Update on Non-Invasive Respiratory Support in the Newborn

Rebecca S Rose, MD, MS
October 8, 2015
Disclosure

• I have no disclosures
At the End of This Presentation, Participants will be able to:

• Discuss the evidence for non-invasive ventilation in the newborn
• Describe the steps for trouble shooting non-invasive ventilation during NRP
• List the types of devices available for non-invasive ventilation
Should All Infants Less than 28 weeks EGA be intubated in the Delivery Room?

David Rambau
COIN Trial

Morley, NEJM. 2008 Feb 14;358(7):700

• RCT: Nasal CPAP in the DR vs Intubation in premature infants (25 - 28 weeks, n = 610)

• Results for Nasal CPAP Infants

  - Incidence of pneumothorax was higher 9% vs 3%
  - Nasal CPAP was started at a pressure of 8 cm of water
  - Lower risk of death or BPD at 28 days
  - Required fewer days of ventilation
  - Incidence of death or BPD at 36 weeks PMA 34% vs 39%, but did not reach significance
SUPPORT Trial
NEJM. 2010 May 27;362(21):1970

• Premature infants 24 - 27 weeks, n = 1316
• RCT: CPAP in the DR vs intubation and SRT
• Nasal CPAP Infants
  ➢ Less frequently required intubation
  ➢ Less need for postnatal steroids for BPD
  ➢ Required fewer days of ventilation
  ➢ Incidence of BPD at 36 weeks PMA 49% vs 54%, but did not reach significance

• Bottom Line: A trial of Nasal CPAP should be considered an alternative to routine intubation in the DR.
# Early CPAP vs. IPPV in extremely low gestational age newborns

<table>
<thead>
<tr>
<th></th>
<th>Death/BPD</th>
<th>IPPV</th>
<th>Surfactant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CPAP/ISX</td>
<td>MV-Surf</td>
<td>CPAP</td>
</tr>
<tr>
<td><strong>COIN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-28 wks</td>
<td>34%</td>
<td>39%</td>
<td>58.7%</td>
</tr>
<tr>
<td><strong>SUPPORT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-28 wks</td>
<td>49%</td>
<td>54%</td>
<td>83.1%</td>
</tr>
<tr>
<td><strong>VON (CPAP)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26-30 wks</td>
<td>31%</td>
<td>37%</td>
<td>52%</td>
</tr>
<tr>
<td><strong>VON (ISX)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>29%</td>
<td>37%</td>
<td></td>
<td>59%</td>
</tr>
</tbody>
</table>
Metaanalysis
Schmölzer, BMJ. 2013;347

• 4 RCTs: Nasal CPAP initiated in the delivery room vs Intubation
  • < 30 weeks, no 23 week infants, very few 24 week infants
  • n = 2782
  • 95% Antenatal steroids

• Results for Nasal CPAP Infants
  ➢ The combined incidence of death or BPD at 36 weeks PMA just reached significance (RR 0.91, 0.84-0.99) favoring Nasal CPAP with number needed to treat of 25.
Avoiding Endotracheal Intubation to Prevent Bronchopulmonary Dysplasia
Fischer and Brüher *Pediatrics* 2013

**TABLE 1** Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Study Name</th>
<th>Year</th>
<th>Intervention</th>
<th>Any eMV Except INSURE %</th>
<th>GA</th>
<th>Randomization</th>
<th>n</th>
<th>Recruitment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morley et al</td>
<td>COIN</td>
<td>2008</td>
<td>nCPAP versus mechanical ventilation</td>
<td>59 vs 100</td>
<td>25 (0%) (1-28%)</td>
<td>At 5 min of age</td>
<td>610</td>
<td>1999–2006</td>
</tr>
<tr>
<td>Rojas et al</td>
<td>CNRN</td>
<td>2009</td>
<td>nCPAP versus INSURE</td>
<td>43 vs 39</td>
<td>27 (0%) (1-29%)</td>
<td>15–60 min of age</td>
<td>146</td>
<td>2004–2006</td>
</tr>
<tr>
<td>Finer et al</td>
<td>SUPPORT</td>
<td>2010</td>
<td>nCPAP versus mechanical ventilation</td>
<td>83 vs 100</td>
<td>24 (0%) (1-27%)</td>
<td>&lt;1 h of age</td>
<td>1316</td>
<td>2005–2009</td>
</tr>
<tr>
<td>Sandri et al</td>
<td>CURPAP</td>
<td>2010</td>
<td>nCPAP versus INSURE</td>
<td>31 vs 33 (c)</td>
<td>25 (0%) (1-29%)</td>
<td>&lt;30 min of age</td>
<td>208</td>
<td>2007–2008</td>
</tr>
<tr>
<td>Dunn et al</td>
<td>DRM</td>
<td>2011</td>
<td>3 groups: nCPAP versus INSURE and mechanical ventilation</td>
<td>52 vs 59 vs 96</td>
<td>26 (0%) (1-29%)</td>
<td>Before delivery</td>
<td>648</td>
<td>2003–2009</td>
</tr>
<tr>
<td>Göpel et al</td>
<td>AMV</td>
<td>2011</td>
<td>nCPAP ± surfactant during spontaneous breathing versus nCPAP ± mechanical ventilation</td>
<td>33 vs 73</td>
<td>26 (0%) (1-28%)</td>
<td>&lt;12 h of age</td>
<td>220</td>
<td>2007–2009</td>
</tr>
<tr>
<td>Kanmaz et al</td>
<td>Take Care</td>
<td>2013</td>
<td>nCPAP ± surfactant during spontaneous breathing versus nCPAP ± INSURE</td>
<td>42 vs 52 (a)</td>
<td>(\leq29%)</td>
<td>&lt;2 h of age</td>
<td>141</td>
<td>2010–2011</td>
</tr>
</tbody>
</table>

- \(a\) Previously unpublished, stratified data for infants \(<30\%\) weeks’ GA.
- \(b\) Number of infants \(<30\%\) weeks’ GA only.
- \(c\) Need for any eMV except INSURE in the first 5 d of life.
- \(d\) Combining prophylactic surfactant and early nasal continuous positive airway pressure study.
## Death or BPD

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Avoid ventilation</th>
<th>Control group</th>
<th>Weight, %</th>
<th>Odds Ratio</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BPD/death</td>
<td>Total</td>
<td>BPD/death</td>
<td>Total</td>
<td>Random effects model (95% CI)</td>
</tr>
<tr>
<td>COIN (2008)</td>
<td>108</td>
<td>307</td>
<td>122</td>
<td>303</td>
<td>0.81 (0.58–1.12)</td>
</tr>
<tr>
<td>CNRN (2009)</td>
<td>53</td>
<td>74</td>
<td>54</td>
<td>72</td>
<td>0.84 (0.40–1.75)</td>
</tr>
<tr>
<td>SUPPORT (2010)</td>
<td>323</td>
<td>663</td>
<td>353</td>
<td>653</td>
<td>0.81 (0.65–1.00)</td>
</tr>
<tr>
<td>CURPAP (2010)</td>
<td>22</td>
<td>103</td>
<td>23</td>
<td>105</td>
<td>0.97 (0.50–1.87)</td>
</tr>
<tr>
<td>DRM (2011)</td>
<td>68</td>
<td>223</td>
<td>138</td>
<td>425</td>
<td>0.91 (0.64–1.29)</td>
</tr>
<tr>
<td>AMV (2011)</td>
<td>15</td>
<td>108</td>
<td>17</td>
<td>112</td>
<td>0.90 (0.43–1.91)</td>
</tr>
<tr>
<td>Take Care (2013)</td>
<td>25</td>
<td>74</td>
<td>30</td>
<td>67</td>
<td>0.63 (0.32–1.24)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>614</strong></td>
<td><strong>1552</strong></td>
<td><strong>737</strong></td>
<td><strong>1737</strong></td>
<td><strong>0.83 (0.71–0.96)</strong></td>
</tr>
</tbody>
</table>

Test for overall effect: $z = 2.55 (P = .01)$

**Figure 2**
Effect of avoiding eMV on death or BPD.

Fischer S H, and Buhrer C. Pediatrics 2013;132:e1351
Respiratory Support in Preterm Infants at Birth

abstract

Current practice guidelines recommend administration of surfactant at or soon after birth in preterm infants with respiratory distress syndrome. However, recent multicenter randomized controlled trials indicate that early use of continuous positive airway pressure with subsequent selective surfactant administration in extremely preterm infants results in lower rates of bronchopulmonary dysplasia/death when compared with treatment with prophylactic or early surfactant therapy. Continuous positive airway pressure started at or soon after birth with subsequent selective surfactant administration may be considered as an alternative to routine intubation with prophylactic or early surfactant administration in preterm infants. Pediatrics 2014;133:171–174
You are called to attend the delivery of an infant at 26 weeks EGA. You are setting up your equipment to use to provide respiratory support for this infant. Which available resuscitation device to you prepare?
Advantages of T-Piece Resuscitator

Provides reliable PEEP

Difficult to give excessive PIP
Disadvantages of T-Piece Resuscitator

Requires a Compressed Gas Source

Must be set up Properly Prior to Use

Requires Practice to Use it Well

Difficult to Quickly Increase PIP During MR SOPA
T-piece resuscitators

<table>
<thead>
<tr>
<th>Response</th>
<th>Self inflating bag</th>
<th>Anaesthetic bag</th>
<th>Neopuff</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean max PIP</td>
<td>44.7 (2.3)</td>
<td>22.6 (0.7)</td>
<td>20.4 (0.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean PIP</td>
<td>30.7 (1.9)</td>
<td>18.1 (0.4)</td>
<td>20.1 (0.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean PEEP</td>
<td>0.15 (0.03)</td>
<td>2.83 (0.23)</td>
<td>4.41 (0.08)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean airway pressure</td>
<td>7.6 (0.8)*</td>
<td>8.5 (0.3)*</td>
<td>10.9 (0.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean rate</td>
<td>47.1 (3.0)*</td>
<td>47.3 (2.7)*</td>
<td>39.7 (1.8)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>% total breaths $\leq 21$ cm H$_2$O PIP</td>
<td>39 (0.07)</td>
<td>92 (0.02)*</td>
<td>98 (0.02)*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% total breaths $\geq 30$ cm H$_2$O PIP</td>
<td>45 (0.07)</td>
<td>0*</td>
<td>0*</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Bottom Line:

• Preterm infants (< 32 weeks EGA) with good respiratory effort should be given a trial of CPAP in the delivery room (institutions expecting to deliver more than 10-15 of these infants per year should strongly consider using a T piece resuscitator for these deliveries)

• Suggested starting pressure 5-6 cm H2O

• Infants requiring intubation for invasive ventilation should be given surfactant within an hour of intubation
Case

• A term singleton infant is born after a delivery complicated by fetal decelerations. The infant is stimulated and dried, but has no respiratory effort. The team suctions the mouth and nose and begins PPV with a self-inflating bag with a mask. After 30 seconds of PPV, the heart rate is 50. At this point the team should:

• 1. Begin chest compressions
• 2. Stop PPV and stimulate the baby
• 3. Trouble shoot their ventilation
• 4. Place an emergent umbilical line and give epinephrine
NRP Facts

• Only 10% of newborn infants will need PPV at birth
• 90% of infants who require PPV in the delivery room will respond with increasing heart rate
• Providing effective PPV is the most important part of newborn resuscitation
Case

• A term singleton infant is born after a delivery complicated by fetal decelerations. The infant is stimulated and dried, but has no respiratory effort. The team suctions the mouth and nose and begins PPV with a self-inflating bag with a mask. After 30 seconds of PPV, the heart rate is 50. At this point the team should:
  • 1. Begin chest compressions
  • 2. Stop PPV and stimulate the baby
  • 3. Trouble shoot their ventilation
  • 4. Place an emergent umbilical line and give epinephrine
• Mask: Correct Size and Good Seal
• Reposition Airway and Mask
• Suction Mouth and Nose
• Open Mouth
• Pressure: Increase
• Alternate Airway
Use MR SOPA

• During resuscitation in the delivery room when initial PPV does not increase heart rate

• Could be considered in any infant in a NICU that does not respond quickly to PPV
  • Do NOT use in known diaphragmatic hernia or gastroschisis, these patients require intubation if their own respiratory effort is not adequate
  • Treat unstable heart rhythms first, if present
POLICY STATEMENT

Respiratory Support in Preterm Infants at Birth

COMMITTEE ON FETUS AND NEWBORN

KEY WORDS
respiratory distress syndrome, preterm infant, neonate, surfactant, continuous positive airway pressure, bronchopulmonary dysplasia

ABBREVIATIONS
BPD—bronchopulmonary dysplasia
CI—confidence interval
CPAP—continuous positive airway pressure
INSURE—intubation, surfactant, and extubation
RDS—respiratory distress syndrome
RR—relative risk

abstract

Current practice guidelines recommend administration of surfactant at or soon after birth in preterm infants with respiratory distress syndrome. However, recent multicenter randomized controlled trials indicate that early use of continuous positive airway pressure with subsequent selective surfactant administration in extremely preterm infants results in lower rates of bronchopulmonary dysplasia/death when compared with treatment with prophylactic or early surfactant therapy. Continuous positive airway pressure started at or soon after birth with subsequent selective surfactant administration may be considered as an alternative to routine intubation with prophylactic or early surfactant administration in preterm infants. Pediatrics 2014;133:171–174

This document is copyrighted and is property of the American Academy of Pediatrics and its Board of Directors. All authors have filed conflict of interest statements with the American Academy of Pediatrics. Any conflicts have been resolved through a process approved by the Board of Directors. The American Academy of Pediatrics recommends that you consult local and national laws and guidelines concerning the legal status of publications in your area. The American Academy of Pediatrics has no commercial interests related to the content of this statement.
If Infant Requires Intubation:

- Risk for developing BPD increases with each day on invasive mechanical ventilation
- Therefore, infants who are hemodynamically stable and have sufficient respiratory drive should be rapidly weaned (within 2-24 hours), and extubated (most to CPAP)
- Reasonable extubation criteria (modified from SUPPORT trial):
  - FiO2 less than 35-40% to keep saturations in the desired range
  - MAP ≤ 8
  - pCO2 ≤ 55 without significant work of breathing
Available Types of CPAP:
High Flow Nasal Cannula Systems

- Flows > 1 LPM that can generate CPAP while delivering supplemental oxygen.
- Provide almost 100% relative humidity, which minimizes nasal drying, bleeding, and septal or mucosal breakdown.
- Humidification allows for the safer use of high flows via nasal cannula to generate nasal CPAP.
- The level of CPAP generated is not measured and has to be estimated by calculation.
High-Flow NC vs Nasal CPAP

- Manley, (NEJM 2013), n=303, < 32 weeks
- Multicenter Randomized Noninferiority Trial: After extubation to HFNC 5-6 LPM vs Nasal CPAP (7 cm)
- Treatment failure with HFNC was noninferior 34% vs 26% with Nasal CPAP
- Significantly less nasal trauma (any) with Nasal Cannula 40% vs 54% with Nasal CPAP

**Bottom line:**

- Efficacy was relatively similar
Nasal Ventilation
Nasal IMV, Nasal SIMV, NIV NAVA, Nasal HFV

- **Major Indications:**
  - A/B/D spells that are unresponsive to Nasal-CPAP therapy
  - Respiratory Acidosis
  - Temporary transition to standard Nasal-CPAP in the recently extubated patient

- **Major Risks:**
  - Incidence of Gastrointestinal Perforation is increased with non-synchronized Nasal IMV (*Pediatrics* 1985;76:406.)
  - Prolonged reluctance to re-intubate with excessive tolerance of spells.
Nasal or Noninvasive Ventilation: Nasal-SIMV, NIPPV or NIV-NAVA

Infant Star - Star Sync

Servo-i

NAVA - Neurally Adjusted Ventilatory Assist

Avea

SiPAP
# N-IPPV vs. N-CPAP in RDS

**Failure: Need for intubation**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>N-CPAP</th>
<th>N-IPPV</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kugelman A. 2007</td>
<td>n = 84</td>
<td>49 %</td>
<td>25 %</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>GA: 24-34 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sai Sunil Kishore M. 2011</td>
<td>n = 76</td>
<td>41 %</td>
<td>19 %</td>
<td>0.036</td>
</tr>
<tr>
<td></td>
<td>GA: 28-34 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BW: ≥ 750 g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lista G. 2010</td>
<td>n = 40</td>
<td>15 %</td>
<td>10 %</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>GA: 28-34 w</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meneses J. 2011</td>
<td>n = 200</td>
<td>34 %</td>
<td>25 %</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>GA: 26-33 w</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## N-IPPV vs. N-CPAP Post extubation

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>N-CPAP</th>
<th>N-IPPV</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friedlich P.</td>
<td>n = 41 BW: 500 - 1500 g</td>
<td>37 %</td>
<td>5 %</td>
<td>0.016</td>
</tr>
<tr>
<td>Barrington K.J.</td>
<td>n = 54 BW: ≤ 1250 g</td>
<td>44 %</td>
<td>15 %</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Khalaf M.N.</td>
<td>n = 64 GA: ≤ 34w</td>
<td>40 %</td>
<td>6 %</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Moretti C.</td>
<td>n = 63 BW: ≤ 1250g</td>
<td>39 %</td>
<td>6 %</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Failure as per defined criteria or need for re-intubation
Synchronized Nasal Ventilation Studies

- Friedlich et al: Nasal-SIMV (Star Sync) rate 10-25, PIP 13-23, PEEP 4-6, IT 0.6 vs Nasal CPAP alone post-extubation.
  - Extubation failure decreased with NP-SIMV (5% vs 37%) (J Perinatol 1999;19:413).

- Barrington et al: NP-SIMV (Star Sync) rate 12, PIP 16, PEEP 6, vs Nasal CPAP (6 cm) alone post-extubation.
  - Extubation failure decreased with NP-SIMV (15% vs 44%) (Pediatrics 2001;107:638).

- Khalaf et al: NP-SIMV (Star Sync) rate same as prior to extubation, PIP + 2-4 cm, PEEP or Nasal CPAP 4-6 cm.
  - Extubation failure decreased (6% vs 40%) (Pediatrics 2001;108:13).

Unfortunately the Infant Star is no longer available!
Noninvasive Ventilation for Prevention of BPD (Nasal IMV)

- Ramanathan, (J Perinatology 2012), n=110, 26-29 weeks
- Multicenter RCT: After surfactant for RDS, extubated when stable to Nasal Intermittent PPV vs Nasal CPAP
- NIPPV Group:
  - Significantly decrease rate of extubation failure at any time before discharge (23% vs 58%)
  - Significantly lower rate of clinical BPD, oxygen use at 36 weeks (21% vs 39%)
  - Significantly lower rate of physiologic BPD, 11% vs 46%, (OR: 6.6, CI:2.4, 17.8, P=0.001)
Noninvasive Ventilation for Prevention of BPD - International Trial

• Kirpalani, (NEJM 2013), n=1009, < 30 weeks, < 1000 g
• 34 centers, 10 countries (RCT): 1st use or initial extubation during first 28 days of life: NIPPV vs Nasal CPAP: BW: 802 and 805 g; GA: 26.1 and 26.2 weeks, ND in death or BPD

• ND in rate of extubation failure, NIPPV (60% vs 62%)
• ND in survival with BPD, 34% vs 31%, (CI: 0.86,1.57)
• WHY the Different Outcomes?
• No specific device was required (>6 types were used)
• NIPPV - delivered by SiPAP (43%) which limits the amount of usable PIP (@ 9 cm above PEEP)
Complications of Nasal CPAP or Noninvasive Ventilation

1) **Pneumothorax** - minimize by using least pressure needed to accomplish aims
   - Always Check a CXR

2) **Nasal Irritation** - mucosal swelling or erosion, excessive nasal dilatation or septal necrosis (nasal prongs)
   - Minimize by proper sizing, positioning and alternating nares (NP-Tube)

3) **Abdominal distention and feeding intolerance**
   - If needed, minimize with the use of continuous feeds, leave the NG/OG tube open to vent and place the infant prone or right side down
Bottom Line on Noninvasive Ventilation

• Many morbidities related to endotracheal intubation and mechanical ventilation for respiratory failure or apnea in the neonate can be potentially reduced:
  • Including:
    • subglottic stenosis
    • volutrauma/barotrauma (death or BPD)
    • nosocomial infections (VAP)

• Consider the use of Nasal CPAP as 1st line therapy in the delivery room for infants > 25 weeks GA
  • Avoid pressures > 6 cm with primary therapy

• Consider primary extubation to Noninvasive Ventilation for infants ≤ 29 weeks GA
  • Always balance the benefit versus the risk of therapy