NONINVASIVE VENTILATION IN THE NEONATE

In neonates with moderate to severe respiratory distress syndrome (RDS), invasive mechanical ventilation can provide lifesaving respiratory support. But it can also result in acute lung injury and serious complications such as bronchopulmonary dysplasia (BPD) and ventilator-induced lung injury (VILI). Given these risks, the use of noninvasive ventilation (NIV) strategies in neonatal patients is increasing. With NIV, constant or variable pressure is used to provide respiratory support without endotracheal intubation. Common types of NIV include nasal continuous positive airway pressure (N-CPAP), nasal intermittent positive pressure ventilation (N-IPPV), and heated, humidified high-flow nasal cannula (HHFNC).

NIV: Physiological Effects and Potential Benefits

- In preterm neonates, an unstable chest wall can contribute to airway collapse. In such cases, NIV may help support airway structure. NIV may help maintain functional residual capacity in premature neonates with surfactant deficient alveoli by augmenting spontaneous respiratory effort and minute ventilation. NIV may help prevent VILI and the development of BPD. It may also prevent the harmful effects of intubation, including hemodynamic instability, increased airway resistance (which can increase work of breathing), airway trauma and risk of infection. Complications of NIV can include nasal trauma and pneumothorax due to higher pressures used in N-CPAP.

Clinical Benefits of N-CPAP

- In a randomized controlled trial (RCT), premature infants receiving N-CPAP had a lower risk of death or need for oxygen therapy at 28 days compared to those getting invasive mechanical ventilation (MV).
  - Infants in the N-CPAP group had fewer days of ventilation and a 50% reduction in the use of surfactant, but the incidence of pneumothorax was three times higher in the N-CPAP group.
  - In another RCT of premature infants randomized to N-CPAP or intubation and surfactant, there was no significant difference between groups with respect to the rate of death or BPD, though infants treated with N-CPAP were less likely to need intubation or corticosteroid therapy for BPD.
  - Infants in the N-CPAP group required fewer days of mechanical ventilation and were more likely to be alive and free from mechanical ventilation by day seven.

Clinical Benefits of N-IPPV

- In short-term studies, N-IPPV appears to be more effective than N-CPAP for reducing apnea in premature infants presenting with frequent apnea, but perhaps less effective in infants with less frequent spells (Figure 1).

N-CPAP
- Uses continuous distending pressure (CDP) to stabilize lung volumes, reduce the work of breathing, improve oxygenation, reduce apnea and attenuate chest wall distortion during inspiration.

Clinical Benefits of N-IPPV
- Uses positive pressure cycles delivered on top of N-CPAP to help provide increased ventilation, higher mean airway pressures, better washout of anatomical dead space and possible stimulation of respiratory drive. Compared with N-CPAP, synchronized N-IPPV appears to have beneficial effects in reducing asynchrony, improving tidal and minute volumes, decreasing respiratory rate and augmenting respiratory drive.

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Apnea Frequency (spells/hour)

<table>
<thead>
<tr>
<th>Study</th>
<th>N-CPAP</th>
<th>N-IPPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lin 1998</td>
<td>1.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Bisceglia 2007</td>
<td>0.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Ryan 1989</td>
<td>0.6</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Figure 1
Clinical Benefits of N-IPPV (cont’d.)

- Randomized, controlled trials in infants with mild to moderate RDS have indicated that N-IPPV is more effective than N-CPAP in reducing the need for invasive ventilation in the first week after birth (Figure 2). [17,20]
- It had a significantly reduced incidence of BPD compared to those treated with N-CPAP (2% vs. 17%). [17]
- In infants (600g to 1250g) with RDS who received surfactant, N-IPPV was associated with a significantly lower incidence BPD and death than conventional ventilation (20% vs. 52%). [17]
- In a large NICU, increasing use of N-IPPV was associated with reductions in BPD, length of hospital stay and cost of care. [17]
- In contrast, in a study of premature infants with RDS, the incidence of BPD was similar for N-IPPV and N-CPAP (26.5% vs. 25%), and in a study of extremely low birth weight infants, no differences in death or survival with BPD were observed between N-IPPV and N-CPAP. [17,22]

Figure 2

<table>
<thead>
<tr>
<th>% Requiring Intubation</th>
<th>Kugelman 2007</th>
<th>Kishore 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td></td>
<td></td>
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<tr>
<td>10.0</td>
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<tr>
<td>50.0</td>
<td></td>
<td></td>
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<tr>
<td>60.0</td>
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</tbody>
</table>

[p = 0.04] [p = 0.036]

Clinical Benefits of HHFNC

- Has gained widespread use in certain settings as an alternative to N-CPAP, though there is little direct evidence supporting its use. [17,20,23]
- Flow rates greater than two L/min can generate unquantifiable positive end-expiratory pressure (PEEP) and result in potentially damaging lung overexpansion. [17,20]
- Use of nonheated and/or nonhumidified air can cause nasal desiccation and bleeding. [17]

HHFNC

- In a trial of premature infants randomized to HHFNC or N-CPAP, no differences were observed for rate of treatment failure within seven days or rate of death before discharge. [17]
- In a randomized study of infants randomized to HHFNC or N-CPAP, no differences were observed for rate of early extubation failure, need for supplemental oxygen and incidence of BPD. [17]

Summary

Overall, NIV in neonates appears to be a safe alternative to routine intubation and mechanical ventilation in preterm infants with spontaneous breathing. Still, more research is needed to elucidate the relative risks and benefits for the different modalities. Randomized, controlled trials comparing N-IPPV to mechanical ventilation have yielded mixed results. There is evidence that N-CPAP utilization can reduce the need for intubation and the incidence of BPD, but more research is needed to evaluate the effects on mortality and long-term outcomes. [17]

Available evidence indicates that N-IPPV may provide significant short-term advantages over N-CPAP, by reducing apneic spells and the need for intubation in infants with mild to moderate RDS, and improving the success of extubation. [17] Evidence also suggests that HHFNC is as safe and effective as N-CPAP for NIV respiratory support in neonates, but more research is needed to support the routine use of this modality. [17]