# Approaches to Noninvasive Respiratory Support in Preterm Infants: From CPAP to NAVA

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## Education Gaps

Invasive mechanical ventilation through an endotracheal tube has been the mainstay of treatment of respiratory distress syndrome in the preterm newborn. Efforts to decrease invasive ventilation have resulted in the development of multiple forms of noninvasive respiratory support. Clinicians should be familiar with these newer modes of noninvasive respiratory support and their long-term effects, if any, on pulmonary morbidities.

## Abstract

Endotracheal intubation and invasive mechanical ventilation have been mainstays in respiratory care of neonates with respiratory distress syndrome. Together with antenatal steroids and surfactant, this approach has accounted for significant reductions in neonatal mortality. However, with the increased survival of very low birthweight infants, the incidence of bronchopulmonary dysplasia (BPD), the primary respiratory morbidity of prematurity, has also increased. Arrest of alveolar growth and development and the abnormal development of the pulmonary vasculature after birth are the primary causes of BPD. However, invasive ventilation-associated lung inflammation and airway injury have long been believed to be important contributors. In fact, discontinuing invasive ventilation in favor of noninvasive respiratory support has been considered the single best approach that neonatologists can implement to reduce BPD. In this review, we present and discuss the mechanisms, efficacy, and long-term outcomes of the four main approaches to noninvasive respiratory support of the preterm infant currently in use: nasal continuous positive airway pressure, high-flow nasal cannula, nasal intermittent mandatory ventilation, and neurally adjusted ventilatory assist. We show that noninvasive ventilation can decrease rates of intubation and the need for invasive ventilation in preterm infants with respiratory distress syndrome. However, none of these noninvasive approaches decrease rates of BPD. Accordingly, noninvasive respiratory support should be considered for clinical goals other than the reduction of BPD.

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**ABBREVIATIONS**

| | |
|---|---|
| BPD | bronchopulmonary dysplasia |
| CPAP | continuous positive airway pressure |
| $Fio_2$ | fraction of inspired oxygen |
| FRC | functional residual capacity |
| GA | gestational age |
| HFNC | high-flow nasal cannula |
| NAVA | neurally adjusted ventilatory assist |
| NCPAP | nasal continuous positive airway pressure |
| NIMV | nasal intermittent mandatory ventilation |
| NIV | noninvasive ventilation |
| PEEP | peak end-expiratory pressure |
| PIP | peak inspiratory pressure |
| RDS | respiratory distress syndrome |

## Objectives After completing this article, readers should be able to:

1. Understand the principles, application, and indications for noninvasive respiratory support in the preterm newborn, including nasal continuous positive airway pressure, high-flow nasal cannula, nasal intermittent mandatory ventilation, and neurally adjusted ventilatory assist.

## INTRODUCTION

Mechanical ventilation through an endotracheal tube (invasive ventilation) has been the mainstay of treatment for preterm neonates with respiratory distress syndrome (RDS). Use of invasive mechanical ventilation, antenatal corticosteroids and postnatal surfactant has accounted for the reduction in neonatal mortality over the past 50 years. (1) However, invasive ventilation has been associated with the development of bronchopulmonary dysplasia (BPD), the primary pulmonary morbidity among survivors of RDS. Importantly, BPD is independently associated with increased risks of adverse neurodevelopmental outcomes. (2) While studies have used different criteria to define BPD, the most clinically important definition of BPD in infants <32 weeks of gestation is the requirement of at least 30% oxygen and/or positive pressure at 36 weeks' postmenstrual age. This definition corresponds to moderate/severe BPD, as defined by the National Institutes of Health severity-based diagnostic criteria. (3) Although arrest of alveolar growth and development is believed to be the primary cause of respiratory morbidity in preterm infants, (4)(5) invasive ventilation-associated lung inflammation and airway injury (6) have long been held to be important contributors. Proposed causes of invasive ventilation-associated injury include delivery of tidal volumes with positive pressure and oxygen toxicity. (7)

Because invasive ventilation has been associated with adverse effects on lung development, noninvasive approaches have been increasingly used. In this article, we present current approaches to noninvasive respiratory support, discussing the mechanism of each and its effects on BPD risk, and providing clinical recommendations for their uses.

## NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE

The development of endotracheal continuous positive airway pressure (CPAP) by Gregory in the early 1970s, as described by Mai et al, revolutionized the treatment of infants with respiratory failure, and significantly improved mortality when compared with tidal ventilation alone. (8) Similar distending pressures can be delivered through the nares by means of large-bore nasal prongs without significant flow restriction. These nasal CPAP (NCPAP) devices deliver airflow that is continuously regulated to produce a set pressure, usually 4 to 7 cm $H_2O$. NCPAP provides distending pressure to the airways and alveoli throughout the respiratory cycle. (9) By distending the lung, NCPAP increases functional residual capacity (FRC), which, in the preterm lung with reduced FRC, increases lung compliance. This increase, and the concomitant decrease in resistance at the distended upper airway, reduces the work of breathing. NCPAP also improves ventilation/perfusion matching, thereby improving oxygenation. Finally, by maintaining lung volume, NCPAP can prevent or reduce atelectasis. (10) As with all positive pressure delivery, NCPAP increases the risk of air leak syndromes, particularly pneumothorax, and is associated with gastric distention. (11) However, a recent randomized clinical trial of 44 preterm infants born at less than 30 weeks' gestation found no difference in time to full feedings with NCPAP compared with high-flow nasal cannula (HFNC). (12)

NCPAP, delivered through large-bore nasal prongs that do not restrict airflow, has been a mainstay of neonatal respiratory support. However, concerns about the comfort of infants during NCPAP treatment and the potential for trauma inside the nares due to pressure from the large-bore cannulas (13) have driven the development of alternate interfaces through which NCPAP is delivered. For example, a commercial nasal cannula (RAM cannula, Neotech, Valencia, CA) featuring small-bore, curved, plastic nasal prongs, has been widely adopted. However, the delivery of pressure through small RAM cannulas depends critically on the amount of leakage at the interface at the nares. Iyer

and Chatburn determined the impact of RAM cannulas on the delivery of peak end-expiratory pressure (PEEP) using a simulated neonatal nose and lung. (14) Neonatal RAM cannulas of 3 sizes were used, with prong external diameters of 3.0, 3.5, and 4.0 mm. The system was first designed to maintain a leak of 30% around the prongs. However, a larger (58%) leak was also created, labeled "worst case," to mimic real-world situations. The outcome measured was the difference in pressures measured by the lung simulator compared with the set PEEP. For a nasal leak of 30%, 70% to 90% of set PEEP (at 5, 6, or 7 cm $H_2O$) was transmitted across the nasal interface. However, with the "worst case," as would occur with a size mismatch between nares and prong diameter, only 8% of PEEP was transmitted. Similar results were seen with tidal pressures delivered through the prongs (peak airway pressures set at 15, 20, and 25 cm $H_2O$, similar to nasal intermittent mandatory ventilation [NIMV], as described later in this article) with peak airway pressures much higher with the smaller leak. Increased leakage of NCPAP prongs at the nose results in decreased transmission of desired distending pressure to the upper airway. (14) Because measurement of intrathoracic pressures developed by application of NCPAP is not clinically available, it is critical for practitioners and respiratory therapists to ensure that prongs are appropriately sized for the patient. The improved comfort of the infant receiving NCPAP through small-bore prongs is likely achieved at the cost of insufficient delivery of the clinically indicated pressure.

Finally, it is incumbent on practitioners and respiratory therapists to understand the extent to which the internal diameter of NCPAP prongs of each interface used provides the primary resistance to flow in the CPAP circuit. The contribution made by the inner diameter of the prongs to the measured pressure can be determined by setting the system to deliver a given pressure on a patient, and then removing the prongs from the patient's nose. The pressure measured when the flow is delivered into the room indicates the intrinsic resistance supplied by the prongs themselves, and therefore, the amount of distending pressure that the patient is not receiving.

Use of NCPAP improves survival and decreases the need for invasive ventilation compared with supplemental oxygen alone. Thus, in a recent, multicenter randomized, controlled trial, neonates born between 24 and 27 weeks' gestation who received early NCPAP in the delivery room had increased survival and a decreased need for invasive ventilation at 7 days of age, compared with neonates who underwent intubation and were given surfactant within 1 hour after birth. (15) Notably, however, 4 large randomized, controlled trials evaluating routine CPAP versus routine intubation together found that 33% to 51% of high-risk infants initially treated with CPAP ultimately required intubation in the first week of postnatal age (Table 1). (15)(16)(17)(18)(19) Furthermore, approximately 25% of neonates required reintubation following surfactant plus a trial of NCPAP. (20) Thus, practitioners wishing to avoid intubation in very small infants may be best served by administering surfactant using a noninvasive approach (eg, the INtubation-SURfactant-Extubation [INSURE] method). (21) Although some randomized, controlled trials found that NCPAP reduces the rate of BPD, the treatment effect is small and has not been consistently reported in other trials. (22)

## HIGH-FLOW NASAL CANNULA

HFNC provides a heated and humidified oxygen mixture delivered via prongs in the nares at a controlled flow rate. In this modality, the pressure that the nasal airflow produces in the airway and chest is not monitored. The prongs typically used to deliver HFNC support have been associated with lower occurrences of nasal trauma compared with the large-bore prongs used to deliver NCPAP. It is a common perception among bedside nurses that these smaller and softer nasal prongs are better tolerated by premature

TABLE 1. **Incidence of CPAP Failure**

| TRIAL | YEAR | SUBJECTS ENROLLED, NO. | GA (WK) | ACS, % (ANY) | CPAP FAILURE, % (5-7 DAYS) |
|---|---|---|---|---|---|
| COIN (17) | 2008 | 610 | 25 0/7–28 6/7 | 94 | 46 |
| SUPPORT (15) | 2010 | 1316 | 24 0/7–27 6/7 | >95 | 51.2 |
| CURPAP (18) | 2010 | 208 | 25 0/7–28 6/7 | >95 | 33 |
| Dunn (19) | 2011 | 648 | 26 0/7–29 6/7 | >98 | 45.1 |

*These large randomized controlled trials evaluated CPAP alone as a primary mode of respiratory support. ACS=antenatal corticosteroids; CPAP=continuous positive airway pressure; GA=gestational age. Reprinted with permission from Wright et al. (16)*

neonates. (23) Parents also prefer HFNC for their neonates, as they are able to better interact with their child and take part in their child's care. (24) Similar to NCPAP, HFNC may improve the work of breathing by reducing resistance in the upper airway and may improve ventilation by providing distending pressure for lung recruitment. (25)

HFNC has become increasingly popular in NICUs. HFNC has been used as primary respiratory support for premature infants. (26) However, evidence is increasing that it is inferior to NCPAP when used as primary therapy—many patients treated with HFNC subsequently require NCPAP or mechanical ventilation. (23) Thus, Conte and colleagues performed a meta-analysis of 6 randomized controlled studies comparing HFNC and NCPAP as initial support for RDS. This analysis, encompassing more than 1,200 infants who were born after 27 weeks' gestation, demonstrated that the initial use of HFNC resulted in a higher rate of intubation (treatment failure) compared with the initial use of NCPAP. (27) Similarly, a study of infants with more than or equal to 28 weeks of gestation supported with HFNC found almost double the rate of treatment failure (25.5%) compared with those receiving NCPAP (13.3%). (28) One reason for these consistent results may be the failure of HFNC to deliver appropriate distending pressures to the preterm lung.

As discussed before, distending pressure is the key to improving function of the preterm lung. With HFNC, the distending pressure resulting from delivered flow varies as a function of the flow and the resistance to flow presented by the inner diameter of the nasal cannula. Locke et al measured transthoracic pressures with an esophageal balloon in preterm infants receiving HFNC at different flow rates using cannulas of varying diameters. (29) Using 0.2-cm-diameter cannulas, distending pressure was not delivered, regardless of the amount of flow that was studied. In contrast, a 50% increase in cannula diameter (which decreases resistance as the fourth power of the radius) resulted in potentially dangerous (and clinically unmonitored) pressures of almost 10 cm $H_2O$. It is not unreasonable to conclude that the distending pressures developed by HFNC at commonly used, higher flow rates (4–5 L/min) may result in complications from overly high airway pressures.

These data indicate that, in the clinical setting, the relationship between the airway pressure developed at a given flow rate in an individual patient receiving HFNC is unknown. As a result, infants may receive either insufficient distending pressure to improve pulmonary function or, worse, too much pressure resulting in lung overdistention, potentially increased work of breathing, and decreased venous return. (30) These limitations make HFNC a less-than-ideal treatment for premature neonates whose primary respiratory requirement, at any time in the RDS course, is distending pressure. In fact, an argument could be made for *never* using HFNC as an alternative to NCPAP, because the delivered pressure is unmonitored. However, infants in whom prolonged NCPAP has led to nasal trauma may be candidates for the brief use of HFNC at low flow rates.

## NONINVASIVE VENTILATION

For many preterm infants with RDS, NCPAP may provide insufficient respiratory support. The concern that invasive ventilation increases BPD risk has led to extensive research into noninvasive forms of ventilation in neonates. (31) In noninvasive ventilation (NIV), pressure-regulated volumes are delivered periodically by a mechanical ventilator to a spontaneously breathing infant through a circuit interfaced to the nose with nasal prongs. NIV supports the infant's spontaneous breathing by periodically increasing intrathoracic pressure above CPAP for a set duration (analogous to inspiratory time in invasive ventilation). (32) Peak pressures and inspiratory times are set on the ventilator, but the extent to which the peak pressure is transmitted from the upper airway to the lung is unclear. Any resultant tidal volumes received by the infant occur as a function of the set peak pressure and the infant's overall respiratory mechanics.

In adults and older children, NIV, delivered by oronasal masks, has been more successful in preventing subsequent intubation than CPAP alone. (32) This increased mean airway pressure aids in maintaining end-expiratory lung volume, increasing FRC, and improving oxygenation. NIV has shown similar success in newborns, preventing intubation in some neonates who would otherwise fail NCPAP. (32) In addition, NIV has been shown to reduce the magnitude and severity of apnea. (33) Commonly used approaches to NIV have been NIMV and neurally adjusted ventilatory assist (NAVA).

## NASAL INTERMITTENT MANDATORY VENTILATION

NIMV is the most commonly used form of NIV in neonates. (32) With NIMV, neonates breathe spontaneously over NCPAP. Mandatory pressure control breaths are used, as described before, and are triggered by patient inspiration or delivered regularly without regard for the infant's respiratory cycle. (34)

One important question when evaluating NIMV is its efficacy in addressing pulmonary function particular to the preterm infant compared with NCPAP, specifically

oxygenation, ventilation, and respiratory drive. In an early study, Friedlich et al randomized 41 preterm infants with RDS (mean gestational age [GA] 27.8 weeks, mean birthweight 954 g) to receive NIMV or NCPAP following extubation and a mean duration of invasive ventilation of 23 days. (35) Infants receiving NIMV were significantly less likely to have respiratory failure using strict criteria. Bisceglia et al randomized 88 preterm neonates with mild to moderate RDS (fraction of inspired oxygen [$F_iO_2$] <0.4, and a chest radiograph suggestive of RDS) to NIMV or NCPAP after birth. Although there was no difference in mean $Pao_2$ values between the groups, infants receiving NIMV had lower mean $Pco_2$ levels, fewer episodes of apnea, and a shorter duration of respiratory support compared with infants receiving NCPAP. (36) Accordingly, the results of this single study support the use of NIMV over NCPAP in infants with mild to moderate disease. In a study of sicker infants, Sai Sunil Kishore et al examined whether infants treated for surfactant deficiency were better supported by NIMV or NCPAP. (37) Seventy-six preterm neonates (mean GA 30.8 weeks, mean birthweight 1,250 g) were randomized to receive NIMV or NCPAP within 6 hours of birth. About 60% of these infants required transient intubation and surfactant administration without mechanical ventilation (ie, the INSURE method). (21) Infants were judged to have failed the assigned treatment, and underwent intubation if they met strict criteria of hypercarbia or apnea within the first 48 hours of treatment allocation. The failure rate in infants randomized to NIMV was less than half the failure rate in infants randomized to NCPAP, (37) suggesting that NIMV may improve ventilation and decrease apnea compared with NCPAP in sicker infants as well.

The decreased intubation rate in NIMV-treated infants described earlier supports the idea that NIMV reduces the requirement for mechanical ventilation compared with NCPAP within the first 48 hours after birth. (37) However, in a larger study of 200 infants with RDS with similar mean birthweights and GAs who were randomized to NIMV or NCPAP, Meneses et al found no significant difference between the groups in the need for intubation and invasive ventilation in the first 72 hours after birth, but the trend favored the NIMV group. (38) Notably, infants were similarly allowed to receive surfactant using the INSURE method, and a similar proportion of infants in each group (~70%) were given surfactant. (21) Moreover, the criteria for intubation and ventilation were almost identical. A comparison of the NIMV settings in the 2 studies reveals no clinically significant differences except for the NIMV rate—in the Sai Sunil Kishore et al study, the NIMV rate was about double that of the Meneses et al study. It seems unlikely that this difference in support could underlie the differences in results between the 2 studies. Consequently, the reasons leading to these divergent conclusions are unclear. However, a recent meta-analysis by Meneses et al (39) of 3 randomized controlled studies of NIMV versus NCPAP after birth, including both studies discussed before, (37)(38) estimated a significant decrease in the need for intubation and mechanical ventilation within the first 72 hours of age in infants treated with NIMV compared with NCPAP.

Following a period of invasive ventilation for RDS, many preterm infants are placed on NCPAP to maintain FRC, reduce apnea, and reduce the risk of reintubation and continued invasive ventilation. The risk reduction, however, is only about 60%, (40) raising the question of whether more aggressive noninvasive support can reduce this risk. In fact, a number of randomized, controlled studies provide support for NIMV in this role. Khalaf et al randomized 64 preterm infants with RDS born before 34 weeks' gestation (mean GA 27.7 weeks, mean birthweight 1,061 g) to treatment with NIMV or NCPAP after extubation. Significantly more children in the NIMV group (94%) remained extubated than those in the NCPAP group (60%). (41) In a contemporaneous study, Barrington et al randomized 54 preterm infants with RDS (mean GA 26.3 weeks, mean birthweight 831 g) to receive NIMV or NCPAP following extubation. (42) In this study, infants were intubated for a mean duration of 7.6 days. A higher percentage of infants randomized to NIMV remained extubated (85%) compared with infants randomized to NCPAP (56%). These early studies have been supported by multiple studies since that time. In fact, a recent meta-analysis of 10 randomized, controlled trials and 1,432 infants comparing NIMV with NCPAP after extubation found statistically and clinically significant reductions in the risk of extubation failure in infants treated with NIMV. (43) Accordingly, the discussion herein supports the idea that NIMV decreases the need for invasive ventilation in preterm infants with RDS both early—at the beginning of the hospitalization— and in infants who require invasive ventilation later—after extubation.

Unfortunately, despite this decreased need for invasive ventilation, the conclusion that use of NIMV fails to reduce long-term pulmonary morbidity is inescapable. The 2001 study by Barrington et al found no difference in BPD risk between infant groups randomized to NIMV or NCPAP after extubation, (42) and the 2011 study by Meneses et al also found no difference in rates of BPD between these same 2 groups. (38) In their meta-analysis, Meneses et al observed no difference in the incidence of BPD in NIMV-treated infants. (39) Finally, in a large multicenter trial, 1,009 preterm infants with RDS (mean GA 26.1 weeks,

mean birthweight 803 g) were randomized to receive NIMV or NCPAP. The assigned treatment was provided either as primary therapy, or after initial extubation. The same proportion (60%) of infants in the groups underwent reintubation after extubation. No difference was found in the combined incidence of death before 36 weeks' postmenstrual age or the incidence of BPD, or the individual incidences of either death or BPD. (44) Accordingly, although there may be nonpulmonary benefits in treatment with NIMV, including ease of care and parental interaction, the use of NIMV to decrease BPD in preterm infants with RDS is unwarranted.

In the same way that modern synchronized ventilation reduces the magnitude of respiratory support required, (45) NIMV synchronized to an infant's spontaneous breathing may be beneficial. Synchronization occurs through detection of the patient's inspiratory flow at the nares. Preterm infants with RDS receiving synchronized NIMV can display increased respiratory comfort (46) and gas exchange (47) compared with infants receiving nonsynchronized NIMV. However, significant patient-ventilator asynchrony can occur because of weak inspiratory efforts and auto-triggering. (48) The few single-center studies comparing synchronized NIMV with nonsynchronized NIMV have found little difference in outcomes. (49)

## NEURALLY ADJUSTED VENTILATORY ASSIST

In light of the potential benefits of synchronized NIMV, perhaps allowing patients to control all parameters of their noninvasive support may affect long-term pulmonary outcomes. NAVA uses the infant's integrated diaphragmatic activity to determine the onset of the assisted breath, the pressure employed during the breath, and the duration of assist. First used in adults, NAVA uses an esophageal electrode to measure the electrical activity of the diaphragm and uses characteristics of this signal to control the ventilator. (50)(51) The ventilator-assisted breath begins when the ventilator detects an increase in diaphragmatic activity greater than the threshold. The delivered pressure increases as a function of the increase in diaphragmatic signal. The magnitude of change in the assist pressure delivered is determined by a multiplier of the instantaneous diaphragmatic signal activity. This multiplier is set by the physician to provide the desired level of pressure support. Following peak diaphragmatic activity, which occurs at the time of peak inspiratory effort, ventilator assist pressure decreases as a function of the decrease in diaphragmatic signal. Once the diaphragmatic activity is 40% to 70% of maximum, inspiratory assist stops and the expiratory phase begins. (52) Thus, the goal of NAVA is to transduce, on a breath-by-breath basis, the timing and intensity of the patient's own inspiratory effort into synchronous support provided by the ventilator. NAVA may be provided through an endotracheal tube, or noninvasively, through nasal prongs. Unlike synchronized NIMV, diaphragmatic activity triggers the ventilator breath and does not depend on patient-driven changes in airflow. (51)

NAVA is used in adult patients to improve patient-ventilator synchrony (53) and reduce overassistance during spontaneous breathing trials. (54) (55) In pediatric patients, a case-control study of 30 pediatric patients in the intensive care unit found that patients who received invasive NAVA demonstrated less agitation, as measured by heart rate and mean arterial pressures, compared with conventional ventilation, and required lower peak inspiratory pressure (PIP). (56) In fact, a systematic review of studies in pediatric patients found that patient-ventilator interaction improves with invasive and noninvasive NAVA, and provides decreased PIP. (57) Finally, Kallio et al randomized 170 pediatric patients to invasive ventilation with NAVA or conventional ventilation. (58) Median ventilator time was not different between the groups. However, when postoperative patients were excluded, significantly less sedation was used during ventilation with NAVA compared with conventional ventilation, suggesting that patient-ventilator interaction and patient comfort were improved. In addition, $FiO_2$, $PcO_2$, and oxygenation index were all lower in the NAVA group. (58)

In preterm infants, several studies have compared invasive NAVA ventilation with conventional ventilation. The primary conclusions in each were that NAVA ventilation is safe and that PIPs required with NAVA were generally lower than with conventional ventilation. (48)(59)(60) In addition, characteristics of patient-ventilator synchrony such as decreased delay to triggered breath onset, delivered inspiratory time, and inspiratory time in excess of demand were all significantly decreased with NAVA ventilation. (48) Finally, the work of breathing has been found to be improved with NAVA compared with conventional ventilation. (61)

Studies in preterm infants that have compared noninvasive NAVA with other modes of noninvasive ventilation have been few. In a randomized, controlled, observational, crossover study of 11 preterm infants, Gibu et al switched infants on NCPAP, HFNC, or NIMV to noninvasive NAVA for 2- to 4-hour periods. When compared with NIMV, NAVA significantly reduced mean PIP and $Fio_2$. Infants receiving NAVA also exhibited fewer and shorter oxyhemoglobin desaturations. Furthermore, infants receiving NAVA

demonstrated unloading of the respiratory effort. (62) These data suggest that NAVA may improve oxygenation, decrease patient-ventilator asynchrony that results in oxyhemoglobin desaturation, and decrease the work of breathing. Finally, Beck et al evaluated patient-ventilator synchrony through simultaneous measurements of diaphragmatic activity and airway pressure. In this small study, esophageal NAVA electrodes were placed in 7 premature infants receiving conventional ventilation (mean GA 29 weeks) who were close to extubation. Infants briefly received invasive NAVA, then underwent extubation and were given noninvasive NAVA. While receiving noninvasive NAVA, infants had lower respiratory rates and better correlation between diaphragmatic electrical activity and airway pressures than with conventional ventilation. These data suggest that noninvasive NAVA provides equivalent patient-ventilator synchrony to invasive NAVA despite delivering support through a nasal interface. (51)

Although noninvasive NAVA is new, early studies suggest that it is safe and may provide improved synchronization, smaller PIPs, and decreased work of breathing compared with NIMV. However, the question of whether these effects have any impact on the duration of ventilation or long-term pulmonary outcomes in preterm infants remains uncertain.

## SUMMARY

Table 2 provides direct comparisons of the risks and benefits of NCPAP, HFNC, NIMV, and NAVA in preterm infants with RDS. NCPAP provides monitored distending pressure to the upper airway, lower airways, and lung, and addresses the atelectasis, decreased lung compliance, and increased work of breathing that characterize RDS in the preterm newborn. Care should be taken to ensure that the pressure delivered is not impeded by the resistance of the nasal prongs. HFNC is indicated in the preterm infant with a stable requirement for supplemental oxygen. Because the distending pressure is not monitored, care should be taken to avoid pulmonary overinflation. HFNC is not a replacement for NCPAP, and should not be used to deliver distending pressure. NIMV may be indicated in the preterm infant who requires more distending pressure than is

TABLE 2. **Approaches, Benefits, and Risks of Noninvasive Forms of Respiratory Support for RDS in Preterm Infants**

| | APPROACHES | BENEFITS | RISKS |
|---|---|---|---|
| Nasal continuous positive airway pressure | Monitored and controlled positive pressure through nonrestrictive nasal prongs | Improves V/Q mismatch<br>Improves oxygenation<br>Maintains FRC<br>Reduces atelectasis<br>Decreases work of breathing | Nasal trauma<br>Air leak syndromes<br>Gastric distention |
| High-flow nasal cannula | Heated, humidified flow of supplemental oxygen through small-bore nasal cannula | Parental acceptance<br>Ease of nursing care<br>Reduced gastric distention | Distending pressure is unmonitored and can be dangerously high or ineffective |
| Nasal intermittent mandatory ventilation | Pressure-regulated, time-cycled positive pressure delivery through restrictive or nonrestrictive nasal prongs<br>Synchronized or nonsynchronized | Improves gas exchange<br>Improves oxygenation<br>Decreases work of breathing<br>Maintains FRC<br>Decreases need for invasive ventilation | Nasal trauma<br>Gastric distention<br>Air leak syndromes |
| Neurally adjusted ventilatory assist | Diaphragm activity-controlled and regulated pressure delivery | Improves patient-ventilator synchrony<br>Improves patient comfort<br>Reduces peak inspiratory pressures | Limited data regarding efficacy<br>Limitations in extremely premature infants with immature respiratory rhythm |

*FRC=functional residual capacity; RDS=respiratory distress syndrome; V/Q=ventilation/perfusion ratio.*

practical with NCAP, and may obviate the need for intubation or reintubation. NAVA may be indicated in the preterm infant who requires more distending pressure than is practical with NCAP. NAVA may increase patient-ventilator synchrony and comfort, and allow decreased respiratory support. None of the noninvasive modes of respiratory support has been shown to decrease the risk of BPD in preterm infants despite large studies. Accordingly, noninvasive respiratory support should be considered for clinical goals other than the reduction of BPD.

## American Board of Pediatrics Neonatal-Perinatal Content Specifications

- Know the clinical strategies and therapies used to decrease the risk and severity of RDS.
- Know the indications for and techniques of continuous positive airway pressure.

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