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# Clinical Application of Neurally Adjusted Ventilatory Assist in Neonates with Respiratory Distress: A Systematic Review

Maliheh Kadivar[1], Razieh Sangsari[1] and Hamid Soltanalian[1,*]

[1]Department of Pediatrics, Tehran University of Medical Sciences, Tehran, Iran

[*]*Corresponding author*: Department of Pediatrics, Tehran University of Medical Sciences, Tehran, Iran. Tel: +98-9388898518, Email: soltanalian.h@gmail.com

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## Abstract

**Context:** Neurally adjusted ventilatory assist (NAVA) is a novel mode of ventilation that coordinates the mechanical ventilator and the patient via electrical impulses of the diaphragm. Using these impulses as neural triggers, the patient's respiration synchronizes with the ventilator. Ventilation with NAVA has successfully been performed in adults with various lung diseases but the application of NAVA in neonates is a novel issue.
**Objectives:** The aim of this review study was to emphasize the NAVA as a new way of neonatal ventilatory support and the importance of ventilator-neonate synchrony in neonatal intensive care units.
**Study Selection:** Several studies have evaluated NAVA in the neonatal period but we described here the cardinal studies. Therefore, we included studies performing NAVA in the neonatal and pediatric population.
**Results:** The review of 10 studies showed that asynchrony was less frequent when using NAVA than when using the pneumatic modes of ventilation. Most of the studies observed a reduction in peak inspiratory pressure (PIP) and $FIO_2$ with NAVA. A reduction in mean airway pressure and work of breathing and an improvement in gas exchange were also observed in some of the studies.
**Conclusions:** We concluded that according to recent studies, the NAVA should be administered in neonates for better synchronization with ventilator and improving the gas exchange and outcomes.

*Keywords:* Neonate, Ventilation, Diaphragm, NAVA

## 1. Context

Asynchrony between mechanical ventilation and spontaneous breathing of the patient can lead to ineffective ventilation and adverse outcomes including increased inspiratory pressure, intracranial hypertension, and fluctuation in blood pressure. Diaphragmatic electromyography (EMG) was first used by Petit et al. in 1959 to evaluate respiratory muscle function (1). Sinderby and Beck expanded this concept with the introduction of embedded electrodes in a nasogastric tube to detect diaphragmatic EMG signal (2). This signal reflects the patient's neural respiratory drive in real time and minimizes artifacts and noises (2). This new minimally invasive bedside technology has been integrated into a commercially available mechanical ventilator (Servo-I, Maquet, Solna, Sweden) that transmits the electrical impulses into a specific assisted breath known as neurally adjusted ventilatory assist (NAVA) (3-5).

This new mode mainly has been employed in the weaning of children from the respirator after cardiac surgery (6). In the neonatal period, weaning is easier to do with the NAVA (7). The NAVA is limited to use in conditions such as neuromuscular diseases, diaphragmatic hernia, and esophageal atresia.

## 2. Study Selection

This review study summarizes 10 studies of NAVA application in the neonatal period (Table 1).

### 2.1. Search Protocol

Relevant studies were searched in MEDLINE from Jan 1950 to Feb 2017 using keywords including NAVA, neurally adjusted ventilatory assist, ventilator, and newborn. The publication type was limited to controlled trials. Other sources also were searched, such as EMBASE (Jan 1980 to Feb 2017). We also included studies that used NAVA in comparison with conventional pneumatic ventilation. All studies that used NAVA in the neonatal period were deemed acceptable.

**Table 1.** Characteristics of the Trials Included in the Review

| Reference | Results (with NAVA) |
|---|---|
| **Alander et al.** (8) | Shorter asynchrony |
| | Lower PIP and MAP |
| | No change in TV, $O_2$ saturation, or vital parameters |
| **Breatnach et al.** (9) | Lower PIP and shorter asynchrony |
| | No change in MAP, TV, RR, $PaO_2$, and $pCO_2$ |
| | No adverse patient events |
| **Stein and Howard** (10) | Lower PIP, $FIO_2$, and $pCO_2$ |
| | Higher pH |
| **Clement et al.** (11) | Lower work of breathing |
| | Lower trigger delay and shorter system response time |
| **Liet et al.** (12) | Lower PIP and oxygen requirement |
| | More comfort for the patient |
| **Stein et al.** (13) | Lower PIP, $FIO_2$, $TcPCO_2$, Edi-peak, and RR |
| | Improved TV |
| **Firestone et al.** (14) | PIP increment until reaching the BrP |
| | Edi gradual decrease after the BrP |
| **Bordessoule et al.** (15) | Shorter asynchrony |
| | Less trigger delay |
| **Zhu et al.** (16) | Lower PIP and Edi |
| | No change in $paO_2$: $FiO_2$ ratio and $pCO_2$ |
| **Jung et al.** (17) | Lower PIP, MAP, $FIO_2$, and work of breathing |
| | Improved $O_2$ saturation |

Abbreviations: Brp, break point; Edi, electronic activity of diaphragm; MAP, mean airway pressure; PIP, peak inspiratory pressure; RR, respiratory rate; TV, tidal volume.

## 3. Results

Alander et al. (8) used the pressure and flow-trigger modes and compared them with NAVA to assess patient-ventilator interactions. The asynchrony between the ventilator and patient was the primary endpoint and vital parameters, mean airway pressure (MAP), respiratory rate, and tidal volume were the secondary endpoints. Asynchrony was shorter in the NAVA group (8.8%) than in the pressure mode group (33.4%) and flow mode group (30.8%) ($P < 0.001$). Peak inspiratory pressure (PIP) of the NAVA group was 2 cm $H_2O$ lower than that of the pressure mode group and 1.9 cm $H_2O$ lower than that of the flow mode group ($P < 0.05$ in both). The respiratory rate was 10 BPM (breath per minute) higher in the NAVA group than in the pressure mode group ($P = 0.001$). The MAP was lower in the NAVA group ($P = 0.047$) but the tidal volume was similar (6.4 - 6.8 mL/kg) in the three groups ($P = 0.55$). Oxygen requirement and vital signs were the same in the three groups, as well.

In Breatnach et al. study (9), patients were ventilated with pressure support ventilation for 30 minutes, followed by the NAVA mode for four hours. The neural way was better than the pneumatic way in the synchronization of triggering and termination. After 30 minutes, a 28% reduction in PIP was observed with the NAVA mode, reaching a 32% reduction after 3 hours, without any change in MAP, minute ventilation, tidal volume (TV), respiratory rate (RR), pulse rate, $PaO_2$, and $PaCO_2$. No adverse patient events or device effects were observed.

Stein and Howard (10) examined 52 patients in the neonatal period that were ventilated with conventional or NAVA modes. The parameters of ventilation and ABG were compared in conventional and NAVA modes, along with their complications. PIP and $FIO_2$ were lower, but pH and $pCO_2$ were higher in the NAVA mode. These parameters sustained for 24 hours. They concluded that in preterm neonates, NAVA improves gas exchange and lowers the PIP and $O_2$ requirements compared to conventional ventilation.

Clement et al. (11) examined 23 patients with bronchiolitis from the neonatal period up to two years of age. The patients were ventilated for 120 minutes with either NAVA mode or volume support. Lower trigger delay (40 vs. 98 ms) and lower system response time (15 vs. 36 ms) were observed in the NAVA mode. The work of breathing was also lower in the NAVA mode.

Liet et al. (12) studied three cases with bronchiolitis aged 28 days, one month, and three years. In all of these patients, $O_2$ requirement was lower with the NAVA mode. This improvement coincided with PIP decrease. They concluded that the NAVA mode produces less aggressive synchronized ventilation, lower peak inspiratory pressure, lower $O_2$ requirements, and more comfort for patients.

Stein et al. (13) studied five premature neonates. The patients were ventilated with the NAVA mode for four hours that changed to PC (pressure control) for another four hours. This cycle was repeated three times. Patients with NAVA had lower PIP, $FiO_2$, transcutaneous $pCO_2$, electronic activity of diaphragm (Edi) peak, and respiratory rate while the tidal volume was higher with NAVA.

Firestone et al. (14) studied the effects of changing the NAVA level on PIP and electrical activity of diaphragm in premature neonates. Nine patients in the neonatal period were studied with the NAVA mode and another 12 patients with the non-invasive NAVA (NIV-NAVA) mode. The peak inspiratory pressure increased to the break point (BrP) and then remained unchanged. Edi gradually decreased after reaching the BrP level. Neonates showed a BrP level that protected the lung parenchyma from overdistention.

Bordessoule et al. (15) performed a study in 10 infants with a mean age of $4.3 \pm 2.4$ months and compared the patient-infant interaction with three modes including NAVA, pressure control ventilation (PCV), and pressure support ventilation (PSV). Failure of ventilation triggering oc-

curred in the PCV and PSV modes but not in the NAVA mode. Trigger delay was shorter in the NAVA mode than in the PCV and PSV modes (93 ± 20 ms vs. 193 ± 87 ms and 135 ± 29 ms, respectively). Asynchrony was seen in 24 ± 11% and 25 ± 9% of patients in the PCV and PSV modes, respectively, compared to 11 ± 3% in the NAVA mode. They concluded that the NAVA mode provides a better ventilator-patient interaction and produces adequate ventilation in infants with variable pressures.

Zhu et al. (16) studied 21 patients that had been operated for CHD with a mean age of 2.9 months and mean weight of 4.2 kg. The infants were ventilated with the NAVA and PSV modes for one hour. PIP and Edi were lower in the NAVA mode than in the PSV mode. After extubation, Edi was larger in patients that needed non-invasive mode or reintubation than in patients who extubated successfully (30.0 - 8.4 vs. 11.1 - 3.6 mV). There were no changes in pulse rate, blood pressure (BP), central venous pressure (CVP), $paO_2$: $FiO_2$ ratio, and $pCO_2$.

Jung et al. (17) compared conventional pneumatic ventilation with NAVA in 29 preterm infants with bronchopulmonary dysplasia (BPD). The values of various ventilatory variables and other measurements were measured one hour before NAVA and 1, 4, 12, and 24 hours after conversion to NAVA. The NAVA significantly improved the PIP, MAP, and work of breathing. Lower $FIO_2$ and improved oxygen saturation were also observed after NAVA. This study suggests the possible clinical utility of NAVA as a weaning modality for BPD in the NICU.

## 4. Conclusions

NAVA is gaining attention as a functional modality for neonatal ventilation. The most important finding of the reviewed studies was that asynchrony was less frequent in NAVA compared to pressure and/or flow-triggered ventilation. Other significant findings are as follows:

1- Most of the studies observed a reduction in PIP and $FIO_2$ with NAVA.

2- Some of the studies observed a reduction in MAP and work of breathing with NAVA.

3- Some of the studies observed the improvement of gas exchange with NAVA.

The age of patients in some of these studies (12 - 15 - 16) was beyond the neonatal period. However, because of similarities in lung mechanic between the infancy and neonatal periods, the results of these studies were also included in this review article.

Based on a growing body of literature, it appears that NAVA improves the patient-ventilator synchrony, abolishes ineffective efforts, results in improved gas exchange, and reduces the need for increasing the ventilator parameter in the neonatal period. There was neither complications nor adverse effects with NAVA. Thus, this novel method should be administered in all neonates with respiratory distress for increasing the synchrony with the ventilator and improving the gas exchange.

## Footnotes

**Authors' Contribution:** Study concept and design: Maliheh Kadivar; analysis and interpretation of data: Razieh Sangsari; drafting of the manuscript, revision of the manuscript for important intellectual content: Hamid Soltanalian.

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