Non-invasive ventilation in the neonate: guidelines for the general pediatrician

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Abstract

Respiratory distress is a frequent problem in preterm and full term neonates. Even though invasive ventilation is necessary in certain situations, adequate knowledge and experienced use of non-invasive ventilation may be sufficient for a large group of neonates.

In this review article, we discuss the recent scope on non-invasive ventilation in late-preterm neonates and propose guidelines on the respiratory support of preterm neonates from 32 weeks of gestation on, not necessarily needing admission to a neonatal intensive care unit.

Introduction

Premature birth is associated with lung immaturity and pulmonary disease is the most important cause of morbidity in preterm neonates. Respiratory distress syndrome, transient tachypnea, apnea of prematurity and persistent pulmonary hypertension are among the most common pulmonary diseases in newborns.

For a very long time, invasive mechanical ventilation was the primary treatment of choice for respiratory insufficiency. Nevertheless, during the last decades, it became clear that invasive mechanical ventilation increases the risk of bronchopulmonary dysplasia (BPD), possibly leading to severe and long-term respiratory and neurologic consequences.

Important advances in neonatology in relation to pulmonary support include therapy with antenatal corticoids and surfactant replacement. Antenatal corticosteroids are given to accelerate fetal maturation in case of risk of preterm birth. Surfactant became a revolutionary treatment for respiratory distress syndrome, leading to better compliance of the lungs and less hypoxic respiratory failure. The combination of all of the above resulted in as significant decrease in mortality and prematurity related morbidity as well as a more prominent position of non-invasive ventilation in neonatal care. Consequently, the last decade showed an increasing interest for non-invasive ventilation modes, giving rise to more knowledge about the different systems and their indications (1,2).

In this review, we would like to discuss the recent scope on non-invasive ventilation in late-preterm neonates and propose guidelines on the respiratory support of preterm neonates from 32 weeks of gestation on, not necessarily needing admission to a neonatal intensive care unit.

Neonatal respiratory distress

The two most common pathologies among newborns are respiratory distress syndrome and transient tachypnea of the newborn (3).

Respiratory distress syndrome or hyaline membrane disease is the most common cause of respiratory distress in preterm neonates. As the type II alveolar cells are immature and produce less surfactant, the surface tension of the alveoli is increased and lung compliance is decreased. This leads to atelectasis causing respiratory distress (retractions, grunting), hypoxia and respiratory acidosis. The typical X-ray shows homogenous opaque infiltrates and air bronchograms. Symptoms might be very scarce at first but increase in the hours after birth when stocks of surfactant become depleted. Endogenous surfactant synthesis will start after 72-96 hours and clinical symptoms can then decrease. However, atelectotrauma and ventilator induced lung injury have well been described and need to be avoided by early intervention.

Transient tachypnea of the newborn is a benign and mostly self-limiting condition caused by residual pulmonary fluid in the alveolar and interstitial space. This is a clinical and radiological diagnosis (parenchymal infiltrates, sunburst sign, intralobar fluid accumulation) more frequently seen in babies of male gender, with macrosomia and after cesarean section. Symptoms can last from a few hours to about 48 hours.

It is important to be aware that during the initial course or during the treatment, especially in the course of hyaline membranes disease, lung damage resulting into chronic lung injury can occur. In case of a sudden onset of respiratory distress with increasing need for oxygen, in a previously stable patient, a pneumothorax needs to be suspected. Other factors causing respiratory distress (infection, persistent pulmonary hypertension, peripartal asphyxia, inborn metabolic disorders, congenital heart disease, …) need to be considered in presence of clinical factors raising suspicion.

In at risk or early symptomatic patients, non-invasive ventilation therapy as a therapy for respiratory distress needs to be started as early as possible. This will significantly reduce the risk for progressive atelectasis.

For further details and guidelines on delivery room management, we refer to the article on the new guidelines in the delivery room developed elsewhere in this issue.

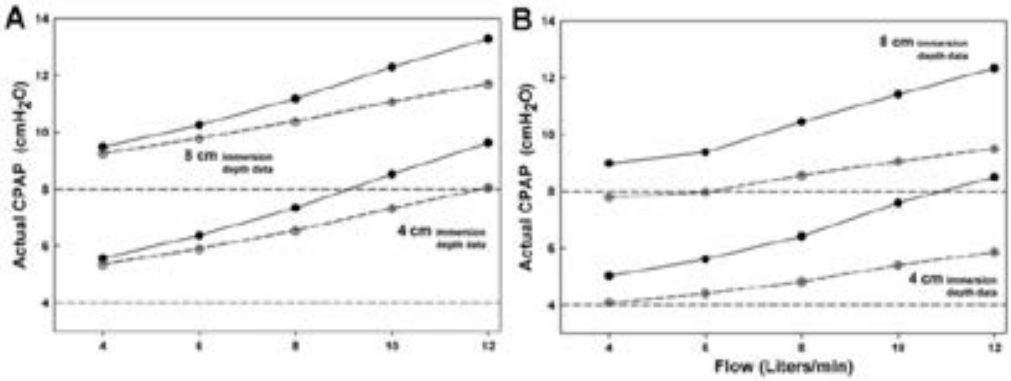
After stabilization in the delivery room, the further choice of respiratory support in the neonatal unit needs to be based upon the newborn's needs and diagnosis.

Modalities for non-invasive ventilation

Nasal CPAP

Nasal CPAP delivers continuous positive airway pressure, preventing alveolar

Figure 1: *The relation between given flow and expiratory limb depth with no and small leak, demonstrating the influence of a good seal on the level of pressure and given support; adapted from Kahn et al. (4)*



Actual B-NCPAP under no leak (*A*) and small leak (*B*) conditions shown for 4 and 8 cm expiratory tubing immersion depth in water. Pprong (•); Pprox (O); Pdistal (small dot). Note that Pprox and Pdistal overlap.

collapse and thus ensuring better gas exchange by stabilizing the functional residual capacity and reducing pulmonary shunts. It also decreases airway resistance and splints the pharyngeal airway, thereby reducing the work of breathing, incidence of apnea and airway collapse (5).

Continuous positive airway pressure was first studied in 1971 by Gregory et al with positive effects in the treatment of respiratory distress syndrome.

CPAP is preferably started immediately after birth while reabsorption of fetal lung fluid and establishment of functional residual capacity are occurring. During the transfer from the delivery room to the neonatal unit, positive pressure should be maintained in case of respiratory distress and this even if there is no need for oxygen supplements.

Two types of CPAP exist: continuous flow and variable flow CPAP.

In continuous flow CPAP the expiratory limb is submersed in a water seal or obstructed by a valve providing the positive end expiratory pressure. The continuous flow is delivered via a flow meter with oxygen blender, heated and humidified. One of the systems providing continuous flow CPAP is also known as bubble CPAP. Figure 1 shows the relation between given flow and expiratory limb depth with no and small leak. It demonstrates that the level of pressure is influenced by the possible presence of a leak on one side and flow on the other side. This might lead to low PEEP (positive end-expiratory pressure) and ineffective support, or to administration of actual pressure which is above the target with risk of lung injury, especially when there is no leak (4,5).

In variable flow CPAP, continuous pressure is generated directly into the nostril or a 'pre-chamber' positioned immediately in front of nasal prongs. A jet of blended oxygen-air is injected towards the nares to provide constant positive pressure. If more inspiratory flow is needed, the venturi action allows additional inspiratory flow. A fluidic flip during spontaneous expiration flips the flow around, leaving via the expiratory limb. The constant but variable gas flow maintains a continuous positive airway pressure, allowing active expiration. This system is also known as Jet-CPAP, or Infant Flow as it's a widely used brand, and reduces the work of breathing as well as increases the lung recruitment.

Nasal CPAP interfaces include mostly nasal masks, prongs or a nasopharyngeal tube (Figure 2) (6,7).

Complications of CPAP are secondary to the pressure administered into the lungs, to the interface irritation directly damaging the nose and to accumulation of air into the stomach and gastro-intestinal tract.

The (excessive) pressure can cause alveolar rupture and air leak syndromes e.g. pneumothorax or pulmonary interstitial emphysema. The positive pressure can also reduce venous return, increase pulmonary vascular resistance and reduce cardiac output. As mentioned above and shown in figure 1, the actual given pressure can exceed the wanted pressure in case of no leak and patients who are very active, moving or crying. In these situations, the given PEEP can increase dramatically and the risk of lung injury rises severely.

The nasal mask or prongs can be too large or too small, or they can cause too much pressure on the nasal area resulting in erosions or necrosis. It requires considerable dedication and skills to apply the nasal interface in a way avoiding complications and still ensuring seal. When trying to increase the seal, there is also a risk of depression of the facial bones. Neonates younger than 30 weeks of gestation are at higher risk of nasal injury than (near) term babies. Very meticulous nursing care is required in order to avoid serious injury and application of barrier dressings is advised. (Figure 3)

Furthermore, as CPAP blows continuous pressure through the nasopharyngeal cavity there is need for the placement of a nasogastric tube to be able to decompress the stomach (8).

Humidified and heated high flow nasal canula (HHHFNC)

HHHFNC delivers humidified and heated gas flow at rates higher than the demanded inspiratory flow. This ensures a variable positive end-expiratory pressure. HHHFNC also reduces dead space and nasopharyngeal airway resistance resulting in decreased work of breathing and more efficient gas exchange.

Practically, the system comprises a flow generator, an air-oxygen blender and a heater-humidifier, all providing flow through bi-nasal prongs. Flow rates range from 2 till 3 liters per kilogram per minute and gas is delivered at 37 degrees and 100% humidity.

The advantages of HHHFNC are the increased comfort for the neonate and the parents, less nasal trauma in comparison with CPAP devices or invasive ventilation and the easy use for the caretaker (9,10).

An important limitation is the variable and consequently less reliable positive end-expiratory pressure.

Nasal interfaces

As mentioned before, an important aspect about noninvasive ventilation in neonates are the interfaces used to deliver the flow and oxygen, if needed. In the case of CPAP, the seal they provide is of major importance. However, in all modes of noninvasive ventilation, the comfort and risk of nasal trauma play a significant role. Masks and prongs are usually alternated in CPAP, while HHHFNC uses a non-sealing interface with protective skin pads. Another interface, gaining popularity, is the RAM cannulaÒ developed by Dr. Ramanathan (11,12). It was first designed for oxygen delivery only, but is now also validated for the administration of high flow therapy and for nasal ventilation (conventional and High Frequency Ventilation). The RAM cannula

Figure 2: *Nasal interfaces*
A CPAP interfaces: nasal mask, nasal prongs (left panel) and nasopharygeal tube (right panel)
B. High flow interfaces: RAM cannula (left panel) en Optiflow® nasal cannula (right panel)

is made of flexible and soft material with thin-walled nasal prongs leading to an increased diameter of the inner prongs. This decrease in airflow resistance results in the ability to provide some degree of positive pressure ventilation, although less efficient compared to known CPAP-devices.

Non-invasive ventilation: other mechanisms

Other modalities for non-invasive ventilation exist.

BiPap (Bi-level nasal CPAP) provides unsynchronized PEEP combined with cycles of low additional pressure at low rate.

NIPPV, nasal intermittent positive pressure ventilation, ensures higher peak inspiratory pressures at a faster rate, resulting in higher tidal volumes and increased functional residual capacity. The inspiratory flow used in NIPPV is not synchronized, forming the most important disadvantage of this ventilation mode (13,14). Earlier studies demonstrate reduced work of breathing when using synchronized non-invasive ventilation, as well as less need for intubation or reintubation and reduced central apneas.

NivNAVA (Noninvasive Neurally Adjusted Ventilation Assist) ventilation supports the respiration in a synchronized way by detecting the diaphragmatic movements using a specialized orogastric tube lined with sensors. Based on the patient's electromuscular signal, pressure support is administered and a back-up inspiratory flow will follow if a set apnea time had passed.

Nasal high-frequency oscillation ventilation applies an oscillatory pressure waveform to the airways using a nasal interface, enhancing alveolar recruitment and CO2 elimination. Although less used in clinical practice, animal models showed promising results.

As these ventilatory modalities are mainly used in neonatal intensive care units, we will not discuss them further.

To CPAP or to High Flow

As High Flow is easier to use and causes less nasal trauma, the question rises whether it can serve as an alternative to CPAP. Several studies have been performed in search of an answer to this question. Yoder et al (n=432) found no difference in efficacy and safety as initial support; they saw however a significant rate of nasal trauma due to CPAP devices (15). The HIPSTER trial (Roberts et al, n=564) and Murki et al (n=272) noted a significantly higher failure rate in the HHHFNC group with good response to rescue therapy with CPAP (16,17). Nasal trauma and pulmonary leaks were on the other hand higher in the nCPAP group. The recently published HUNTER trial (n=754) confirmed that among preterm babies of more than 31 weeks of gestation, the use of HHHFNC as a primary support was inferior to CPAP with a significantly higher incidence of intubation (10). On the other hand, studies showed significantly better scores on the COMFORT scale in groups with HHHFNC compared to groups treated with nCPAP (Spentzas et al, n=46) (9).

In our opinion, in late preterm infants it is of major importance to start respiratory support early enough. With a team trained in its use, CPAP is preferable for neonates with moderate to severe respiratory distress. In cases of mild distress with little need for oxygen, high flow can serve as an alternative. (Table 1)

Table 1: Comparison between characteristics, side effects and goals of CPAP and HHHFNC

CPAP	HHHFNC
Constant PEEP	Less reliable PEEP
Maintenance of FRC and less airway collapse	Washout of nasopharyngeal dead space
Higher success rate in RCT	Higher failure rate and need for intubation in RCT
More nasal trauma	Less nasal trauma
Knowledge of device and good seal is necessary for adequate therapy	Easy use
More air leak syndromes	Possible air leak syndromes

Adjunctive management

Beside the respiratory management, the patient should be managed in an optimal environment to allow for better stabilization.

First, respiratory drive can be optimized with caffeine therapy if evaluated insufficient (18).

As much as possible, the patient should be kept in a calm and stimulus free condition ensuring minimal touch protocol. Careful attention must be paid to the limitation of unnecessary noise and light. The patient should be placed in a comfortable position, e.g. swaddled, in a suitable nest or skin to skin if the parents are available and the infant is stable.

Metabolic stability (glucose, temperature) must be maintained to limit energy consumption. This includes evaluation for the need of IV glucose infusion even if minimal feedings can be started early. As early as possible, minimal enteral feedings should be initiated (10-20 ml/kg/d) to optimize maturation and function of the gastrointestinal tract.

Detection and management of other non-respiratory complications (infection, feeding intolerance, pain, hemodynamics…) need to be evaluated but are out of the scope of this article.

Timely referral to NICU

As we speak about late preterm neonates with respiratory distress, the need for escalation of care needs to be noticed in a timely matter. More specifically we address the cases where neonates on non-invasive ventilation suffer from increasing respiratory distress and/or increasing need for oxygen. Early communication between neonatal (intensive) care wards is of major importance. The indication for surfactant therapy to treat RDS (currently set on worsening when FiO_2 >0.30 on CPAP pressure of at least 6 cm H_2O according the European guidelines (19) needs to be foreseen ensuring timely referral to a tertiary hospital with neonatal intensive care unit.

Conclusion

Non-invasive ventilation has a prominent role in the respiratory support of late preterm and term neonates. The two most used devices are nasal CPAP and HHHFNC. Early respiratory support in the delivery room with CPAP is important and the decision between above named modalities needs to be made based upon diagnosis, the patient's needs and team competence.

Disclosure

The authors have no conflict of interest to declare with regard to the subject discussed in this manuscript.

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