A PRACTICAL APPROACH TO NON-INVASIVE RESPIRATORY SUPPORT

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Plan

- Indications
- Modalities of NRS
- How to start on each modality?
- How to manipulate/adjust on each modality?
- Short term side effects and physiologic effects
- Practical hints
- How to wean?
- NRS in outlying units
- Essentials to remember

NRS - Indications

- NRS has been used for:

1. The initial treatment of RDS,
2. Post extubation as a "bridge" to spontaneous unsupported breathing,
3. Apnea of prematurity.

Nasal Respiratory Support (NRS)

- NCPAP - nasal continuous positive airway pressure
- NIMV - nasal intermittent mandatory ventilation
- HFNC – high flow nasal cannula (?)

Introduction

- Owen (Arch Dis Child Fetal Neonatal Ed. 2008) recently concluded that in the practical approach in England, NIMV is commonly used, with considerable variability in the techniques applied.
- The wide range of clinical approaches highlights the paucity of evidence available.
- Data on term infants are lacking and we will focus on preterm infants.
- The following suggested practical approach is based on the current literature.

- *Initiating nasal respiratory support (NRS)*

Nasal continuous positive airway pressure *(NCPAP)*

- NCPAP goal in infants with RDS is to maintain lung recruitment or functional residual capacity (FRC).
- The level of pressure should achieve this goal without compromising circulatory or ventilatory function.
- A pressure of 4-6 cm H_2O usually will be adequate.
- Meta-analyses of CPAP studies suggest that a pressure of at least 5 cm H_2O is needed to provide benefit over ambient oxygen.
- Higher pressures up to 8 cm H_2O were used by some investigators, but at least in one study the rate of pneumothorax using such pressure was relatively high (Morley CJ, *N Engl J Med*. 2008).

Nasal intermittent mandatory ventilation *(NIMV)*

- The ventilator settings used for NIMV or nasal synchronized intermittent mandatory ventilation (NSIMV) are not similar in all studies.

- The effects of different initial settings on the success of NIMV and of manipulating the settings on clinical status have not been investigated.

PEEP during NIMV

- No study has investigated the optimal level of positive end expiratory pressure (PEEP) during NIMV.
- It is probably adequate to adopt the recommendations for NCPAP, as CPAP to maintain FRC in treating RDS is the basis for NRS and the intermittent mandatory ventilations used in NIMV are just added on top of the CPAP.

PIP during NIMV

- No studies have investigated optimal peak inspiratory pressure (PIP) during NIMV.
- Some NIMV studies used a PIP similar to that used during ventilation, whereas others used pressures 2–4 cm H2O higher than pre-extubation PIP.
- One study used enough pressure ‘‘to see the chest rise’’, and others chose specific target pressures (16–20 cm H2O).
- Ryan *et al* (Am J Dis Child 1989) noted that despite a set pressure of 20 cm H2O the pressure generated at the proximal end of the nasal prongs was highly variable (range 8–21 cm H2O; mean 10 cm H2O).

Rate and Flow on NIMV

- The optimal rate of inflation during NIMV has not been investigated.
- A range of rates have been used, mainly 10–25/minute.
- There were reports on the use of assist control mode, in which every infant-initiated breath is supported by a ventilator inflation.
- No study has investigated the flow to use in the circuit during NIMV.
- The circuit flow, and the leak from the device, will influence the PIP achieved during each inflation.

Summary NIMV

- We suggest (Kugelman A, *J Pediatr.* 2007) choosing the initial ventilator settings according to the indication for NIMV.

NIMV- Ventilator settings

(Kugelman A *J Pediatr.* 2007).

- Initial treatment of RDS:
  - Rate of 12-30 breaths per minute (according to $PaCO_2$),
  - Inspiratory time of 0.3 seconds,
  - PEEP of 6 cmH_2O,
  - PIP of 14-22 cmH_2O according to chest excursion and the infant's weight.
  - FiO_2 to keep oxygen saturation by pulse oximetry between 88-92%

NIMV- Ventilator settings

- After extubation:
  - Those used on endotracheal ventilation prior to extubation, or,
  - Only "sigh" ventilation

Nasal flow

- Its use is popular because it allows easy access to the infant and enables the parents to hold the infant.
- Nasal cannulae have been used to deliver oxygen at flow rates of 0.5 liter/minute to as high as 6 liter/minute, usually with no intention of delivering CPAP.
- However, a significant amount of CPAP is generated ("inadvertent CPAP"), and is not measured continuously at the bedside (Sreenan. Pediatrics 2001).

NC

- Standard or low flow nasal cannula is limited by inadequate humidification and unheated air flow.
- Delivery of such a gas may lead to airway dysfunction and negative respiratory outcomes.
- Cooling and loss of water from the airways may impair mucociliary transport, increase fluid osmolality, promote bronchospasm, and increase the viscosity of airway secretions.
- Moreover, considerable energy is required to heat and to humidify gas delivered into the nose, potentially interfering with optimal nutrition and growth.

NC

- On the basis of studies with VLBW infants undergoing ventilation, the delivery of nonhumidified gas may lead to increases in air leaks, more-severe chronic lung disease, impaired surfactant activity, and changes in pulmonary mechanics.
- Delivery of cold, relatively dry gases, particularly at high flow rates, to the nose may also lead to nasal mucosal injury and bleeding, resulting in pain and creating a portal of entry for infectious agents.
- The warmed and humidified new delivery HFNC devices overcome the disadvantages of commonly used nasal cannula therapy.

HFNC

- HFNC delivers flow rates that exceed patient inspiratory flow rates at various minute volumes.
- High flows result in washout of anatomical and physiological dead space and contribute to improved fractions of alveolar gases with respect to carbon dioxide as well as oxygen.
- One must exercise caution when delivering flow rates greater than 2 liter/minute via nasal cannula without knowing the amount of pressure delivered.
- This is also true for the warmed and humidified new delivery systems.

HFNC

- Kubicka *et al* (Pediatrics. 2008) concluded that HFNC therapy using cannulae of 0.2-cm outer diameter can generate some level of CPAP when the mouth is closed.

- The amount of pressure generated was related to the flow rate, the size of the leak around the nasal cannula, and the degree of mouth opening.

- They also raised the important safety and monitoring issues for the use of these devices.

HFNC

- They speculated that if the nasal leak is eliminated with the use of cannulae that obstruct the nares completely, then dangerously high distending pressures may be generated when the mouth is closed.
- Thus, they suggested that HFNC therapy should not be used as a routine replacement for CPAP therapy.
- To use HFNC we suggest: create/allow leak by using the nasal prongs no larger than 1/2 the diameter of the nares and do not allow chin rap.

Suggested protocol and rationale for HFNC

- There are no precise data currently on the relationship between flow and generated CPAP on HFNC, and fluctuations may occur depending on flow, infant weight and the level of leak according to cannula size and opening of the mouth.

- Continuous CPAP measurements on HFNC are not feasible yet.

- We depicted our flows by integrating the known information from the literature taking margins of safety and not aiming to create CPAP.

HFNC

- Kubicka (Pediatrics. 2008 has shown that the highest mouth pressure achieved was 4.5 cm H2O (flow rate: 8 l/m) with outer diameter cannula of 0.2 cm.
- Others used esophageal pressure measurements to estimate distending pressures generated in premature infants and found conflicting results.
- Locke *et al* (Pediatrics 1993) reported that the equivalent of 9.8 cm H2O could be generated with only 2 l/m of flow by using a nasal cannula of 0.3 cm outer diameter.
- Sreenan *et al* (Pediatrics 2001) reported that clinically relevant levels of CPAP could be generated with flow rates of 1 to 2.5 l/m.
- Saslow (J Perinatol 2006) found no significant increase in end distending pressure from baseline with flow rate lower than 5 l/m.

HFNC

- Recently, Quinteros et al (SPR, Baltimore, 2009) measured hypopharyngeal pressures delivered by nasal cannula in premature infants (989±556 g) at 43±25 days, and reported maximal pressures (median [range]) of 4.7 [1.3-19] on 1 l/min and 5.4 [4.0-20.4] cm H2O on 2 l/min.

- Peak pressures >15 cm H2O were frequently observed with gas flows >2 l/min in infants <1000 g.

- On the other hand such fluctuations are an integral part of the treatment with NIMV using peak inspiratory pressure (PIP) of 14-22 cmH2O, and these were found to be safe.

HFNC- protocol

- Flows will be started on 1 l/m.
- Flows between 1.0-3.0 l/m in infants <1000 g, and between 1.0-5.0 l/m in infants >1000 g (where the leak may be larger).
- FiO2 will be set to keep oxygen saturation by pulse oximetry between 88-92%.

- *Ventilator settings adjustments during NRS therapy*

Nasal continuous positive airway pressure *(NCPAP)*

- Pressures may be increased for lung recruitment in severe RDS (usually up to ~8 cm H2O), while monitoring the hemodynamic effects in the individual patient and chest radiograph to avoid hyperinflation.
- When treating the acute phase of RDS in the very premature infant, one should consider intubation and surfactant administration instead of increasing the CPAP level.
- NCPAP pressure may be weaned in the recovery stages of RDS as lung compliance improves to avoid over-distention.
- We wean infants to spontaneous unsupported breathing from 4-6 cm H2O.
- We usually do not use lower pressures.

Nasal intermittent mandatory ventilation *(NIMV)*

- The setting of NIMV during the time the infant requires NRS are adjusted to maintain the goals of adequate oxygenation and ventilation (permissive hypercapnia).
- Oxygenation is maintained by FiO2 and mean airway pressure (inspiratory time [IT], peak inspiratory pressure [PIP] and CPAP level), and ventilation by the respiratory rate, expiratory time, PIP, and maintaining adequate CPAP, according to the rules of conventional endotracheal ventilation.
- Yet, this routine was not tested in controlled trials.

Nasal intermittent mandatory ventilation *(NIMV)*

- For example, no study has shown that higher rates on the ventilator change the $PaCO_2$, while the baby is breathing spontaneously and complements the NRS.
- Yet, increasing the rates may decrease the work of breathing.
- Meta analysis of two trials comparing NIMV and NCPAP in infants with apnea demonstrated no difference with regard to carbon dioxide levels after 4-6 hours of support (Tarnow-Mordi WO, *J Pediatr.* 1989).
- Nasal ventilation respiratory settings need to be further studied to allow evidence based recommendation.

Nasal flow-HFNC

- Oxygen should be monitored to keep the required oxygen saturation.
- An oxygen/room air mixer/blender is required to assure limitation on the higher level.
- The CPAP created at different flows of HFNC needs to be studied to guide a controlled use, if one's intention is to create CPAP with nasal flow.

HFNC

- Flows can be increased at intervals of 1 l/m according to the infant's weight and as needed according to the clinical condition (respiratory [retractions, respiratory rate, grunting] and hemodynamic [blood pressure and heart rate]), and according to ABG (ventilation [PaCO2] and oxygenation).

- There are fluctuations that are not continuously measured and this may create obstacles in using formulas created according to flow, gestational age and weight (Kubicka. Pediatrics. 2008).

- Certainly, a high flow limitation should be kept to avoid the complications of air leak.

Criteria for failure of nasal support

- Differer between studies, and in our study (Kugelman A. *J Pediatr.* 2007) were:
- Clinical deterioration [increased respiratory distress] accompanied by at least one of the following or worsening of the following:

1. pH < 7.20 and $PCO_2 > 60$ mmHg,
2. $PaO_2 < 50$ mmHg or arterial oxygen saturation by pulse-oximetry (SpO_2) $< 88\%$ on $FiO_2 > 50\%$,
3. Recurrent significant apnea requiring repeated stimulation or bag-and-mask ventilation despite the use of methylxanthines or adequate nasal support (proper ventilatory settings and no technical problems).

- It is possible to switch from NCPAP to NIMV in order to try to minimize endotracheal intubation.

- *NRS side effects*

Short term side effects

- NRS seems to be safe.
- Of some concern is the study of Morley *et al* (*N Engl J Med*. 2008) that reported higher incidence of pneumothorax (9%) in the CPAP group (8 cmH2O), as compared with 3% in the intubation group ($P<0.001$).
- However, other studies did not report such high rates of pneumothorax on NCPAP or on NIMV.

GI

- There was a concern that NIMV might cause more gastrointestinal complications than NCPAP because of gastric distention leading to cessation of feeds or perforation.

- However, no gastrointestinal complications were reported in other studies and time to full feeds was similar in the two methods.

Early NCPAP and NEC in preterm infants (Aly. Pediatrics 2009).

- Data on 343 premature infants were collected for this study.
- Mean BW was 999±289 g and GA was 28±2.6 weeks.
- The majority of patients were managed with ENCPAP, with only 13% of patients intubated in the delivery room.
- The overall incidence of NEC was 7% (n=24).
- The exposure to ENCPAP did not increase the risk for NEC.

NRS - Short term effects

- The discomfort related to NRS may be of importance and deserves our attention for two main reasons:

- First, our aim is to be gentle and to keep a policy of ‘minimal handling' in the care of premature infants (avoid pain, noise, local trauma).

- Second, an irritable infant who ‘fights’ the NRS may be exposed to a higher risk of pneumothorax.

Discomfort

- NRS may irritate the infants because the nasal flow causes high noise-levels.

- Surenthiran *et al* (*Arch Dis Child Fetal Neonatal Ed.* 2003) reported mean noise intensity in the ear at 1 kHz of 55 dB, higher on NCPAP compared with spontaneous breathing or conventional ventilation, and up to 102 dB at some frequencies.

Discomfort

- NRS may cause pain and irritation in relation to nasal flow, high pressure in upper airways and local pressure and trauma.

- Adequate techniques for fixation of the NRS devices that minimize the friction and direct pressure on the nose may decrease these undesired local effects.

- Devices that deliver humid and warm nasal flow were shown to reduce the rate of nasal mucosa injury as compared to standard HFNC.

Oral CPAP following nasal injury. (Carlisle. *Arch Dis Child Fetal Neonatal Ed. 2010*)

Figure 1 A. Premature infant with nasal septum erosion. B. Dummy continuous positive airway pressure (CPAP) device. C. Oral CPAP in place on the infant. D Pharyngeal pressure measurements.

Physiological parameters

- NRS may affect physiological parameters during RDS and while the babies are stabilized, at the phase of recovering from RDS.
- Yu *et al* (*Acta Paediatr Scand.* 1977) concluded that with correct use of NCPAP, an improvement in oxygenation generally occurs without obvious adverse cardio-respiratory effects.
- However, when appropriate pressures are exceeded it is possible that both circulatory and ventilatory function might be severely compromised, possibly by over distension and a decrease in the venous return.

Physiological parameters AND Discomfort

- Kugelman *et al* (*Acta Pediatr*. 2008) concluded that NRS in 'stable' premature infants is associated with increased blood pressure and increased discomfort, despite a decreased respiratory rate.
- The clinical importance of these effects was modest.
- While these findings are reassuring when NRS is needed, they should be considered when the medical team balances its need and advantages with its adverse effects according to the clinical condition of the infant.
- To minimize the discomfort related to NRS, we should shorten its use when possible

Practical hints for neonatal NRS application

- Different techniques of NRS are available.
- Short binasal prong devices are more effective than single prongs or nasopharyngeal prong (De Paoli. *Cochrane Database Syst Rev*. 2008).
- Infant flow driver uses a fluidic flip system that has been shown to assist spontaneous breathing and reduce work of breathing by reducing expiratory resistance and maintaining a stable airway pressure throughout the respiratory cycle.
- It was also shown to provide better lung recruitment compared to continuous flow NCPAP.
- However, the infant flow driver was found to be as effective as conventional CPAP in preventing extubation failure among ELBW infants (Stefanescu. *Pediatrics*. 2003).

Bubble CPAP

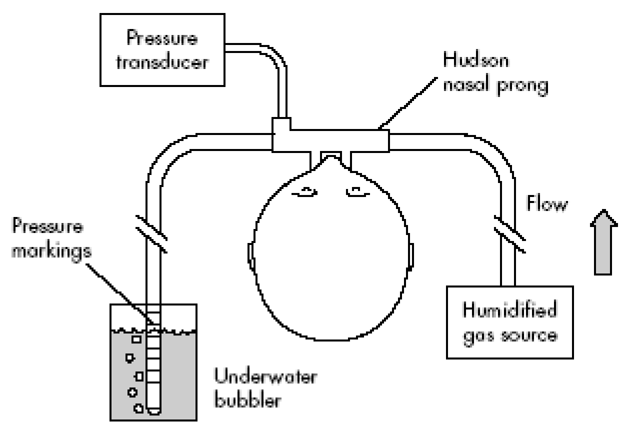

Figure 1 Diagram of "Bubbly Bottle" nasal continuous positive airway pressure (CPAP) system.

- Bubble CPAP, is accomplished by submerging the expiratory limb of the respiratory circuit within a fluid column.
- The generated pressure is determined by the depth of submersion and is independent of flow rate.
- It has been shown to be more successful than the standard CPAP (Pillow JJ *Am J Respir Crit Care Med*. 2007, Narendran V *J Perinatol*. 2003).
- Bubble CPAP may also provide an inexpensive form of CPAP with some characteristics of noninvasive HFV.

Bubble CPAP

- In a randomized crossover trial (Morley. Arch Dis Child Fetal Neonatal Ed. 2005), 26 babies treated with nasal prong CPAP from a bubbling bottle, received vigorous, high amplitude, or slow bubbling for 30 minutes.
- Pulse oximetry, transcutaneous carbon dioxide, and respiratory rate were recorded.
- The bubbling rates had no effect on carbon dioxide, oxygenation, or respiratory rate.

Synchronized NIMV

- Finally, there are different methods that try to synchronize NIMV.
- However, while NSIMV may be preferred over NIMV, this was not demonstrated and synchronization is probably not mandatory (Kugelman A, J Peds 2007).

Nursing during NRS

- Good quality nursing during NRS care is of uttermost importance.

- The success of the treatment relies on optimal positioning of the baby, maintaining patency of the upper airways and avoiding loss of the positive airway pressure.

Key points for NRS nursing care according to Bohlin *et al* (*Neonatology*. 2008) and our own experience:

- Keep an open nasal passages;
- Find the optimal comfort body position for the infant and keep the head in mild extension to keep an open airway with a neck support;
- Use preterm pacifier to minimize loss of pressure from open mouth or keep the mouth close with chin support to achieve adequate CPAP; caution!!
- Try to avoid suctioning the nose and use saline drops instead and then suction the oropharynx;
- Use adequate humidification and temperature of gases;

Key points for NRS nursing care according to Bohlin *et al* (*Neonatology*. 2008) and our own experience:

- Avoid using excessive force when fixating the nasal prongs;
- Do not pull tightly the nosepiece against the nose and keep it under the nose;
- Protect the nose with manufactured or "home made" materials;
- Use the largest size prong that will sit without support in the nose;
- Inspect the fixation when you see that the nosepiece is pressing too tightly against the nose or the NRS pressure is difficult to hold;
- Change to a larger prong as the baby grows.

Key points for NRS nursing care according to Bohlin *et al* (*Neonatology*. 2008) and our own experience:

- Some studies suggested using a gastric tube, open to air, to avoid gaseous distension of the stomach during NIPPV, although there is no evidence that this works.

- We remove the air from the stomach at least twice every 8 hours to avoid over-distention and open the NG 1 hr after feeding.

Weaning NRS

- Weaning by slowly reducing CPAP pressures has been shown to be superior to intermittent pausing (Singh S, Abstract, Europediatrics, Barcelona, October 2006).

- Logically, pausing can result in alternating hyperinflation with collapse of alveoli (atelectato-trauma) known to be associated with development of BPD.

Weaning from non-invasive respiratory support in the premature infant

- Length of NRS depends on the indication (RDS or apnea), gestational age, weight and possible side effects and there are no clear guidelines as to when to stop NRS.

- Infants with RDS were allowed to stop NRS

1. FiO2 <30%,
2. Normal blood gases
3. No respiratory distress or apnea

- ((Kugelman A, *J Pediatr.* 2007).

Weaning NRS

- Two approaches to weaning from NRS are possible.
- 1. Wean pressures and rate as performed while on conventional ventilation, weaning first those parameters that may cause lung damage.
- 2. Use cycles of NRS and spontaneous breathing and allow exercising the respiratory muscles.

Weaning NRS

- The preferred method of weaning from NRS needs to be studied.

- The way to wean from NRS may be important, but it is possible that this issue has a neglected role in the final outcome.

Potential hazard of the Neopuff T-piece resuscitator in the absence of flow limitation.

(Hawkes CP, Arch Dis Child Fetal Neonatal Ed 2009)

- Even an increase in flow from 5 to 15 l/min will bring about a fourfold increase in PEEP, a serious potential hazard of the Neopuff.

Neopuff (**Morley.** *Arch Dis Child Fetal Neonatal Ed. 2009)*

- The practical message for all who use the Neopuff is that it should be used according to the manufacturer's instructions.
- 1. The recommended operating gas flow range is 5 to 15 l/min. It specifically says, "Do not attempt to use a flow higher than 15 l/min."
- 2. Adjust the gas supply to the desired flow rate between 5 and 15 l/min. Only then, set the PIP and PEEP.
- 3. The Neopuff should only be used on a baby after checking that correct pressures will be delivered to the baby.

Neopuff (**Morley.** *Arch Dis Child Fetal Neonatal Ed. 2009)*

- The practical clinical messages are simple:

1. Choose a flow rate you are going to use; we suggest 8 l/min should be more than adequate; set the PEEP and PIP, and then do not alter the flow.

2. If the PEEP and PIP are not being delivered during the resuscitation, this is due to a large leak between the mask and face, and that should be corrected by altering mask position and hold, and not by increasing the flow.

NASAL VENTILATION IN OUTLYING NICUs

- Even the basic procedure of endotracheal ventilation requires skills that are not trivial.
- Only 62% out of 60 attempts were successful in 31 infants during neonatal resuscitation (O'Donnell CP *Pediatrics*. 2006).
- Success rates and mean±SD time to intubate:
  - Residents: 24%, 49±13 sec;
  - Fellows: 78%, 32±13 sec;
  - Consultants: 86%, 25±17 sec.
- Infants frequently deteriorate during intubation attempts.
- Thus, to avoid these, NRS is required.

NASAL VENTILATION IN OUTLYING NICUs

- Modern mechanical ventilation requires skilled personal and expensive equipment.
- NRS and Surfactant reduce need for mechanical ventilation (avoiding transport).
- CPAP was found to be safe for transport (Murray, Pediatrics 2008).

NASAL VENTILATION- Experience

- The use of NRS is also more successful in experienced medical teams.
- Aly (*Pediatrics.* 2004) showed that the number of ELBW infants who were started on early NCPAP but intubated within 1 week (CPAP failure) decreased over time (38.5% vs. 13.8% vs. 7.4%, respective to 3 terciles since the institution of early NCPAP system).
- They concluded that the frequency of use of early NCPAP in ELBW infants and its success improved in their unit over time.

Essentials to remember:

- 1. Maintaining FRC is essential for the treatment of RDS in all modes of NRS. This is not the rule for HFNC.
- 2. Data on ventilator settings on NRS needs to be further studied for effective and safe use.
- 3. NRS is safe. However, possible side effects should be monitored and prevented.
- 4. NRS is beneficial, but when the infant is "ready" to wean, try to take him off NRS.
- 5. The comfort of the infant needs no be maintained while on NRS.

Thank you !!!!!