LUNG PROTECTION STRATEGIES IN PRETERM NEONATES

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Outline

- Journey Towards Lung protection
- Goals of lung protection
- Strategies
- Summary
- Conclusion
The Journey Towards Lung Protective Respiratory Support in Preterm Neonates

- Before 1960: Oxygen; impact assessed clinically.
- The 1960s: President JFK, Ventilators → ↓ mortality; The march Towards BPD.
- The 1970s: Giant Leaps Forward; ANS, CPAP
- The 1980s: Another Huge Jump; Surfactant
- The 1990s: Further Steps in the Right Direction; better ventilators.
- Mortality in (< 1000 g, ELBW) has reduced but the overall BPD incidence has not changed ... NICU graduates transferred to PICU with LRTI and right heart failure.
Changing appearance of BPD
Fetal Lung Development
Major Goals of Lung protective strategies

- FiO2 – *Oxygen toxicity*
- PIP – *Barotrauma*
- Tidal volume – *Volutrauma!!*
- “Collapsed” lung regions – *Atelectotrauma*
- Lung inflammation - *Biotrauma*
CPAP should be used early.

During bag-mask ventilation
  ◦ PEEP valves should be used to establish stabilize functional residual capacity.
  ◦ ventilation with large tidal volumes is avoided.

Reduce the risk of oxygen toxicity→ BPD, ROP

Provision of supplemental oxygen must be guided by pulse oximetry…Target in NICU 90–95%.
Antenatal counseling. Team briefing and equipment check.

Birth

Term? Tone? Breathing or crying?

No

Warm and maintain normal temperature, position airway, clear secretions if needed, dry, stimulate.

Apnea, gasping, or HR below 100 bpm?

No

Labored breathing or persistent cyanosis?

Yes

Position and clear airway. Spo2 monitor. Supplemental O2 as needed. Consider CPAP.

No

Post-resuscitation care. Team debriefing.

1 minute

PPV. Spo2 monitor. Consider ECG monitor.

Yes

HR below 100 bpm?

Yes

Post-resuscitation care. Team debriefing.

Check chest movement. Ventilation corrective steps if needed. ETT or laryngeal mask if needed.

No

HR below 60 bpm?

Yes

Intubate if not already done. Chest compressions. Coordinate with PPV. 100% O2. ECG monitor.

No

HR below 60 bpm?

Yes

IV epinephrine.

If HR persistently below 60 bpm: consider hypovolemia, consider pneumothorax.

Stay with mother for routine care: Warm and maintain normal temperature, position airway, clear secretions if needed, dry, ongoing evaluation.

Pre-ductal Spo2 Target

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Target</th>
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<tbody>
<tr>
<td>1 min</td>
<td>60%–65%</td>
</tr>
<tr>
<td>2 min</td>
<td>65%–70%</td>
</tr>
<tr>
<td>3 min</td>
<td>70%–75%</td>
</tr>
<tr>
<td>4 min</td>
<td>75%–80%</td>
</tr>
<tr>
<td>5 min</td>
<td>80%–85%</td>
</tr>
<tr>
<td>10 min</td>
<td>85%–95%</td>
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</table>
Early CPAP (Avery et al 1987)

Columbia Presbyterian

500-1500 gm Infants: Variation in CLD

Survival, MV, Surfactant, Indocin, %CLD

New York, Boston

*p<0.0001

Intubation/Ventilation vs. CPAP

Death or BPD at 36 Weeks

<table>
<thead>
<tr>
<th></th>
<th>Intubation/Ventilation</th>
<th>CPAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>COIN</td>
<td>38%</td>
<td>30%</td>
</tr>
<tr>
<td>SUPPORT</td>
<td>55%</td>
<td>52%</td>
</tr>
<tr>
<td>VON</td>
<td>34%</td>
<td>32%</td>
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</table>
INSURE- STRATEGY

- Intubation for surfactant administration followed by rapid extubation to CPAP is known as “INSURE”
- A Cochrane review indicates that preterm infants with or at risk for RDS treated with INSURE less likely to:
  - Require MV
  - Develop BPD
  - Lower rates of air leaks
Intubation/Ventilation vs. InSurE

Death or BPD at 36 Weeks

VON DR Trial
Less Invasive Surfactant Administration

- Intrapartum/pharyngeal administration
- Administration via laryngeal mask airway (LMA)
- LISA: Thin catheter using placed using Magill's forceps; baby spontaneously breathing.
- MIST: Rigid vascular catheter; baby spontaneously breathing.
Practical Approach

Non invasive ventilation: SUMMING IT UP!

Approach to VLBWI After Birth

Depressed - Poor resp effort
- ET tube IPPV
- Surfactant if RDS
- When stable extubate to NCPAP or NIMV

Active - Good resp effort
- Start NCPAP
- Deterioration, Increasing FiO2, PaCO2, Apnea
- ET tube-IPPV-Surfactant if RDS
- When stable extubate to NCPAP or NIMV
- Stable-Continue NCPAP

BANCALARI, 2013
Synchronization of spontaneous breathing efforts with inflations.

- Consistent TV
- Improved oxygenation
- less use of sedatives/analgesic drugs, and shorter duration of MV.
Neurally Adjusted Ventilatory Assist (NAVA)

Observational studies have shown better synchrony, less PIP and sedation with similar ABG.
Further research needed to determine effects on outcome.
From experimental and clinical studies in the late 1980s and 1990s in adults, it became increasingly evident that Volume not pressure that causes significant lung injury.
Rat lungs after IPPV @ 45 cmH20

control

5 min

20 min

Dreyfuss and Sauman. Am J Respir Crit Care Med 1998
Non invasive ventilation: WHY INTEREST IN NIV??

Volume Targeted Ventilation

Concept: deliver the set Vt at the lowest airway pressure possible

Clinician (re) selects
VT set, PIP, PEEP,
Ti, Flow

Ventilator delivers
next breath

Ventilator adjusts
PIP to make
VT = VT set

No

VTdelivered = VT set?

Yes

PIP remains unchanged
Advantages of volume targeted ventilation

A significant increase in lung compliance, such as following exogenous surfactant administration will lead to a proportional increase in delivered VT unless the inflating pressure is reduced.

As the VT increases due to improving compliance after surfactant administration, the ventilator automatically drops the PIP.

Volume Targeted Ventilation

- VTV reduces
  - variability of $V_T$ delivery compared with PLV.

- Decreasing $V_T$ fluctuations
  - leads to a more stable PaCO$_2$ and less hypocarbia.
  - Reduces fluctuations in cerebral blood decreases the risk of brain injury.
Atelectasis results in accumulation of protein-rich fluid leading to:
- surfactant inactivation
- Release of inflammatory mediators.

The repeated collapse and re-expansion of alveoli with low end-expiratory volume contribute further to VALI.

This process is known as atelectotrauma
In the presence of extensive atelectasis, as seen in the right lower corner, there are two populations of alveoli with very different critical opening pressures.
Pressure and Volume Swings

- During CMV, there are swings between the zones of injury from inspiration to expiration.
- During HFOV, the entire cycle operates in the “safe window” and avoids the injury zones.
Review: Elective high frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants

Comparison: 01 HFOV vs CV (all trials)
Outcome: 08 Death or CLD at 36-37 weeks PMA or discharge

<table>
<thead>
<tr>
<th>Study</th>
<th>HFOV</th>
<th>CV</th>
<th>Relative Risk (Fixed) 95% CI</th>
<th>Weight %</th>
<th>Relative Risk (Fixed) 95% CI</th>
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</thead>
<tbody>
<tr>
<td>Clark 1992</td>
<td>11 / 37</td>
<td>16 / 28</td>
<td>11.1 [0.29, 0.94]</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>Gerstmann 1996</td>
<td>17 / 64</td>
<td>28 / 61</td>
<td>17.5 [0.35, 0.94]</td>
<td>0.58</td>
<td></td>
</tr>
<tr>
<td>Morissette 2001</td>
<td>55 / 139</td>
<td>57 / 134</td>
<td>35.5 [0.70, 1.24]</td>
<td>0.93</td>
<td></td>
</tr>
<tr>
<td>Plavka 1999</td>
<td>5 / 21</td>
<td>10 / 20</td>
<td>6.3 [0.20, 1.15]</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>Rettwitz-Volk 988</td>
<td>5 / 46</td>
<td>4 / 50</td>
<td>2.3 [0.39, 4.75]</td>
<td>1.36</td>
<td></td>
</tr>
<tr>
<td>Thorne 1998</td>
<td>46 / 140</td>
<td>45 / 144</td>
<td>27.2 [0.75, 1.48]</td>
<td>1.05</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>139 / 447</td>
<td>160 / 437</td>
<td>100.0 [0.70, 1.00]</td>
<td>0.84</td>
<td></td>
</tr>
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Test for heterogeneity chi-square = 9.09 df = 5 p = 0.1056
Test for overall effect Z = -1.92 p = 0.06
PERMISSIVE HYPERCAPNIA

- Permissive hypercapnia: Tolerance of (PCO2)>45mmHg.
  - Low tidal volumes
  - More unloading of oxygen to the tissues (Bohre's effect)
  - Increase in Respiratory drive...Less apnea
  - Facilitate early weaning.

- Retrospective observations in preterm infants showed that low levels of carbon dioxide (CO2) <30mmHg an increased risk of BPD.

- Permissive Hypercapnia (45-55mmHg)
  - Reduced BPD
  - Reduced PVL

- Keep PH> 7.25
Clinical experience

- Normocapnia: 35–45 mmHg
- Permissive Hypercapnia: 45–55 mmHg

Graph showing the duration of assisted ventilation (hours) for infants on assisted ventilation. The graph compares infants on Normocapnia and Permissive hypercapnia. The p-value is less than 0.005.
Caffeine

- CAP trial showed
  - Reduced apnea
  - Caffeine group Weaned from the ventilator one week earlier.
  - Caffeine group had lower incidence of BPD (OR 0.63; P < 0.001).
Summary

- A single recommendations on optimal LPVS cannot be made.
- Different modes of LPVS may be combined or individually.
  - Establish an FRC Early and use of non-invasive ventilation
  - if indicated use Surfactant early and deliver it in minimally invasive manner
  - Open the lungs and keep it open
  - Look out for hidden oxygen toxicity
  - Chose a synchronised mode of ventilation and control your tidal volumes
  - Permissive hypercapnia.
- Remember less is more….IF possible avoid mechanical ventilation!!