Non-Invasive Ventilation Neonatal Physiology, Best Evidence & Applications

Beatrice Stefanescu, MD MS
UNM Neonatology

Non-Invasive Ventilation (NIV):
Outline of points

• Evidence based physiology
• Evidence based decisions
  – NIV vs Mechanical Ventilation (MV)
  – HHHFNC (Heated Humidified High Flow NC) vs CPAP
    (Continuous Positive Airway Pressure)
  – HHHFNC vs NIPPV (Non-invasive Positive Pressure Ventilation)
• Alternative (newer) directions
  – NIV-NAVA (Neurally Adjusted Ventilatory Assist)
  – N-HFV (Nasal High Frequency Ventilation)

Why NIV

• Invasive ventilation causes volu-barotrauma and along with biotrauma results in ventilator induced lung injury (VILI)

Animal models:

• “only 6 manual inflations of 35 to 40 mL/kg given to preterm lambs injures lungs and reduces response to surfactant therapy” (Bjorklund et al, 1997)
• 15 min ventilation with Vt 15mL/kg in preterm lambs initiates injurious process (Hillman et al, 2007)

Respiratory mechanics

Effect of mechanical ventilation on preterm lamb lung

At 0 hour
- Without surfactant
- With surfactant

At 24 hrs
- Without surfactant
- With surfactant

Vermont Oxford Network (VON) data for 1994 to 2014
VON annual meeting Chicago, Sept 2016

Pinkerton et al, 1994
Non-Invasive Ventilation Neonatal

**Pathophysiology schematics in Respiratory Distress Syndrome (RDS)**

- Insufficient, Delayed Atelectasis
- Immature Immature
- Capillary leak
- V/Q mismatch
- Collapse easily
- Decreased Clave will complain

**CPAP: EVIDENCE BASED PHYSIOLOGY**

- **History of CPAP**
  - Introduction of the "respirators" for neonatal intensive care in 1959 did not improve outcomes
  - Gregory et al. 1971: introduced the clinical use of distending pressure in neonates via ETT or a head box

- **Pulmonary effects**
  - Effect of CPAP on FRC (Functional Residual Capacity)
    - Increased alveolar volumes result in a greater surface-area exposure of alveolar gas and capillary blood
    - This is a primary mechanism by which CPAP affects gas exchange

- **Pulmonary effects**
  - Regularization of respiration and decrease WOB
  - Splinting of airways and stabilization of chest wall (Kattwinkel et al., 1976)
  - Decrease total airway resistance (Katz et al., 1983)
  - Protective effect on surfactant (Lawson et al., 1979)
  - Redistribution of extravascular lung water (Malo, 1984)

- **Less lung inflammation**
  - Jobe, 2002: Indicators of lung injury
    - There were fewer neutrophils in the alveolar washes (A) of the CPAP lambs than the mechanically ventilated lambs
    - Less H2O2 was in the cells from the alveolar washes (C) of the CPAP lambs than the ventilated lambs (CPAP vs ventilation)
Importance of **STRETCHING**

- During fetal development physiological stretching helps drive lung growth and maturation *(Mustafa, 2014)*
- Total lung capacity after 2 wks was 40% higher in the CPAP-exposed animals than in the control animals *(Zhang, 1996)*

Central Venous Pressure (CVP) and CPAP level

**Adverse effects from CPAP**

- Nasal septum injury

  Prevention is key:
  - Staff skilled with use of device
  - Protocols for prevention and treatment of nasal septum breakdown

**Adverse effects from CPAP**

- Air leak syndrome
  - Usually from high level CPAP
  - Sudden/more gradual clinical decompensation
  - Needs immediate attention

*Subcutaneous scalp emphysema, pneumo-orbitis and pneumocephalus in a 29 weeks GA on 4LPM HFNC at 36 DOL* *(Jasine et al, 2008)*

**CPAP: CLINICAL APPLICATIONS**

- Atelectatic disorders
- Apnea of prematurity
- Postextubation in preterm
- Transitory tachypnea of newborn

**Other**

- Pneumonia
- Meconium aspiration syndrome (MAS)
- Pulmonary edema/hemorrhage
- Airway malacia syndromes
- Patent ductus arteriosus (balance between cardiac output and pulmonary blood flow)
Modified DOWNE Scoring System for Assessment of RD Severity

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Rate (rate/min)</td>
<td>&lt;60</td>
<td>60-80</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Retractions</td>
<td>None in RA</td>
<td>None with O2 support</td>
<td>Cyanosis in spite of O2 support</td>
</tr>
<tr>
<td>Grunting</td>
<td>None</td>
<td>Audible with stethoscope</td>
<td>Audible without stethoscope</td>
</tr>
<tr>
<td>Air entry</td>
<td>Good</td>
<td>Decreased</td>
<td>Barely audible</td>
</tr>
</tbody>
</table>

Score:
- <4: Mild clinical respiratory distress
- 4-6: Moderate clinical respiratory distress, monitor arterial blood gases
- 7-8: Impending respiratory failure

CPAP in Meconium Aspiration Syndrome (MAS)
- Pathology of MAS: atelectasis
  + large and small airway obstruction
  + V/Q abnormalities
- Apply of moderate level CPAP
- Result: resolution of atelectasis, stabilization of terminal airway

CPAP in Apnea of Prematurity (AoP)
- The application of low-level CPAP decreases the AoP incidence
- Experts recommend early use CPAP for prophylaxis of apnea (Cochran meta-analysis 2014)

Clinical Evidence for Primary Treatment of RDS

Ho et al, 2002: CPAP vs no CPAP (Hood oxygen)
- Reduced neonatal mortality (RR 0.52, 95% CI 0.32, 0.87)
- Reduced rate of the combined outcome of death or assisted ventilation (RR 0.70; 95% CI 0.55, 0.88) with CPAP use
Initial stabilization with CPAP at delivery

<table>
<thead>
<tr>
<th>GA (wks)</th>
<th>Enrolled</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 ‐ 26</td>
<td>405</td>
<td>Intubation +/− Surfactant</td>
</tr>
<tr>
<td>24 ‐ 26</td>
<td>1316</td>
<td>Intubation/surfactant</td>
</tr>
</tbody>
</table>

Primary outcome for 3 studies: death or BPD at 36 wks PMA

No significant difference between groups

Summary evidence for CPAP

- CPAP safe to use in DR
- When compared to intubation CPAP reduces need for mechanical ventilation
- With CPAP, early selective better than prophylactic surfactant in decreasing MV
- INSURE strategy better than later selective surfactant with continued ventilation

AAP Committee of Fetus and Newborn, 2014

"Using CPAP immediately after birth with subsequent selective surfactant administration – an alternative to routine intubation"

NON-INVASIVE POSITIVE PRESSURE VENTILATION (NIPPV)

Lemyre et al, 2014: NIPPV vs CPAP after extubation

- Reduction of extubation failure within 48 hours to one week more effectively with NIPPV (RR 0.71 [0.61, 0.82]) with NNT 3
- No difference in BPD or mortality

Kirpalani et al, 2013: The NIPPV International Randomized Controlled Trial

- RCT, 1009 infants enrolled
- NIPPV does not confer benefit above nasal CPAP for infants with birth weight <1000 g

HEATED HUMIDIFIED HIGH FLOW NASAL CANNULA (HHHNC)
Non-Invasive Ventilation Neonatal

Meta-analyses of HHHNC vs other NIV in preterm infants

**Kotecha et al, 2015**
- HFNC similar in efficacy and safety to other conventional modes of NIV when used as primary support as well as after extubation

**Wilkinson et al, 2016**
- Similar conclusion

There were only small numbers of extremely preterm and late preterm infants

**Taha et al, 2016**
Retrospective, HHHNC vs CPAP in ELBW infants; n=2820

<table>
<thead>
<tr>
<th></th>
<th>HFNC ± CPAP vs CPAP</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPD or death</td>
<td></td>
<td>1.085 (1.035-1.137)</td>
<td>0.001</td>
</tr>
<tr>
<td>BPD</td>
<td></td>
<td>1.168 (1.118-1.220)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Severe IVH</td>
<td></td>
<td>1.077 (0.804-1.441)</td>
<td>ns</td>
</tr>
<tr>
<td>PDA requiring therapy</td>
<td></td>
<td>0.937 (0.786-1.116)</td>
<td>ns</td>
</tr>
<tr>
<td>NEC Bell stage 2 or higher</td>
<td></td>
<td>0.893 (0.656-1.217)</td>
<td>ns</td>
</tr>
<tr>
<td>ROP requiring laser</td>
<td></td>
<td>1.283 (0.961-1.712)</td>
<td>ns</td>
</tr>
</tbody>
</table>

**NIV-NAVA**
- **Fischer et al, 2015**: 17% of NICUs in 5 well developed European countries use n-HFOV
- **Colaizy et al 2008**: 14 VLBW infant who were stable on NCPAP were placed on N-HFOV (Infant Star, frequency 10 Hz) for 2 hrs and showed lower PCO2 levels
- RCT comparing nHFOV vs nCPAP immediately after extubation of VLBW infants ClinicalTrials.gov: NCT02340299
- **Conclusions**
  - Use lung injury preventative strategies when ventilating infants
  - CPAP is a good alternative to mechanical ventilation in preterm infants
  - Information on initial use of CPAP versus HHHNC in ELBW infants is limited
  - Long-term respiratory and neuro-developmental outcomes of NIV as compared to MV needs to be evaluated

Beth Israel Hospital Boston - Respiratory Care
Non-Invasive Ventilation Neonatal

THANK YOU