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Non-invasive Respiratory Support in the Neonatal Intensive Care Unit

By Kathleen Deakins, RRT NPS

Non-invasive respiratory support in the neonatal intensive care unit (NICU) is a mainstay to reduce complications of invasive mechanical ventilation. Nasal Continuous Positive Airway Pressure (CPAP) in infants is used for situations such as respiratory distress syndrome, apnea of prematurity, bronchomalacia with terminal airway collapse, and in other conditions that require positive pressure. Types of CPAP used in neonates include continuous flow CPAP, variable flow CPAP, bubble or underwater seal CPAP, bi-level CPAP, synchronized non-invasive positive pressure ventilation, high flow nasal cannula, and nasal high frequency ventilation (NHFV). Changes resulting from research and product development have generated new ideas and different types of CPAP prongs or masks that accommodate the infant's needs, with an emphasis on non-invasive devices. Overall, non-invasive respiratory support strategies for the management of RDS in the neonatal intensive care unit continue to evolve. Early CPAP is practiced regularly in the delivery room to encourage spontaneous breathing and promote surfactant production in the smallest infants. Comprehensive strategies to prevent chronic lung disease and oxygen dependence are essential for survival and quality of life in these patients.

Panel Discussion: Non-invasive Respiratory Support in NICU

Moderator: *Jen-Tien Wung MD, FCCM*

Panelists: *Brian Walsh, RRT-NPS, RPFT*
Bradley A. Yoder MD
Hany Aly MD
Scott Pettinichi RRT

Current evidence supports the early use of Continuous Positive Airway Pressure (CPAP) to reduce the need for intubation and surfactant therapy for some very low birth weight (VLBW) infants. CPAP also facilitates weaning from mechanical ventilation to reduce lung injury. However, there remains a lack of consensus on the CPAP therapy for these vulnerable babies. Not all CPAP devices are created equal. There is a learning curve for CPAP therapy. In this panel discussion, a number of experts address some of the key issues in using CPAP in neonatal care.

2009-0150 Rev 00

This program is provided by an education grant from
Teleflex Medical Incorporated

Non-invasive Respiratory Support in the Neonatal Intensive Care Unit

By Kathleen Deakins, RRT NPS

Non-invasive respiratory support in the neonatal intensive care unit (NICU) has been used for more than 35 years as a means to reduce complications of invasive mechanical ventilation.[1] Specific types of non-invasive support have been implicated in preventing respiratory failure in spontaneously breathing infants, especially those with Respiratory Distress Syndrome (RDS). Technological progress, along with a better understanding of the applications of equipment, advances in the care of the neonate, and documented favorable patient outcomes have translated into trends that continue to promote non-invasive respiratory support for care of the neonate.

Nasal CPAP in the Neonate

Nasal Continuous Positive Airway Pressure (CPAP) is a non-invasive positive pressure modality used to maintain an elevated baseline transrespiratory system pressure during spontaneous breathing.[2] Nasal CPAP is applied to infants for a variety of clinical conditions including respiratory distress syndrome, apnea of prematurity, bronchomalacia where terminal airway collapse is evident, and in other conditions that require positive pressure, including patent ductus arteriosus, some congenital heart abnormalities, or other conditions that produce atelectasis.[3] The indications for CPAP include evidence of signs of respiratory distress including nasal flaring, grunting, retractions, and increase oxygen requirement.[1] (Table 1) The physiologic benefits of CPAP include alveolar stabilization and maintenance of lung volume, increased functional residual

> Technological progress, has translated into trends that continue to promote non-invasive respiratory support for care

capacity (FRC), decreased atelectasis, decreased ventilation perfusion mismatch, airway stabilization, possibly increased lung compliance and improved gas exchange.[4] Other positive effects of CPAP include a decrease in airway resistance attributed to laryngeal dilation, preservation of surfactant accomplished by alveolar stabilization, a reduction in respiratory rate,[1] minute ventilation as atelectasis resolves, and reduction of intracardiac left-to-right shunt. Contraindications for using CPAP include the presence of a pneumothorax, conditions where the nose is not patent such as choanal atresia, in conditions where risk of intra-abdominal distention is lethal, such as congenital diaphragmatic hernia (preoperative) or tracheal esophageal fistula, or evidence of cardiac failure or hemodynamic instability.[5] CPAP is also not recommended in patients with cleft lip or palate as there is an inability to control anatomical leaks.[5] Risks and complications caused by using nasal CPAP are related to the effects of positive pressure, the condition of the patient's lungs and the type of CPAP setup used.[6] Nasal CPAP risks that may produce complications include pressure sores around the nose, gastric distention, extension of pulmonary air leak, increased intracranial pressure, decreased renal blood flow, and changes in cardiac output.[1]

Table 1. **Indication for CPAP Therapy:**

1. Diseases with low FRC, e.g. RDS, TTN, CPIP, PDA, pulmonary edema, etc.
2. Apnea and bradycardia of prematurity
3. Meconium aspiration syndrome (MAS)
4. Airway closure disease, e.g. bronchiolitis, BPD
5. Tracheomalacia
6. Partial paralysis of diaphragm
7. Respiratory support after extubation

Types of CPAP used in Neonates: CPAP Delivery Varies Amongst Devices

Continuous Flow CPAP

Continuous flow CPAP systems use a preset flow of gas to maintain CPAP through nasal prongs. CPAP delivered is dependent upon the flow rate and the resistance created by the exhalation valve that is housed in the breathing circuit.[2] Typically, ventilator-driven CPAP represents a continuous flow system.[7] Following the earlier versions of bubble CPAP devices, continuous flow CPAP became popular because of its ease of use and pressure stability. Because of the presence of an exhalation valve, patients must exhale against a fixed resistance, thus resulting in a higher induced work of breathing.[7]

Variable Flow CPAP

Variable flow CPAP technology incorporates a flow driver that delivers fresh gas through a breathing circuit to a dual injector generator with a specially designed valve, mask or nasal prongs. Gas enters at the point of the interface on inspiration and shunts flow away through an expiratory gas channel as the patient desires on exhalation.[8,9] CPAP levels are stabilized and maintained by a change in the flow rate at the generator with little variability, unless there is a leak at the patient's interface.[9]

The positive effects of variable flow CPAP have been described as a decrease in respiratory rate, increase in tidal volume, and increase in lung compliance, which translate to a decrease in the work of breathing.[10] Variable flow CPAP represents a sophisticated technology of CPAP delivery with visual and audible alarms and physiologic monitoring. The feasibility and effectiveness of its application are reasonable but require specific pieces of equipment such as flow drivers, generators and circuits that are somewhat expensive to provide.[6]

Bubble or Underwater Seal CPAP

Bubble CPAP, the earliest version of CPAP, was described by Gregory in 1971.[11] This is a simple, inexpensive method of CPAP delivery involving nasal prongs attached to a circuit with a gas source delivering flow of 6-10 liters per minute on the inspiratory side of the circuit and submersion of the expiratory tubing under water at a designated level that represents CPAP (one cm below the water is equivalent to one cm H_2O of CPAP).[6] Bubble CPAP is a type of continuous flow CPAP that differs from other systems in that it lacks physiologic monitoring. There is no audible pressure disconnect alarm, and no warning when there are leaks in the system. Visual alarms of "no bubbling" and clinical observations of the patient are essential to maintaining the system and maintaining patient safety.[3] The advantages of its simplistic design include portability and mobility of the system for transport. One unique feature of bubble CPAP is that the bubbles create airway pressure oscillations that may or may not contribute to gas exchange.[3,12] Although this method of CPAP is a labor intensive intervention that requires attention to detail and continuous education, centers using bubble CPAP have been successful in preventing atelectasis in very low birth weight groups.[12]

Bi-Level CPAP Applications

Bi-level CPAP, known by different acronyms such as SiPAP™ or biphasic CPAP or nasal BIPAP, is another type of CPAP that allows spontaneous breathing at two levels of CPAP.[13] A sigh level of CPAP is reached for a preset defined interval of time (set as inspiratory time) and a low level, the baseline CPAP is maintained continuously.[14] The number of sighs is determined and preset by the caregiver. The difference created by these two levels of pressure is minimal, however; it may be associated with small changes in volume and associated increases in functional residual capacity (FRC), which can be integral to recruitment.[15] The goal of this bi-level CPAP is to achieve some higher level of alveolar recruitment and prevent alveolar collapse, and it implies some assumption that it will decrease the work of breathing required by the infant.[14] In addition, the higher mean airway pressure generated by two levels of CPAP may be responsible for accelerating the surfactant production of a spontaneously breathing infant and also stimulating the respiratory center of very low birth weight infants.[15] Recommendations for using the SiPAP version of bilevel CPAP are to use low frequencies of about 5-6 breaths per minute and a minimum of 1-second duration for sigh breaths..[15] When it was introduced into practice, bi-level CPAP showed clinical evidence of greater improvement in gas exchange compared to CPAP alone.[15] However, in the incidence of extubation failure, bi-level CPAP and CPAP remain similar. The ability to achieve bi-level CPAP requires either a ventilator or a specific flow generator that can function as a bi-level CPAP generator.

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Synchronized Non-Invasive Positive Pressure Ventilation

Synchronized non-invasive positive pressure ventilation (SNIPPV) is another method to deliver positive pressure breaths through nasal prongs or a mask. In SNIPPV, gas flow issues from a flow driver used in variable flow CPAP or through a mechanical ventilator.[15] Baseline CPAP pressures are typically set at +5 cm H20, while inspiratory pressures may range from 10-20 cm H_2O. A ventilator requires a minimum driving gas flow of 8 L/minute to accomplish the desired pressure in the face of leaks. Flow driver CPAP pressures used in some centers are dependent on the flow rate in the circuit. SNIPPV has been shown to decrease work of breathing in infants with respiratory distress syndrome compared to nasal CPAP alone.[16]

Nasal High Frequency Ventilation

Nasal high frequency ventilation (NHFV) is a type of non-invasive ventilation that provides high frequency breaths through nasal prongs using below dead space tidal volumes and a step by step inflation method that stabilizes at a desired pressure.[17] The benefits of NHFV include aggressive maintenance of FRC and MAP and reduced CO_2 retention. Maintaining the circuit and interfaces of NHFV is a challenge because spontaneous movement of the patient may cause disconnection and de-recruitment. Anecdotal reports indicated that NHFV resolved atelectasis within 24 hours after failure of standard variable flow CPAP. Utilization of this type of non-invasive ventilation has fallen out of favor because the equipment is not readily available. Studies continue

to test its efficacy and assess the feasibility of its delivery.

CPAP Interfaces: What Works and What Needs Improvement?

There are many types of interfaces used with CPAP. Examples include long (40-90 mm) or short (6-15 mm) binasal prongs, contoured masks, and shortened endotracheal tubes.[14] Short binasal prongs are the most commonly used interface because of they are simple to insert, they maintain patency, and it is easy to inspect the nares without detaching the setup from the infant. Long bi-nasal prongs and endotracheal tubes are slightly more difficult to handle and require meticulous care to maintain patency.[18] Complications of inappropriate position of the prongs, or fixation devices may result in damage to the shape of the skull on an already soft bony structure, damage to the nasal septum that results from pressure applied to the cartilage between the nares, narrowed nasal passages, orbital edema, bumps, bruises or bleeding on any of the areas where pressure exists.[18] In a comparison between mask and nasal prong CPAP, Yong revealed that nasal prongs had a higher incidence of complications (35% to 29%) than the CPAP mask used with the infant flow driver variable flow CPAP, although patients on nasal prongs were generally on CPAP longer.[16]

The incidence of complications with CPAP interfaces is improving, showing that lessons learned about care of the infant with nasal CPAP are paying off. CPAP has been a standard of care for newborns with RDS for more than three decades and will most likely continue to remain as a key component in stimulating surfactant production and reducing the need for invasive mechanical ventilation.[3]

Changes resulting from research and product development have generated new ideas and different types of CPAP prongs or masks that accommodate the infant's needs. Minimizing the amount of equipment applied to the head and face may help decrease the incidence of complications as long as CPAP levels can be maintained. Well established CPAP interfaces such as those used with bubble CPAP have not correlated with a significant degree of nasal injury, while other interfaces have not fared as well.[3] Managing CPAP properly is important and requires careful attention, including frequent assessment at least every 4-6 hours, constant inspection of the nares, adequate positioning of the infant and careful selection of the CPAP cap, fixation device and securing band for the head.[3,18]

Measuring esophageal pressure is the best method of assessing positive pressure delivered, but it may be difficult to accomplish at the bedside.

Other Non-invasive Devices

High Flow Nasal Cannula

The heated and humidified high flow nasal cannula (HH-HFNC) is a simple, non-invasive method of oxygen delivery that can produce positive pressure in a premature infant (usually at >1 liter per minute.[18] (See Figure 1) The distending pressure generated is dependent on the size of the nasal cannula, the composition of the infant's airway structure, and the flow rate.[19] The benefits of HH-HFNC in infants are simplicity of use, less risk of damage to the nares and nasal septum, and lower incidence of structural change of the head shape in the absence of a fixation cap or head band. The risks of using HH-HFNC on infants <2 kg lie in the inability to effectively measure distending pressure. In addition the hazard of developing of inadvertent escalation of expiratory pressure is possible. Measuring esophageal pressure is the best method of assessing positive pressure delivered, but it may be difficult to accomplish at the bedside. The safety of delivering oxygen or airflow through a HH-HFNC using minimum flows of two liters per minute has been improved on selected types of devices. Pressure diversion through a pop-off valve assembly allows additional system pressure to be vented to the atmosphere instead of being transmitted to the infant, although these pressures can be in excess of 40 cm H_2O.[20]

Figure 1. Conchatherm Neptune Heated Humidified High Flow Nasal Cannula (Teleflex Medical)

In summary, it appears that HH-HFNC compares favorably to conventional types of CPAP, but potential side effects and unknown pressure delivery seen in the clinical arena has some neonatologists questioning its safety and efficacy. Early studies of HH-HFNC showed that it was comparable to CPAP in managing obstructive or mixed apneas.[21] In one study, HH-HFNC was able to prevent intubation, reduce the work of breathing, and prevent mucous membrane damage, although the study appeared to be underpowered.[16] However when comparing HH-HFNC and CPAP prongs in VLBW infants gram-negative bacteria was associated with damage to the mucosa caused by using cannulas. The degree of infection risk in HH-HFNC versus CPAP prongs remains to be seen.[22]

Despite lack of efficacy and safety documentation, Shoemaker et al revealed no differences in negative out-

Figure 2. Infant Nasal Prong CPAP (Teleflex Medical)

comes when using the HH-HFNC or CPAP in infants < 30 weeks gestation.

Applications and Expectations of Non-invasive Respiratory Support

CPAP was initially used in infants as a response to visible respiratory distress. Today initiation of CPAP begins in the earliest hours of life, as in the delivery room (Figure 2). CPAP is now considered a preferred "first line" therapy for infants with RDS because improved antenatal management (including steroid administration) has benefited lung development in premature infants.[16] According to Finer, there is still lack of evidence supporting the advantage of initiating CPAP in the delivery room for low birth weight infants.[23] About 50% of <28 week gestation infants still required intubation and surfactant in the delivery room despite attempts to use non-invasive means to support these infants.[23] There are mixed reports about the efficacy of early versus late administration of CPAP. Infants who received CPAP shortly after birth have demonstrated good outcomes in terms of survival (78%-84%) and survival without oxygen dependence at 28 days (58%-79%).[16] There are no studies comparing long-term outcomes of non-invasive respiratory support devices (such as the HH-HFNC versus CPAP), therefore, the HH-HFNC has not been widely accepted as a standard of care, despite its simplicity.[20]

Conclusions

Non-invasive respiratory support strategies for the management of RDS in the neonatal intensive care unit continue to evolve. NICU's across the country have been diligently proactive in promoting early initiation of CPAP as a first line treatment for premature infants. CPAP strategies have also taken many centers back to the basics, using the tried and true methodology of Gregory for weaning off of CPAP in 1 cm H_2O increments.[9] Early CPAP is practiced regularly in the delivery room to encourage spontaneous breathing and promote surfactant production in the smallest infants. To date, the role of HH-HFNC in acute and long-term management of RDS and other neonatal respiratory conditions is unknown. Comprehensive strategies to prevent chronic lung disease and oxygen dependence are essential for survival and quality of life in these patients.

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Kathleen M. Deakins, RRT NPS, is Supervisor for Pediatric Respiratory Care at Rainbow Babies & Children's Hospital of University Hospitals, Cleveland, Ohio. She is the author or coauthor of many publications and abstracts on pediatric respiratory care and is the recipient of the 2005 Bird Education Award and the 2006 Viasys HealthCare Fellowship for Neonatal and Pediatric Therapists. She lives in Chardon, Ohio.

Panel Discussion: *Non-invasive Respiratory Support in NICU*

Moderator:
Jen-Tien Wung, MD, FCCM
Professor of Clinical Pediatrics
Columbia University

Panelists:
Hany Aly, MD, FAAP
Associate Professor of Pediatrics and Obstetrics and Gynecology
George Washington University

Scott Pettinichi, Med, RRT, NP
Senior Clinical Director, Division of Respiratory Care
Cincinnati Children's Hospital

Brian Walsh, RRT-NPS, RPFT, EMT-E, FAARC
Clinical Research Coordinator, Respiratory Care
Children's Hospital, Boston

Brian Yoder, MD
Associate Medical Director, NICU
University of Utah School of Medicine

Mechanical ventilation (MV) is commonly used in the neonatal intensive care unit (NICU) for ventilatory support of infants. However, there are numerous complications associated with endotracheal intubation and positive pressure ventilation. In addition, there is a strong association between MV and brain injury. Therefore, there is need for a less invasive alternative for respiratory support, such as CPAP (continuous positive airway pressure), to reduce baro/volutrauma and the development of bronchopulmonary dysplasia (BPD). CPAP is to apply a positive pressure to the airway of a spontaneously breathing patient throughout the respiratory cycle to increase transpulmonary pressure. In recent years, there is a wealth of experimental and clinical data regarding CPAP therapy. In this panel, we have have gathered 4 experts to discuss contemporary issues such as the use of CPAP in respiratory distress syndrome.

> CPAP is both a corrective and a supportive therapy; that allows premature lungs to grow while helping the process of gas exchange.
>
> - Wung -

How effective is CPAP in infants with respiratory distress syndrome (RDS)?

Aly: Nasal CPAP has been associated with positive results in preterm infants with RDS. In 1997, we started using CPAP in our unit at the George Washington University Hospital. At that time the incidence of chronic lung disease (CLD) in very low birth-weight infants (<1500g) was 33%. Each year we experienced a consistent and significant decrease in CLD. Our current rate is 5%. We also observed the need for experience to achieve satisfactory results. (After adopting the early CPAP policy from Columbia University, it took us almost 6 years to match Columbia's outcome results.) Many other experiences are reported in the recent literature. After a visit to our NICU and adopting our practice with early use of the bubbl nasal CPAP, Birenbaum and colleagues reported a decrease in CLD from 47% to 22%.[1]

Pettinichi: I agree, CPAP is an effective modality for managing respiratory distress, especially in preterm babies. The main indications for CPAP are RDS and apnea of prematurity. CPAP has been shown to decrease the need of invasive and costly mechanical ventilation. Short binasal prong devices are more effective than single prongs for reducing the rate of reintubation in preterm infants who have been extubated to NCPAP after intermittent positive pressure ventilation for RDS. This is also true for infants treated with NCPAP soon after birth. The improvement in respiratory parameters suggests that short binasal prongs are more effective than nasopharyngeal CPAP in the treatment of early RDS.

Walsh: CPAP has been a standard of care for managing infants with RDS for a few decades. Nasal CPAP in particular has lead to a significant improvement in patient outcomes, particularly in low birth-weight, premature infants. CPAP is clinically indicated in infants with both obstructive and restrictive lung diseases, and can improve oxygenation, counter atelectasis[2-6] and stabilize the chest wall. It is also used to stent open airways and lower airway resistance to gas flow in patients with obstructive lung disease and apnea.[7-12] CPAP is frequently used to maintain airway patency in infants with obstructive apnea[13-18] and obstructive airway diseases.[19-22]

Yoder: It had been over 3 decades since Gregory and colleagues first demonstrated the benefit of CPAP in the management of RDS.[23] The relative reduction in mortality they reported has not been equaled by any other therapeutic intervention in the NICU. Numerous observational studies have reported CPAP's effectiveness (primarily via nasal prongs) for managing neonatal RDS (nRDS). Although nasal CPAP has been widely used in Europe since the Gregory report, use increased in the US only after the comparative observational studies of Avery et al[24] and Van Marter et al.[25]

Adequately sized randomized controlled trials are the gold standard for evaluating CPAP for nRDS. To date there is only one large randomized trial published, the COIN Trial.[26] This study showed that early use of nasal CPAP in preterm infants (25-28 weeks gestation) with respiratory compromise resulted in a 50% reduction of subsequent intubation, ventilation and surfactant therapy. The greatest reduction was found among infants > 26 weeks gestation, confirming the observational results reported by Ammari et al.[27]

Wung: Nasal CPAP increases the functional residual capacity and airway diameter, prevents alveoli from collapsing, improves respiratory compliance, and conserves surfactant. In our experience since 1973 with early application of CPAP therapy, usually within five minutes of life, to prevent alveoli collapse, 75% of these infants (<1500 grams) did not need intubation and surfactant therapy. The extended use of CPAP can also stimulate the growth of alveoli. CPAP is both a corrective and a supportive therapy; that allows premature lungs to grow while helping the process of gas exchange. Over the past 4 decades, evidence has accumulated to support the use of CPAP to treat infants with various respiratory distress diseases and to facilitate weaning in intubated infants.

Do you prefer water bubble CPAP (threshold resistors) or respirator-derived CPAP (variable pressure-flow resistor)? State your reason(s) why. What are the components of a good CPAP device ?

Aly: The saying "if it is not broken, do not fix it" is often true. We know that reports of the best outcomes and the least incidence of CLD come from neonatal units using the bubble CPAP. We also know that bubble CPAP does not require any extra expenses. In fact, it is actually less expensive to use than a ventilator-derived CPAP. Therefore, it is hard to justify the use of other types of

We know that reports of the best outcomes and the least incidence of CLD come from neonatal units using the bubble CPAP.

– Aly –

CPAP. There are some speculations that water bubbling produces some oscillatory changes in the pressure created inside the lung causing better recruitment of alveoli. However, there is not enough evidence to support these claims. On the other hand, bench research demonstrated a less stable pressure when using bubble CPAP when compared to ventilator-derived CPAP.[28] Besides a flaw in the methodology, the animal researchers could not provide a reason for the discrepancy between their results and the reality in neonatal practice.

Pettinichi: The respirator-derived CPAP is better tolerated by neonatal patients because flow sensing allows the patient to exhale against low resistance as opposed to bubble CPAP. I have not seen evidence that bubble CPAP is beneficial to respirator-derived CPAP in this respect. Noise associated with bubble CPAP can be a concern with low birth-weight infants. The components of a good CPAP device are first and foremost patient safety. CPAP setups should be professional grade, meaning that they are not home built by RT or medical staff. A pressure monitor and oxygen analyzer are to be placed in line the CPAP device.

Walsh: I truly believe that this is a user preference, as there appears to be little evidence for one type of device over another. I prefer respirator-derived CPAP systems because they contain alarms that provide careful monitoring of the system during therapy. This is not necessarily true with many of the home-grown bubble CPAP type systems. In many instances CPAP can be a life saving intervention. Infants are obligate nose breathers and any device that seals the nose should be monitored for functionality. If it is not properly monitored and a malfunction occurs (disconnect or dislodged) the end result could be distress and/or desaturation. Many feel that physiologic monitors are enough to provide safe monitoring, however I feel this could lead to poor care. For example, when a desaturation occurs due to an interruption in gas flow or drop in pressure, a system monitor would have alerted the practitioner to this failure prior to the end result – desaturation or worse. Regarding the components of a good CPAP system – I think we are almost there. We need CPAP systems that promote comfort, provide high relative humidity at close to body temperature without drowning the infant, are alarmed for functionality, and encourage developmental care.

Yoder: We use both bubble and ventilator derived CPAP, though only ventilator-CPAP is available in each of our units. Where bubble-CPAP is available, it is our primary choice of initial non-invasive support because of decreased cost. If an infant is extubated directly from a ventilator capable of supporting CPAP (i.e., not a high frequency ventilator), then ventilator-CPAP is typically used. The benefits of bubble CPAP are primarily ease of set-up and low cost. The benefits of ventilator CPAP are stability of pressure support[29] and an effective alarm system. The optimal CPAP support device would be one that is low cost, easy to set-up and manage, provides pressure stability, has low resistance to exhalation and has the option for providing intermittent supplemental breaths.

Wung: A good CPAP system should include the following criteria: (1) Easy to set-up, apply and keep connected to infant's airway, (2) Easy to control pressure, temperature, humidity and FiO2, (3) Low resistance and applicable to very low birth weight infants, (4) Simple, safe and understood by care givers, (5) Comfort to patient and cost effective.

What complications can occur with CPAP and how can we avoid them?

Aly: There are 3 complications: acute, chronic, and care-dependent. The acute complication is pneumothorax, which usually occurs between the first and third day of life, depending on the size of the infant. The incidence varies between 0.5% - 2%. The pneumothorax is usually small, when compared to intubated infants on mechanical ventilation, where pneumothorax is more frequent (15%-22%) and more serious. A recent clinical trial reported a high incidence of pneumothorax (9%) in association with the use of CPAP. In that trial they used unusually high CPAP pressure (8 CmH2O), while we and many authors use only a pressure of 5 CmH_2O[26]

The use of CPAP for a prolonged time can result in abdominal distention that has been described as benign gaseous distention. It is not a precursor to necrotizing enterocolitis. It can be minimized if the gas in the stomach is evacuated routinely every 3 hours and if an open-to-air orogastric tube is maintained while on CPAP. The third complication is nasal septum damage. This occurs when an inexperienced caregiver pushes the nasal prongs or the face attachment piece of the CPAP apparatus tightly against the nasal septum. Another cause for damage is when inappropriate size prongs are used that "pinch" the nasal septum, or if there is careless suction of nasal secretions. All these care-related problems are preventable with appropriate training and clear unit policy. In our practice, infants <1000 g in birth-weight are assigned only to the most experienced nurses in the NICU during the first week of life.

> In many cases, I see HFNC and NCPAP as exchangeable on the lower end of CPAP therapy.
>
> - Pettinichi -

Pettinichi: In addition to these complications, one can see skin breakdown around nares and oral areas. To avoid this, monitor sight closely and ensure proper fitting of the patient interface. A third complication is decreased venous return at higher levels. To avoid this, maintain moderate settings -- regular monitoring of patients on CPAP is needed at all times.

Walsh: There is an objective scoring system that can ensure that everyone is on the same page with monitoring skin breakdown. In extreme situations a neonate may need to be intubated to rest the affected area. Pneumothorax can still occur, but less likely at lower pressures (< 6 cm H_2O). Developmental care is something I think many of the current CPAP systems miss. Many very low birth-weight neonates wear CPAP for weeks if not months with few breaks. Most CPAP systems partially block the view of the child and are heavy enough to prevent them from spontaneously moving their head, keeping them from interacting with their environment. It makes sense to try to remove the visual obstruction and allow for easier head movement of the neonate.

Yoder: Injury to the nasal soft tissues can be minimized by attention to proper prong size and position, minimizing tubing torque, gentle intermittent cleansing, and proper gas heating and humidification.[30] Loss of pressure may occur, either through prong malposition or via an open oral airway. Pressure alarms or attention to bubbling can minimize this. Air leak syndromes are also a risk during CPAP therapy. In the COIN trial, pneumothorax was significantly higher (3-fold) in the early CPAP group compared to early intubation, but had no apparent effect on clinical outcomes.

Previous studies on CPAP show different results, and some show no decrease in the incidence of bronchopulmonary dysplasia . What do you think are the reasons for this difference?

Aly: This is related to the difference in experiences among facilities. Despite the discrepancies between different reports, there is not a single report or trial that demonstrated increased incidences of Chronic Lung Disease (CLD), mortality or long-term disability in association with CPAP. It is therefore fair to conclude that the use of CPAP is at least as good as mechanical ventilation. The focus for care givers should be to reproduce the outcomes that the best CPAP facilities have reported.

Pettinichi: The time at which CPAP is initiated is a factor in reducing incidence of BPD. The sooner CPAP is started, the better the outcome in most instances. The proper use of a high flow nasal cannula (HFNC) can also be of benefit if initiated early.

Walsh: This just shows you how complex this disease is as well as all the other confounding factors. For example the use of prenatal steroids became standard of practice in late 1990's or early 2000's, after many of the surfactant studies in which roughly half of the mothers received steroids prior to delivery. This makes you wonder if many of those studies are still relevant in today's

practice.

Yoder: Most studies supporting the beneficial effect of CPAP on BPD have been from single centers where care providers are experienced and a consistent approach has been developed. The importance of clinical experience on improving the effectiveness over time of CPAP support has been shown by Dr. Aly and colleagues (Pediatrics 2004, 2005). Of the two large multicenter randomized controlled trials neither demonstrated a reduction in BPD rates despite overall decreases in the need for intubation and mechanical ventilation.[26,31] Multicenter trials introduce a variety of potential problems including variations in expertise, variance in population genetics, differences in sepsis patterns and nutritional support, and patterns of postnatal steroid use, among others.

Some practices advocate the INSURE (Intubate-SURfactant-Extubate) strategy. What is your opinion of this approach?

Aly: The use of surfactant is one of the few interventions that showed evidence of improved outcomes in premature infants. The surfactant trials were done in mechanically ventilated infants and conducted at a time when CPAP was not widely used, so one cannot really extrapolate those results to infants on CPAP. The major objection to the application of the INSURE strategy is the need for tracheal intubation, which is the most traumatic procedure that can be done to a neonate. INSURE-associated mechanical ventilation, even for a short period of time, also has consequences. My inclination is to reserve the INSURE strategy for infants who are likely to require intubation anyway. For example infants born at a gestational age <26 weeks are often lacking the central drive and the adequate muscle bulk required for efficient breathing and they often require mechanical ventilation. These infants, if intubated at birth and received surfactant, could have possibly done better on CPAP. This is a personal opinion rather than evidence-based. In this respect, I would like to caution readers of neonatal literature to be critical of recent studies on INSURE strategies. For example, a recent randomized controlled trial by Rojas et al demonstrated that INSURE strategy decreased the incidence of CLD in VLBW infants from 59% to 49%.[32] In the USA, the overall incidence of CLD in VLBW infants is 29% that is one half of what is reported in the Rojas trial. The inferior baseline outcome makes it hard to make any conclusion out of this trial.

Walsh: I am a big advocate for this type of strategy. Many of these extremely premature infants are surfactant-deficient. Intubation and surfactant delivery appear to be fairly safe. Anytime you can keep a patient off positive pressure ventilation and achieve adequate gas exchange, you are providing better patient care. We all understand that ventilator-induced lung injury is real, and keeping an endotracheal tube in place sets the infant up for ventilator-associated pneumonia.

Yoder: A recent meta-analysis of several small randomized trials evaluating the INSURE approach concluded that this approach was associated with less need for mechanical ventilation, reduced frequency of air leak and decreased rates of BPD.[33] However, very few of the infants enrolled in these trials were <27 weeks gestation; thus the benefit of this approach in very immature infants is not as well established. We have utilized this approach within our units, more in the management of slightly older preterm infants (28-36 weeks) with signs of early RDS, and found it quite effective as a tool to decrease ventilator need.

Wung: The INSURE strategy includes intubation, prophylactive surfactant and early extubation. At our institution, 84.6% and 30.2% of ≥26 weeks and ≤26 weeks of gestation VLBW infants respectively were successfully treated with CPAP without intubation and surfactant. If we adopted the INSURE strategy, many VLBW infants would have been intubated, received surfactant and stressed unnecessarily. However, if there is a high possibility that an infant will need mechanical ventilation, surfactant should be given and one should try to extubate early. Unfortunately, in VLBW infants (≤26 weeks of gestation), extubation after surfactant therapy is usually not possible because of deterioration from intubation.

Some practitioners use high flow nasal cannula (HFNC) in infants as an alternative to CPAP. Do you think both modalities are exchangeable? Is there any evidence to support the use of HFNC? If so, in what indications?

Aly: I do not see a good reason to change an infant from CPAP to HFNCT. I am not aware of any study that could associate HFNCT with improvement of clinical outcomes.

Pettinichi: In many cases, I see HFNC and NCPAP as exchangeable on the lower end of CPAP therapy. As the need for support increases, NCPAP allows the caregiver to administer more consistent levels of oxygen than CPAP Studies have shown that while HFNC can deliver measurable levels of CPAP, they are dependent on the mouth being open or closed. Back pressure within the HFNC system is also a concern in larger patients. In our PICU, high levels of back pressure in HFNC circuits have been an issue, requiring us to limit its use. HFNC should be used with a pressure limited valve in line.

Walsh: I am unsure if they are interchangeable at this point. HFNC appears to be safe and I feel this therapy could be the bridge during the growth process that we need without sacrificing safety, developmental growth, and comfort. That being said, I will continue my same plea for monitoring of these devices.

Yoder: I prefer to use the term HHFNC (Humidified High Flow Nasal Cannula) as it emphasizes the importance of adequate humidification with this mode. (One should probably add a third H for Heated as that is another important variable of neonatal respiratory gas therapy.) I'm not sure the two therapies are completely exchangeable, but there does appear to be an overlap. The use of HHFNC remains controversial, primarily due to concerns over the potential for undocumented increased pressure delivery, though the most recent studies suggest this more a theoretical concern than a practical one.[34-36] Despite this concern, HHFNC for respiratory support in the NICU is becoming increasingly frequent. Observational studies suggest HHFNC can be used in place of nasal CPAP in the management of premature infants.[37,38] In these studies HHFNC nearly completely replaced CPAP use with no increase in reintubation rates, air leak, feeding intolerance or other adverse effects. There are no randomized trials comparing the use of HHFNC to nCPAP for support of respiratory compromise. We have the only active trial registered on ClincalTrials.gov, however maintaining equipoise among the clinical care providers has been difficult.

What is your opinion of the use of nasal intermittent positive pressure ventilation (NIPPV), also referred to as "IMV via CPAP prong."

Aly: Some infants supported with CPAP may show signs of CPAP failure. We identified some criteria of CPAP failure that included: a) increased oxygen requirement to >60%, b) increased PCO2 >65 mmHg, c) intractable acidosis with base deficit >-10 mEq/dl, and d) severe apnea or chest wall retraction. Infants who meet the criteria of CPAP failure need escalation of respiratory support, such as tracheal intubation and mechanical ventilation. In our practice, we tend to use more of mechanical ventilation without intubation or NIPPV as an alternative before reaching the final resort of intubating an infant. Recently some reports advocated the use of NIPPV as the primary mode of support. However, we advise beginning with the least invasive approach (i.e. bubble CPAP) before escalating to NIPPV.

> Observational studies suggest HHFNC can be used in place of nasal CPAP in the management of premature infants.
>
> - Yoder -

Walsh: NIPPV has been around for years without huge success in preventing apnea and or re-intubation. However, I wonder if we are not seeing a different patient population than when these studies were conducted. Studies of NIPPV in adults showed it can worsen outcomes in the wrong patient population. This raises the question that when we try this therapy, do we draw a clear line for escalating therapy, or just prolong unacceptable results such as frequent apneas, frequent hypoxic events, oxygen toxicity, and/or hypoventilation? A second issue is that ventilation often simply increases the mean airway pressure. We tend to be a little phobic of CPAP or PEEP. We typically do not go far above 5 cmH_2O, but will quickly put someone on NIPPV at 8/5 with a MAP of 6.5, crediting the mode when maybe 6 or 7 of CPAP would have worked just as well.

Yoder: Meta-analysis of the few small randomized trials suggests that synchronized NIPPV results in a greater extubation success rate among immature infants compared to CPAP alone.[39] There is currently inadequate evidence that NIPPV results in decreased BPD rates, but study numbers have been small. We are currently involved in a multicenter randomized trial, sponsored by the Canadian Institutes of Health Research (PI, Dr. H Kirpalani, Philadelphia), designed to answer this question.

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Hany Z Aly, MD, FAAP is Associate Professor of Pediatrics and Obstetrics & Gynecology, George Washington University, Washington, DC. He completed his medical and surgical training at the Ain Shams University in Cairo, Egypt, and his pediatrics and neonatal-perinatal training at Hahnemann University Hospital, Philadelphia, Penn, and Columbia University, New York. Dr. Aly is author or coauthor of over 32 publications in the area of pediatric respiratory care and in 2002, he was the recipient of the Patient Safety Award, District of Columbia Hospitals Association.

Jen Tien Wung, M.D., FCCM is Professor of Clinical Pediatrics at Columbia University, New York. He received his MD degree from Taipei Medical University in 1966 and completed post-graduate training and residencies in obstetrics-gynecology and anesthesiology, and fellowship in combined pediatrics and neonatal intensive care medicine at Columbia in 1973. He is the recipient of many awards for excellence in teaching and neonatal care and is a pioneer in nasal CPAP therapy. He has published dozens of peer-reviewed articles and book chapters in his area of expertise and is an active journal reviewer. He is an active international lecturer on neonatal respiratory care and has directed an annual conference on "Respiratory Care of the Newborn-A Practical Approach" at Columbia University and recently in Taiwan since 1988.

Scott M Pettinichi Med, RRT, NPS is Senior Clinical Director, Division of Respiratory Care, Cincinnati Children's Hospital, Cincinnati, Ohio where he is responsible for competency, professional standards and clinical practice for 190 respiratory therapists as well as budget and revenue, JCAHO standards, recruitment and retention. He has 14 years experience as Senior Clinical Director, 6 years experience as Clinical Education Coordinator, and 22 years of neonatal and pediatric experience. He has made over 25 presentations and written a dozen publications on pediatric airway management and other topics in respiratory care. Mr. Pettinichi lives in Cincinnati.

Bradley Allen Yoder, MD is Associate Medical Director, NICU Primary Children's Medical Center, Department of Pediatrics/Neonatology, University of Utah School of Medicine, Salt Lake City, Utah. He assists in NICU policy development and implementation, as well as resident, fellow and NNP training. He author or coauthor of over 75 publications, 6 book chapters, and 50 abstracts on respiratory care and has made over 100 presentations on the topic. On the research side, he is an alternate PI with the Neonatal Network Research Consortium (funded by NICHD) and is a co-investigator in the Nasal Intermittent Positive Pressure Ventilation in Premature Infants (NIP) Trial, funded by the Canadian Institutes of Health Research.

Brian Kendall Walsh, RRT-NPS, RPFT, EMT-E, FAARC is Clinical Research Coordinator, Respiratory Care Department and the Department of Critical Care, Children's Hospital, Boston, where he conducts translational and clinical research, develops protocols and budgets, monitors adverse reactions, lectures, and presents research findings to the investigation review boards. He has coauthored 3 textbook chapters and 14 scientific articles on respiratory care topics. He is the 2008 recipient of the Outstanding Alumnus Award from Central Virginia Community College Alumni Association. He is also Chair for the American Association for Respiratory Care Neonatal and Pediatric Section and has been appointed by the Governor of Virginia to advise the Virginia Board of Medicine on Respiratory Care Issues. Mr. Walsh lives in Norfolk, Mass.

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Please direct your correspondence to:

Saxe Healthcare Communications
P.O. Box 1282
Burlington, VT 05402
info@saxecommunications.com

Questions

1. **Applying CPAP in the delivery room has been shown to have what effects on neonates <28 weeks gestation?**
   a. Prevent Bronchopulmonary Dysplasia
   b. Showed favorable outcomes related to survival
   c. More than half of the infants still required surfactant delivery and intubation
   d. b and c
2. **The physiologic effects of nasal CPAP include:**
   a. decreased the incidence of non-homogenous lung disease
   b. alveolar stabilization
   c. maintain lung compliance
   d. b and c
3. **What type of CPAP delivery system and interface has demonstrated to create a higher work of breathing with the infant?**
   a. Nasal pillow
   b. Mechanical ventilator and binasal prongs
   c. Variable flow CPAP device
   d. Heated and humidified high flow nasal cannula
4. **What type of CPAP interface had the greatest degree of complications using the variable flow device?**
   a. Bi-nasal prongs
   b. Short nasal prongs
   c. Nasal mask
   d. Endotracheal tube
5. **The greatest benefit of bi-level CPAP compared to standard CPAP is:**
   a. Better synchronization
   b. Extubation failures are less with bi-level CPAP
   c. Work of breathing is decreased
   d. Gas exchange is greater with bi-level CPAP
6. **The goal of CPAP delivery earlier in the course of an infant with RDS is to:**
   a. Stimulate the respiratory center to breathe
   b. Stimulate surfactant production
   c. Increase airway resistance
   d. a and b
7. **High flow nasal cannula may generate positive distending pressure in premature infants when the beginning with a flow rate of:**
   a. .25 liters per minute
   b. 1 liter per minute
   c. 1.5 liter per minute
   d. 2 liters per minute
8. **Continuous flow CPAP includes which of the following?**
   a. Ventilator driven CPAP
   b. Bubble or underwater seal CPAP
   c. Flow driver CPAP
   d. a and b
9. **Although HH-HFNC has a lesser incidence of complications related to its interface, the greatest risk to its application includes:**
   a. Inability to measure precise FiO2
   b. Inability to easily measure distending pressure
   c. Cannot support neonatal apnea compared to CPAP
   d. Does not prevent intubation compared to other CPAP devices
10. **The suggested method for weaning CPAP involves reducing the pressure level by how many cm H_20:**
    a. 1 cm H_20
    b. 2 cm H_20
    c. 3 cm H_20
    d. Take directly off without weaning CPAP
11. **The standard of care for the management of RDS in infants is:**
    a. Nasal High Frequency Ventilation
    b. CPAP
    c. High Flow Nasal Cannula
    d. NIPPV
12. **What are the complications associated with CPAP?**
    a. Skin breakdown
    b. Pneumonthorax
    c. Abdominal distension
    d. All of the above
13. **The INSURE strategy has been associated with:**
    a. Increased risk for CLD
    b. Increased rates of BPD
    c. Improved outcomes in premature infants
    d. None of the above
14. **Observational studies suggest Humidified High Flow Nasal Cannula (HHFNC) can be used in place of nasal CPAP in the management of premature infants.**
    a. True
    b. False

This program has been approved for 2.0 contact hours of continuing education (CRCE) by the American Association for Respiratory Care (AARC). AARC is accredited as an approver of continuing education in respiratory care.

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Participant's Evaluation

The goal of this program is to educate healthcare professionals on Non-invasive Respiratory Support in the NICU

1. What is the highest degree you have earned? Circle one. 1. Diploma 2. Associate 3. Bachelor 4. Masters 5. Doctorate
2. Indicate to what degree the program met the objectives:

Objectives

Upon completion of the course, the reader was able to:

1. Identify the physiologic indications for CPAP in the Neonate

   Strongly Agree 1 2 3 4 5 6 Strongly Disagree

2. Compare the clinical advantages of the various forms of non-invasive support in neonates.

   Strongly Agree 1 2 3 4 5 6 Strongly Disagree

3. Identify how historical applications and CPAP interfaces are utilized in clinical practice.

   Strongly Agree 1 2 3 4 5 6 Strongly Disagree

4. Please indicate your agreement with the following statement. "The content of this course was presented without bias of any product or drug."

   Strongly Agree 1 2 3 4 5 6 Strongly Disagree

Answers

1	☐	☐	☐	☐	9	☐	☐		
2	☐	☐	☐	☐	10	☐	☐	☐	☐
3	☐	☐			11	☐	☐	☐	☐
4	☐	☐	☐	☐	12	☐	☐		
5	☐	☐	☐	☐	13				
6	☐	☐			14				
7	☐	☐	☐	☐	15				
8	☐	☐	☐	☐	16				

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