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Noninvasive Ventilation in the Neonate

Debbie Fraser Askin, MN, RNC

One of the most common and concerning complications seen in low-birth-weight infants is chronic lung disease. A variety of factors have been implicated in the etiology of chronic lung disease including lung inflammation and injury. Noninvasive ventilation (NIV), a term applied to a variety of devices capable of supporting neonatal ventilation without the use of an endotracheal tube, is receiving increasing attention as means to reduce damage often incurred with mechanical ventilation. This article will review the history of continuous positive pressure ventilation and will provide an overview of some of the other types of NIV being used in neonates. The literature supporting the use of NIV is reviewed, and nursing care of the infant receiving NIV is examined.
Key words: *bronchopulmonary dysplasia*, *CPAP*, *neonate*, *ventilation*

Despite advances in technology, chronic lung disease (CLD) or bronchopulmonary dysplasia (BPD), a condition seen primarily in neonates who are born at 24 to 26 weeks of gestation, remains a significant cause of morbidity and in some cases, mortality. According to a review done by Bhandari and Panitch, the incidence of BPD, defined as oxygen need at 36 weeks of postmenstrual age, is about 30% for infants with birth weights less than 1000 g.[1] The etiology of CLD is known to be multifactorial; however, positive pressure ventilation with its resultant barotrauma and volutrauma appears to be an important contributing factor.

Focus on reducing the use of mechanical ventilation in neonates has led to a renewed interest in continuous positive pressure ventilation (CPAP) and the introduction of other types of noninvasive ventilation (NIV) to support neonates with respiratory diseases. The use of NIV is contingent upon a thorough understanding of the equipment being used and on astute assessment of the neonate to determine the appropriate ventilation strategy. This article reviews the history of neonatal CPAP and provides an overview of some of the other types of NIV. Indications and benefits of NIV are reviewed and nursing care of the infant receiving NIV is presented.

Author Affiliation: The St Boniface General Hospital and Faculty of Nursing University of Manitoba, Winnipeg, Manitoba, Canada.

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Corresponding Author: Debbie Fraser Askin, MN, RNC, Faculty of Nursing University of Manitoba, Winnipeg, Manitoba, Canada R3T 2N2 (Debbie_Fraser@umanitoba.ca).

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HISTORY OF CPAP

Use of CPAP was first described in adults in the 1930s.[2] In 1971, the first article was published on the use of bubble CPAP to treat respiratory distress syndrome (RDS) in neonates.[3] CPAP did not gain widespread acceptance until the early 1980s and, with improvements in technology later in that decade, CPAP was largely replaced by mechanical ventilators as the primary mode of respiratory support for premature infants with lung disease.[4]

Despite the use of sophisticated ventilators and the development of exogenous surfactant, CLD continued to complicate the course of low-birth-weight newborns with RDS. In a sentinel article published in 1987, Avery and colleagues compared survival rates and rates of CLD in 8 American NICUs and found that, while survival rates were similar across centers, the incidence of CLD was significantly lower at Columbia Presbyterian Medical Center in New York. The primary difference between Columbia and the other centers was an approach to ventilating small babies that included early use of nasal prong CPAP and less dependence on intubation and mechanical ventilation.[5] The release of

Table 1. Types of phasic ventilation

Ventilation Strategy	Acronym
Nasal ventilation	NV
Synchronized nasal intermittent positive pressure ventilation	SNIPPV
Synchronized nasal intermittent mandatory ventilation	SNIMV
Nasal intermittent mandatory ventilation	NIMV
Nasopharyngeal synchronized intermittent mandatory ventilation	NPSIMV
Non invasive positive pressure ventilation	NIPPV

this article combined with ongoing research into CLD resulted in renewed interest in the use of nasal CPAP to avoid the potential hazards of mechanical ventilation. Ongoing interest in the use of NCPAP to avoid or shorten the duration of mechanical ventilation has spawned a number of studies that are reviewed later in this article.

TYPES OF NONINVASIVE VENTILATION

In addition to nasal CPAP, improvements in sensors and flow delivery systems have resulted in the introduction of a variety of other NIV strategies. Confusion has resulted from both the definitions and acronyms used to describe these systems. CPAP is sometimes included in the category of NIV[6] while other definitions describe NIV as a separate category of devices capable of delivering positive pressure throughout the respiratory cycle (CPAP) with the addition of phasic increases in airway pressure.[4] Acronyms representing some of the phasic ventilation strategies are listed in Table 1.

CPAP

CPAP, the application of continuous pressure throughout the respiratory cycle, can be provided by a variety of devices ranging from simple bubble CPAP to sophisticated dedicated mechanical ventilators. CPAP pressure is generated by 1 of 2 mechanisms: varying the flow rate (variable flow devices) or providing a constant flow of gases and varying the pressure by another mechanism (continuous flow devices).

Continuous flow devices include the following: neonatal ventilators that provide a continuous flow of fresh gas and vary the level of positive pressure by controlling gas outflow; and bubble CPAP that generates pressure by submerging the expiratory tubing in a water chamber with the level of water determining the level of CPAP. Bubble CPAP creates chest wall vibration similar to that of high-frequency ventilation that may increase gas exchange[7] although this is disputed.[8]

Variable flow devices are less common in North America and rely on flow generators or drivers with specialized prongs to maintain the appropriate level of airway pressure. Of the variable flow devices available, the Infant Flow System (VIASYS, Conshohocken, Pennsylvania) has been most extensively evaluated.[9] Limited comparisons of types of CPAP delivery systems have been published. In one study of variable flow nasal CPAP in comparison with bubble CPAP in 18 infants weighing less than 1500 g, variable flow NCPAP was found to result in less work of breathing and breathing asynchrony than bubble CPAP.[10] One study of twenty-four 800- to 1200-g preterm infants randomized to constant flow or variable flow CPAP found that work of breathing decreased between 13% and 29% with variable flow CPAP in comparison with constant flow. However, the authors cautioned that overdistension of the lung may result with variable flow CPAP when pressures of greater than 6 cm H_2O were used.[11] Another study found that variable flow CPAP was also superior to continuous flow CPAP in lung recruitment perhaps because the mean airway pressure (MAP) was more constant with the variable flow device.[12]

High-flow nasal cannula

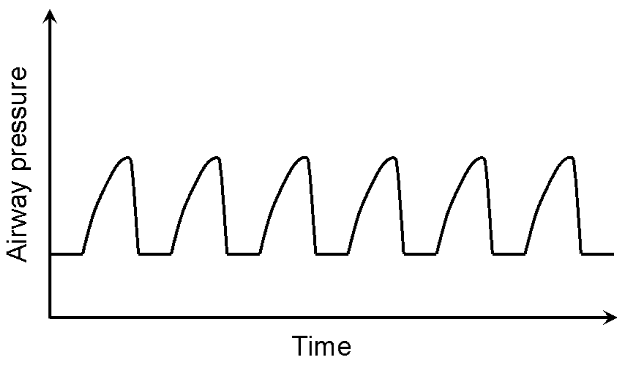
Positive pressure is also generated with the use of nasal cannula. The level of pressure generated by nasal prongs varies according to the flow rate, the type of cannula used, and infant size.[4] Using nasal cannula with an external diameter of 0.3 cm in a group of 1400-g neonates, researchers estimated that flows of 2 L/min generated positive pressures with a mean of 9 cm H_2O. A few studies have compared high flow nasal cannula to NCPAP and to NIPPV.[13] A study of 40 infants less than 29 weeks with apnea who received either NCPAP of 6-cm pressure or nasal cannula with flows of up to 2.5 L/min (adjusted to generate an esophageal pressure of +6 cm) found no difference between the groups in frequency or duration of apnea.[14] In a study of 18 infants weighing less than 2 kg, researchers compared a humidified high-flow nasal cannula (HHFNC) system at flows of 3, 4, and 5 L/min to NCPAP at 6-cm pressure and found no difference in infant work of breathing between the groups. They concluded that HHFNC was comparable in support to NCPAP.[15] In a similar study comparing high-flow cannulas to the Infant Flo CPAP device, the authors noted that infants receiving NCPAP by cannula at a calculated pressure of 4.5 cm had a significantly higher rate of reintubation compared to those on the infant flow.[16] Another study also reported a higher incidence of gram-negative sepsis in infants on positive pressure by nasal cannula, speculating that nasal mucosal damage may be responsible.[17]

Concerns remain regarding the use of high-flow nasal cannula, including leaking around the cannula that may affect flow delivery, inability to adequately monitor the pressure level delivered by a given flow and achieving adequate humidity.[18] Others have expressed concern about the generation of unknown levels of positive pressure without the benefit of a safety pressure relief valve.[4] To prevent potential damage from unregulated pressure with nasal cannula, the American Association of Respiratory Care recommends limiting the flow to less than 2 L/min.[19]

Phasic positive pressure devices

As described previously, phasic NIV consists of positive pressure applied across the respiratory cycle combined with periods of increased airway pressure (Fig 1). Intermittent increases in airway pressure (breaths) may be delivered at regular intervals (nonsynchronized) or synchronized with infant inspiratory efforts. The majority of systems currently in use in North America feature some type of synchronization; synchronized NIPPV has also received the most attention in clinical trials.

Physiologic benefits have been described in NIPPV. An evaluation of synchronized nasal intermittent positive pressure ventilation (SNIPPV) in 15 premature infants (27–32 weeks) found that compared to NCPAP, SNIPPV resulted in a decrease in work of breathing.[20] It has also been shown to stabilize the chest wall and reduce asynchronous motion between the chest and the abdomen[21] and to improve tidal volumes and minute ventilation.[22] SNIPPV may create additional end expiratory airway pressure that recruits collapsed alveoli and increases FRC.[23]



In phasic ventilation, periodic increases in airway pressure are added to the background level of continuous positive pressure normally seen in CPAP.

Figure 1. Phasic ventilation.

There have been a limited number of studies comparing NIPPV to CPAP in treating infants with apnea of prematurity. A randomized trial of 34 infants between 25 and 32 weeks' gestation to either nonsynchronized NIPPV or NCPAP demonstrated a greater reduction in apnea frequency (events per hour) with NIPPV compared to NCPAP.[24] A Cochrane review of studies in which NIPPV was used for treating apnea of prematurity concluded that NIPPV appears to reduce the frequency of apnea more effectively than NCPAP but that more safety and efficacy data are required before recommending NIPPV as standard therapy for apnea.[25]

SNIPPV has been found to be more effective than NCPAP in weaning infants with RDS from the ventilator.[23,26] A Cochrane review comparing NIPPV to NCPAP after extubation reviewed 3 studies[27–29] and concluded that in each trial there was a significant benefit of synchronized NIPPV compared to NCPAP for preventing reintubation.[30] The authors of the review note that the MAP generated during NIPPV may be higher than that in nasal CPAP and therefore the differences in outcomes may be due simply to a higher MAP in the NIPPV group.[30]

NIPPV has also been shown to lower the rates of BPD in low-birth-weight infants. In 2 studies,[27,29] a trend to lower rates of BPD was noted in infants treated with NIPPV, although the numbers did not reach statistical significance. A recent study found that in 84 infants aged 28 to 33 weeks, those randomized to NIPPV for the initial treatment of RDS were significantly less likely to require ventilation than those in the CPAP group (25% vs 49%) and had significantly lower rates of BPD (5% vs 33%, $P < .05$, for infants <1500 g).[31]

BENEFITS OF NONINVASIVE VENTILATION

The application of positive pressure results in a number of physiologic benefits, including stabilization of the airways, diaphragm and chest wall, increased lung volumes, reduced obstructive apnea, and decreased airway resistance and work of breathing.[32–36] The mechanisms responsible for these effects are outlined in Table 2. It is important to note that excessive CPAP pressure, especially when applied to normal lungs, may actually reduce lung compliance and lead to airleaks.[38]

Since the original work,[3] NIV has been primarily used to treat premature infants with RDS. Other neonatal respiratory conditions are also treated with NIV, including transient tachypnea of the newborn, pneumonia, and apnea of prematurity. Randomized controlled trials of

Table 2. Physiologic effects of NIV[37]

Effects	Mechanism
Decreased intrapulmonary shunting	Recruits additional alveoli, decreases pulmonary vascular resistance
Increased compliance and functional residual capacity and prevention of atelectasis	Recruits additional alveoli and splints the airways
Improved oxygenation	Decreases pulmonary vascular resistance
Decreased thoracoabdominal asynchrony	Splints the airways and diaphragm, stabilizes chest wall
Decreased obstructive and mixed apnea	Splints the airways and diaphragm, stabilizes chest wall; regularizes and slows respiratory rate
Conservation of surfactant	Recruits alveoli, improves pulmonary blood flow, improves oxygenation
Improved lung growth	Stretches lung tissue

NIV have been primarily focused on 3 issues: preventing extubation failure, treating apnea of prematurity, and treating RDS.

A number of studies examined the use of NCPAP following extubation to decrease work of breathing and prevent the need for reintubation.[38–41] A Cochrane review examined 8 trials, and the authors determined that NCPAP was effective in preventing extubation failure.[42]

The use of CPAP for apnea of prematurity is less well studied. An early study comparing face mask CPAP at 2- to 3-cm pressure to theophylline found that theophylline was more effective in reducing the number of prolonged apneas and bradycardias and in reducing the need for intubation.[43] The Cochrane review of this topic urged more study of CPAP's role in apnea of prematurity.[44]

Many of the studies examining CPAP for the treatment of RDS were done in the presurfactant and preantenatal steroid era, rendering them less relevant to current premature infants. A meta-analysis of these studies concluded that early CPAP use improved survival in infants weighing more than 1500 g.[45]

Current attention has focused on the use of NIV to prevent lung injury in extremely low-birth-weight (ELBW) infants. Unanswered questions remain including the timing of NCPAP and whether early NIV should be used to avoid intubation and mechanical ventilation or whether ELBW infants should be intubated, given surfactant and rapidly extubated to NIV.[36] The latter approach has been dubbed INSURE (INtubation SURfactant Extubation).[46] Use of the INSURE protocol at one institution in Sweden resulted in a 50% reduction in the number of infants requiring mechanical ventilation.[46]

NIV to avoid mechanical ventilation

A growing number of studies have provided support for the use of NIV to avoid the need for mechanical ventilation in the ELBW infant with the ultimate aim of reducing the incidence of CLD.[47–50] Kamper and Ringsted examined the outcome of 81 infants weighing less than 1500 g, 68 of whom were treated with early nasal CPAP, and found that 61 infants were managed with CPAP or oxygen alone with none developing CLD. They concluded that CPAP from birth could be successfully used in most infants of more than 25 weeks' gestation.[51]

Prophylactic CPAP

Unlike earlier studies examining CPAP used in infants experiencing respiratory distress, the application of CPAP immediately after delivery and before the onset of respiratory distress is an area of more recent investigation. In a retrospective study of all infants born at their center between 2000 and 2001, Narendran and colleagues found that early bubble CPAP reduced delivery room intubations, days on mechanical ventilation, and postnatal steroid use, and was associated with increased postnatal weight gain with no increased complications.[52] Sahni et al reported a very low incidence of BPD (7.4%) in infants weighing less than 1250 g, primarily managed with "bubble" NCPAP.[53] Another retrospective study of 234 infants weighing less than 1500 g identified variables that influenced the decision to initiate NCPAP in the delivery room. Nasal CPAP was started successfully in the delivery room for 65% of infants, and 35% smaller and sicker infants were intubated. The use of NCPAP in the delivery room increased with experience over time.[54]

Other studies report mixed results. Ammari and colleagues report their experience in using bubble CPAP from birth in 261 infants weighing 1250 g or less. CPAP was successful in 76% of infants having 1250 g or less birth weight and in only 50% of infants weighing 750 g or less.[55] A pilot study of 104 infants examined the feasibility of randomizing infants of less than 28 weeks' gestation to CPAP during resuscitation after delivery with infants treated with CPAP intubated only when they were receiving a Fio_2 greater than 0.3, had a $Paco_2$ greater than 55 mm Hg, or had apnea requiring bag-and-mask ventilation. Forty-seven required intubation for resuscitation in the delivery room—49% of the CPAP group and 41% of the control infants. Overall, 80% of infants in this study were intubated within the first 7 days of life.[56] A systematic review of randomized controlled trials of prophylactic CPAP found 2 eligible studies[57,58] involving 312 infants. No significant differences were found between CPAP and control infants in the variables studies. Both of the studies noted a nonstatistical increased risk of intraventricular hemorrhage.[59]

SURFACTANT THERAPY AND NCPAP

The early use of surfactant in the ELBW infant has been shown to confer an advantage over rescue therapy.[60] A multicenter trial in which infants with RDS were randomized to CPAP alone or a single dose of surfactant followed by CPAP found that 85% of the infants on CPAP alone were eventually ventilated compared with 43% of the infants given surfactant.[61]Another study by the same group again found a decrease in mechanical ventilation (68% vs 25%) in infants less than 30 weeks who were treated with surfactant and NCPAP.[62]

The Cochrane review comparing early surfactant replacement therapy with extubation to NCPAP to rescue surfactant replacement and mechanical ventilation found that prophylactic surfactant and extubation to CPAP is associated with a reduced need for mechanical ventilation and increased utilization of exogenous surfactant therapy. This review did not find sufficient evidence to evaluate the effect on BPD or CLD but did find a trend toward a decreased risk of air leaks.[63] Four trials were included in this review.[64–67]

USING NIV

Despite the unanswered questions, CPAP is now widely used for a number of neonatal respiratory conditions. Some practical questions that continue to go unanswered include the optimal type of prong with which to administer NIV, recommended pressure levels and the criteria, or approach to weaning an infant from NIV. Contraindications to the use of NIV are outlined in Table 3.

Table 3. Contraindications to NIV[9,68]

Respiratory failure defined as pH < 7.25, Pco_2 > 60
Congenital malformations of the upper airway (T-E fistula, choanal atresia, cleft palate)
Congenital diaphragmatic hernia, bowel obstruction, oomphalocele, or gastroschisis
Severe cardiovascular instability
Poor respiratory drive

NIV Prongs

Originally CPAP was primarily given through an endotracheal tube.[3] Subsequently, other devices were developed including short nasal prongs, longer nasopharyngeal prongs, a single nasopharyngeal prong (usually a shortened endotracheal tube), and face masks. Limited data are available comparing one type of prong to another.[9] De Paoli and associates found that short binasal prongs are more effective than nasopharyngeal tubes in preventing reintubation.[18]

Few studies have compared different types of binasal prongs. One study comparing the Argyle prongs (Sherwood Medical, St Louis, Missouri) with the Hudson prongs (Hudson RCI, Temecula, California) across 3 weight classifications of low-birth-weight infants concluded that both types of prongs were equally effective in delivering CPAP; however, the researchers did note an early onset of nasal irritation in the infants of 1000 g or less weight class wearing the Argyle prongs. The neonates weighing between 1000 and 1500 g had a higher number of episodes of prong displacement with the Argyle prongs than those with the Hudson prongs.[69] Anecdotal discussions among clinicians suggest that the ease with which the prongs can be stabilized plays a significant role in the success of the therapy. Optimal characteristics for nasal prongs are outlined in Table 4.

Face mask CPAP has been used extensively in adults; however, early mask CPAP devices for neonates were not popular because of the difficulty in obtaining an adequate seal and an association with cerebellar hemorrhage.[71] Soft silicone masks are now available and in use in some settings; however, there have been no published reports regarding their efficacy.[72] In this author's experience, face mask devices can be

Table 4. Desirable characteristics of nasal prongs[70]

Soft, short, wide and thin walled
Available in a variety of sizes to ensure a good fit
Easy to secure and adjust
Do not put excessive pressure on the face or septum
Flexible light weight tubing

successfully alternated with nasal prongs in some infants to reduce irritation of the nares sometimes seen with nasal prongs.

Recommended pressure levels

To date no research has been done which defines the optimal level of pressure to use in NIV. It has been shown that bubble CPAP generates chest wall vibrations that may contribute to its ventilatory effect[7] and that pressures generated during variable flow CPAP may be higher than that of conventional CPAP.[30] Most of the literature suggests beginning with 5 to 7 cm of water pressure and titrating up to 10 cm according to the infant's disease process and degree of respiratory distress.[72] Clearly, an infant with decreased compliance resulting from RDS may require more pressure than an infant being treated for apnea of prematurity. One study of infants of 27 to 32 weeks' gestation with mild RDS comparing CPAP of 2, 4, 6, and 8 cm H_2O demonstrated the highest end-expiratory lung volumes, lowest respiratory rate, and the least thoracoabdominal asynchrony at a pressure of 8 cm H_2O.[73]

Weaning from NIV

The optimal approach to weaning an infant from NIV has not been defined. General criteria for weaning include the absence of significant episodes of apnea, minimal work of breathing, and low-level supplemental oxygen requirement. For NIPPV, the rate is usually weaned and the infant switched to CPAP alone before support is discontinued. CPAP pressures are usually weaned to 5 cm H_2O before discontinuing support. In many institutions, infants are weaned from positive airway pressure to nasal cannula before being tried without any airway support. In the case of infants requiring short-term NCPAP for problems such as transient tachypnea of the newborn, a move from CPAP to room air may be feasible. Readiness to wean from NIV may be noted by the infant's tolerance to short periods without support such as during bathing or weighing.

For infants on NIV support for extended periods of time, some clinicians prefer to trial progressively longer periods of time without NIV before completely discontinuing support. There have been no published studies addressing these approaches.[72]

Failure criteria for NIV

Determining when an infant has "failed" NIV and requires intubation and mechanical ventilation is individual and dependent on gestational age and birth weight as well as the underlying disease condition and overall clinical status. No clearly defined criteria have been identified. De Paoli and Morley suggest the following intubation criteria for infants with RDS: persistent and significant apneic episodes, $Paco_2$ of >60 mm Hg, and Fio_2 of >0.6 to maintain acceptable oxygen saturation.[74]

Table 5. Complications of NIV

Nasal septal irritation and necrosis
Gastric distension
Pneumothorax
Increased intracranial pressure
Difficulty keeping prongs in place
Overdistension of the lungs (inadvertent PEEP)
Mucous obstruction of the airway

NURSING CARE

Nasal CPAP is labor intensive for nursing staff. To be most effective, the prongs need to be in the nose and the infant's mouth closed. With variable flow systems, properly securing the prongs is even more critical than with continuous flow systems.[9] Nursing care is directed toward assessing the effectiveness of CPAP, managing the airway, and assessing for, preventing, and managing the complications of CPAP (Table 5).

Assessing CPAP effectiveness

Neonates receiving NIV require frequent and careful assessment to determine therapy effectiveness and readiness for weaning and monitoring for complications. They should be placed on cardiorespiratory and oxygen saturation monitors. Blood gases should be obtained according to infant clinical condition.

Signs that NIV therapy is effective include a decreased work of breathing and improvements in oxygen saturation and blood gas values. Tachypnea may be decreased with NIV although some neonates will continue to demonstrate rapid shallow breathing despite a decrease in work of breathing. Signs of worsening distress signal the need to reevaluate the infant's clinical condition and level of support provided.

Positioning the infant

Excessive movement increases the risk of nasal septum irritation. Swaddling is helpful in minimizing movement and drag on the CPAP tubing. The infant should be positioned prone where possible, with the neck slightly extended.[72] A pacifier may reduce pressure loss by encouraging the infant to suck; some units use a chin strap to keep the mouth closed.[70] More research is needed to study nasal prong devices and methods of securing the prongs and tubing.

Protecting the airway

Nasal septum irritation or injury has been noted as a side effect of CPAP,[75] but with good nursing care and appropriate equipment, these problems should be avoidable. One report found an incidence of nasal injuries of up to 20% in a 6-month review of CPAP given by flow driver. Injuries included necrosis of the columella nasi, flaring of nostrils, and snubbing of the nose.[76] Septum injury is usually the result of a combination of friction, pressure, and excessive moisture. Selection of appropriate prongs and hat is the first step in avoiding nasal injury. Table 4 outlines some factors to consider when selecting NCPAP equipment. Other considerations include the fit of the hat used to anchor the prongs, proper positioning of the neonate and the prongs to avoid excessive movement or pressure, use of a Velcro "mustache" to keep pressure off the face, and avoiding the use of hydrocolloid products on the upper lip.

Another aspect of care is maintaining patency of the nares and airway. Even with adequate humidification of the inspired gases, an infant on nasal prong CPAP is likely to have increased secretions and a decreased ability to clear those secretions. Airway patency should be assessed at least every 2 to 3 hours and nares suctioning done as needed. Normal saline drops may help lubricate the nasal passages and liquefy secretions. In the presence of thick secretions, the temperature and humidity level on the CPAP device should be reevaluated.

Gastric distension

Some infants receiving NIV develop gastric distension and feeding intolerance. An early study of infants receiving CPAP suggested that this distension is benign and resolves once CPAP is discontinued.[77] A 1985 study reported an increased risk of gastrointestinal perforation in infants receiving NIPPV.[78] The 2001 Cochrane review of NIPPV found that in the 3 studies reviewed[27–29] no infants developed gastrointestinal perforation and the rates of feeding cessation because of intolerance were no different between infants receiving NIPPV and CPAP.[30]

It remains important to distinguish distension caused by swallowed air from that caused by more serious problems such as necrotizing enterocolitis. Skin discoloration, absent bowel sounds, abdominal rigidity, and systemic signs of illness are more likely to be seen in cases of NEC than in CPAP distension. Continuous or transpyloric feedings may be an option for infants with feeding intolerance secondary to gastric distension.[4]

SUMMARY

Noninvasive ventilation is not a new therapy but has received new attention in the interest of preventing lung injury. Numerous research studies and meta-analyses have demonstrated the benefits of NIV for the treatment of RDS and the reduction in the need for intubation and mechanical ventilation. Multiple devices and components for providing NIV are available, some more thoroughly studied than others. Optimal implementation of NIV requires basic understanding of the mechanics, capabilities, and limitations of these various devices.

Care of the infant receiving NIV is based on an ongoing assessment of the infant's clinical condition and response to therapy. The literature has clearly demonstrated that the success of NIV therapy increases with increasing experience of the clinicians administering the therapy. A significant number of studies have been published in the past 10 years but a number of unanswered questions remain. Further research is required to enhance our understanding of the optimal application of NIV therapies.

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