Closed loop control of inspired oxygen for the premature newborn

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Disclosure

The algorithm for Closed Loop FiO₂ was developed and patented by Drs. Claure and Bancalari, who are Faculty of the University of Miami. The University of Miami, the assignee for this patent, has a licensing agreement with CareFusion.
Prolonged need for oxygen supplementation in preterm infants

(Infants born at UM-JMH, GA 24-31w Years 2008-2009)
Improving the outcomes: Adequate oxygenation vs. toxicity in the premature infant

**Insufficient O$_2$**
- CNS hypoxia
- Organ/tissue hypoxia
- Pulmonary vasculature
- Hemodynamic adaptation
- Risk of mortality?

**Excessive O$_2$**
- Eye injury
- Lung injury
- Oxidative stress
- CNS damage
## Actual vs. intended SpO₂

<table>
<thead>
<tr>
<th></th>
<th>Below intended range</th>
<th>Within intended range</th>
<th>Above intended range</th>
</tr>
</thead>
<tbody>
<tr>
<td>All 14 NICUs</td>
<td>16%</td>
<td>48%</td>
<td>36%</td>
</tr>
<tr>
<td>Postnatal week 1</td>
<td>51%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postnatal week 4</td>
<td></td>
<td>44%</td>
<td></td>
</tr>
</tbody>
</table>

80 infants GA<28w (on O₂),
Hypoxemia spells and postnatal age in premature infants

Di Fiore et al. J Pediatrics 2010
Fluctuations due to respiratory instability
Manual FiO₂ titration in infants with frequent fluctuations in SpO₂
Nurse:patient ratio and maintenance of SpO$_2$
Compliance to SpO$_2$ alarms

Low alarm  
(should be @ 85%)  

High alarm  
(should be @ 94%)  

Clucas et al. Pediatrics 2007 (infants on O$_2$)
Improving the maintenance of SpO$_2$

Reproduced from data by Ford et al. Pediatrics 2006
Factors affecting the maintenance of SpO₂ targets in neonatal intensive care

- Respiratory instability of the preterm infant
  - Postnatal age
  - Changes in the underlying lung disease
- Inadequate manual adjustment
  - Insufficient weaning / tolerance of high SpO₂
  - Delayed response
- Staff limitations
  - High workload
  - Education and awareness
  - Poor alarm compliance
Ideal manual FiO$_2$ adjustment

29±17 adjustments per hour by a fully dedicated nurse at bedside
Closing the Loop

Oximeter → Ventilator

Ventilator to Automated FiO₂ algorithm

SpO₂ → Ventilator

FiO₂ → Ventilator
Automated FiO₂ adjustments

- Rule-based algorithm
- FiO₂ is ↑ or ↓ step-wise if SpO₂ is < or > the target range, respectively
- Magnitude and frequency of FiO₂ adjustments are determined by:
  - difference between SpO₂ and target range
  - time outside range
  - trend in SpO₂
  - baseline FiO₂
- Baseline FiO₂ is adjusted gradually to FiO₂ needed to keep SpO₂ within range – indicator of lung disease
Closed Loop FiO₂

SpO₂

FiO₂

[0, 60]
Automatic vs frequent manual FiO₂ changes
Automated FiO$_2$ in preterm infants
Automatic FiO₂ control in infants with frequent fluctuations in SpO₂

<table>
<thead>
<tr>
<th></th>
<th>Manual</th>
<th>Auto</th>
</tr>
</thead>
<tbody>
<tr>
<td>% time SpO₂ 87-93% or &gt;93% at 21% O₂</td>
<td>39</td>
<td>47 *</td>
</tr>
<tr>
<td>% time SpO₂ &gt; 93% on &gt; 21% O₂</td>
<td>37</td>
<td>21 *</td>
</tr>
<tr>
<td>% time SpO₂ &gt; 98% on &gt; 21% O₂</td>
<td>5.6</td>
<td>0.7 *</td>
</tr>
<tr>
<td>% time SpO₂ 80-86%</td>
<td>15</td>
<td>20 *</td>
</tr>
<tr>
<td>% time SpO₂ &lt; 80%</td>
<td>9.5</td>
<td>9.8</td>
</tr>
<tr>
<td># episodes SpO₂ &lt; 85%, &gt;2 min (per 24h)</td>
<td>35</td>
<td>22 *</td>
</tr>
<tr>
<td># episodes SpO₂ &lt; 75%, &gt;1 min (per 24h)</td>
<td>10</td>
<td>3 *</td>
</tr>
<tr>
<td>Manual FiO₂ adjustments per 24 h</td>
<td>112</td>
<td>10 *</td>
</tr>
</tbody>
</table>

32 infants on MV and O2 with frequent hypoxemia episodes
GA: 25 w, Age: 26 d
4 NICUs in the U.S. under IDE by FDA

(*: p< 0.01) From Claure et al. Pediatrics 2011
Automatic FiO\textsubscript{2} control in infants with frequent fluctuations in SpO\textsubscript{2}

32 infants on MV and O2 with frequent hypoxemia episodes
GA: 25 w, Age: 26 d
4 NICUs in the U.S. under IDE by FDA

From Claure et al. Pediatrics 2011
Automatic control of FiO$_2$
Automatic FiO₂ control in keeping two SpO₂ target ranges in preterm infants

80 infants who require O2 while on MV, CPAP or NIV
GA: 26 w; Age: 18 d
8 NICUs in Europe and 1 in Canada

Van Kaam et al. ESPR 2014
Closed loop FiO₂: Proposed as a clinical tool to improve the outcomes in premature infants

- Undertakes two issues that limit the maintenance of SpO₂
  - Respiratory instability of the infant
  - Staff limitations to conduct repetitive/laborious task
- Can improve the maintenance of SpO₂ within the target
- Target range is selected by the clinician
- Reduces exposure to extreme high/low SpO₂
- Reduces exposure to supplemental oxygen
- Does not prevent, only attenuates hypoxemia fluctuations
- Not a substitute for adequate clinical monitoring and assessment of ventilation
Improving outcomes: Adequate oxygenation vs. oxygen toxicity

CNS hypoxia
Organ/tissue hypoxia
Pulmonary vasculature
Ductal patency
Risk of mortality?

Eye injury
Lung injury
Oxidative stress
CNS damage

Respiratory instability and fluctuations
Limitations in newborn intensive care

Can closed loop FiO₂ contribute to this goal?