versus noninvasive NAVA in preterm neonates with apnea of prematurity: a pilot study with a novel approach. *Journal of Perinatology,* 1-5. doi:10.1038/s41372-020-0661-x

Firestone, K. S., Fisher, S., Reddy, S., White, D. B., & Stein, H. M. (2015). Effect of changing NAVA levels on peak inspiratory pressures and electrical activity of the diaphragm in premature neonates. *Journal of Perinatology,* 1-5. Retrieved November 9, 2020 from ResearchGate. doi:10.1038/jp.2015.14

Hussain, S., Lubarsky, D., Firestone, K., Protain, A., & Stein, H. (2020). The effect of NIV NAVA 0 on ventilation in premature neonates. Akron Children's Hospital Poster.

Jones, M., Bai, S., Thurman, T., Holt, S., Heulitt, M., & Courtney, S. (2018). Comparison of work of breathing between noninvasive ventilation and neurally adjusted ventilatory assist in a healthy and a lung-injured piglet model. *Respiratory Care*, 63(12), 1478-1484.

Lubarsky, D., Firestone, K. S., Mukherjee, R. K., & Stein, H. M. (2020). Changes in electrical activity of the diaphragm in response to painful procedures in neonates. *Neonatology Today,* 15(5), 3-8. Retrieved October 6, 2020 from ResearchGate.

Matlock, D. M., Bai, S., Weisner, M. D., Comtois, N., Beck, J., Sinderby, C., & Courtney, S. E.

(2020). Work of breathing in premature neonates: noninvasive neurally adjusted ventilatory assist versus noninvasive ventilation. *Respiratory Care*, 65(7), 946-953. doi: 10.4187/respcare.07257

Rauf, A., Gupta, D., Sachdev, A., Gupta, N., Gupta, S., Kumar, P., & Sabharwal, R. Neurally adjusted ventilatory assist: an early clue to diagnosis of congenital central hypoventilation syndrome. (2019). *Indian Journal of Critical Care Medicine,* 23(11), 536-537. Retrieved March 28, 2021 from CINAHL.

Schmidt, M., Dres, M., Raux, M., Deslandes-Boutmy, E., Kindler, F., Mayaux, J., Similowski, T., & Demoule, A. (2012). Neurally adjusted ventilatory assist improves patient-ventilator interaction during postextubation prophylactic noninvasive ventilation. *Crit Care Med,* 40(5), 1738-1744.

Stein, H. & Firestone, K. (2018). Chapter 15 B: Neurally adjusted ventilatory assist (NAVA) in neonates.

Verbrugghe, W., & Jorens, P. G. (2011). Neurally adjusted ventilatory assist: A ventilation tool or a ventilation toy? *Respiratory Care*, 56(3), 327-335.

Weber, C. D. (2016). Applying adult ventilator-associated pneumonia bundle evidence to the ventilated neonate. *Clinical Issues in Neonatal Care,* 16(3), 178-190. doi: 10.1097/ANC.0000000000000276