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Oxygen in the Delivery Room: An 2016 Update

Oxidative stress, free radicals & antioxidants

Nomogram of urinary lipid peroxidation byproducts in preterm infants

- Lipid peroxidation by products have been associated with severe conditions in preterm infants.
- Non-invasive methods (urine) have been validated in analytical and clinical studies.
- Screening of metabolic profiles for the evaluation in vivo of oxidative stress and inflammation could be a useful tool for the clinician.

Isoprostanes & Isofurans

Kuligowski J et al Antioxid Redox Signal 2015

Kuligowski J et al Antioxid Redox Signal 2015
Neurofurans & Neuroprostanes

Clinical experience

Biomarkers of oxidative damage in hypoxia / reoxygenation in asphyctic term babies: Redox status.

Biomarkers of oxidative damage in hypoxia / reoxygenation in stabilization of preterm infants: isoprostanes

**Kuligowski J et al.** AnKoxid Redox Signal 2015

**Kuligowski J et al.** AnKoxid Redox Signal 2016

**Vento M et al.** Pediatrics 2009

**Vento M et al.** Pediatrics 2003
Biomarkers of oxidative damage in hyoxia / reoxygenation in stabilization of preterm infants: Isofurans

Oxygen saturation in ELBW after birth

Defining the reference range for oxygen saturation

Data set characteristics

Term Neonates ≥ 37 weeks’ gestation

Preterm < 37 weeks gestation
Suggested level for administration of oxygen

Oxygen saturation (%)

Minutes after birth

How can SpO2 centiles be used to inform decision making in the DR?

Titration of FiO2 against measured SpO2

TRANSITIONAL OXYGEN TRACKING SYSTEM

What initial FiO2 is recommended for term and preterm infants in the delivery room?

ILCOR 2010 Treatment Recommendation

In term infants receiving resuscitation at birth with positive pressure ventilation, it is best to begin with air rather than 100% oxygen.

If despite effective ventilation there is no increase in heart rate or if oxygenation (guided by oximetry) remains unacceptable, use of a higher concentration of oxygen should be considered.

October 18th 2010
Flow diagram

Studies included in quantitative synthesis (meta-analysis) \( (n = 8) \)

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Studies included and mortality

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>( \text{PaO}_2 )</th>
<th>Gestational age (wks)</th>
<th>Death</th>
<th>High</th>
<th>Low</th>
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<tbody>
<tr>
<td>Wang (2008) USA</td>
<td>0.21 vs. 1.0</td>
<td>26.4</td>
<td>13%</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Escrig (2008) Spain</td>
<td>0.30 vs. 0.90</td>
<td>28.0</td>
<td>21%</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Vento (2009) Spain</td>
<td>0.35 vs. 0.90</td>
<td>28.0</td>
<td>15%</td>
<td>7%</td>
<td></td>
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<tr>
<td>Rabi (2011) Canada</td>
<td>0.21 vs. 1.0</td>
<td>27.0</td>
<td>0%</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>Kapadia (2012) USA</td>
<td>0.21 vs. 1.0</td>
<td>26.0</td>
<td>7%</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Aguir (2014) Spain</td>
<td>0.30 vs. 0.60</td>
<td>26.5</td>
<td>12%</td>
<td>27%</td>
<td></td>
</tr>
<tr>
<td>Rook (2014) The Netherlands</td>
<td>0.30 vs. 0.65</td>
<td>26.5</td>
<td>15%</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Oei (2015) Australia/NZ/others</td>
<td>0.21 vs. 1.0</td>
<td>27.0</td>
<td>19%</td>
<td>6%</td>
<td></td>
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</tbody>
</table>

Death before hospital discharge for preterm < 28 weeks gestation

- Low oxygen: 13.5%; High oxygen: 12.4%
- Low oxygen: 10.2%; High oxygen: 21.7%
- Low oxygen: 15.7%; High oxygen: 8.0%

Death before hospital discharge preterm < 28 weeks gestation; only unmasked studies

BPD in survivors
Intraventricular hemorrhage

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Low oxygen</th>
<th>High oxygen</th>
<th>Risk Ratio</th>
<th>Year</th>
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</thead>
<tbody>
<tr>
<td>Total (n=31)</td>
<td>11</td>
<td>20</td>
<td>0.92</td>
<td>2016</td>
</tr>
<tr>
<td>Term</td>
<td>2</td>
<td>3</td>
<td>0.58</td>
<td>2016</td>
</tr>
<tr>
<td>Preterm</td>
<td>8</td>
<td>17</td>
<td>0.62</td>
<td>2016</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>20</td>
<td>0.92</td>
<td>2016</td>
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</tbody>
</table>

Necrotizing enterocolitis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Low oxygen</th>
<th>High oxygen</th>
<th>Risk Ratio</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (n=36)</td>
<td>26</td>
<td>10</td>
<td>1.05</td>
<td>2015</td>
</tr>
<tr>
<td>Term</td>
<td>9</td>
<td>5</td>
<td>0.72</td>
<td>2015</td>
</tr>
<tr>
<td>Preterm</td>
<td>17</td>
<td>5</td>
<td>0.62</td>
<td>2015</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>10</td>
<td>1.05</td>
<td>2015</td>
</tr>
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</table>

Retinopathy of prematurity

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Low oxygen</th>
<th>High oxygen</th>
<th>Risk Ratio</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (n=28)</td>
<td>17</td>
<td>11</td>
<td>0.77</td>
<td>2013</td>
</tr>
<tr>
<td>Term</td>
<td>17</td>
<td>6</td>
<td>0.77</td>
<td>2013</td>
</tr>
<tr>
<td>Preterm</td>
<td>11</td>
<td>5</td>
<td>0.77</td>
<td>2013</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>17</td>
<td>0.77</td>
<td>2013</td>
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</tbody>
</table>

Canadian Neonatal Network Retrospective Study

- Retrospective study
- 17 NICUS 2328 infants ≤ 27 wks
- 1/246 (n=580) vs. 1/236 (n=580)
- AOR for severe neurologic injury or death:
  - OX2005 vs. OX100 AOR 1.36 (95% CI 1.11, 1.66)
  - OX2005 vs. OX2006 AOR 1.33 (95% CI 1.04, 1.69)
- Higher risk of severe Neurologic Injury or Death among preterms ≤ 27 wks with reduced initial FiO2

Oxygen in the DR in preterm infants at limit of viability

- Eligible (n=133)
- 22 – 26 weeks (n=22)
- 25 – 26 weeks (n=27)
- 27 – 28 weeks (n=34)
O₂ in the DR in preterm infants at the limit of viability: % of time in bradycardia.

Discussion

• Recommendations regarding initial FiO₂ especially in ELGA remain inconclusive
• Evidence is based on small studies with different designs
  – Masked studies have better outcomes
  – Greater resources
  – University centers with trained personnel
• Timing: better outcomes after 2009
  – Learning curve in the DR?
• Caution using low FiO₂ and keeping ELGA in low SpO₂’s and HR even for minutes

What initial FiO₂ could be recommended for preterm infants in the delivery room?

Guidelines to administer O₂ in the DR

• Optimal initial FiO₂ (guided by HR first 3 min)
  – < 29 weeks → 30%-50%
  – <26 weeks → 40%-50%
  – 29-32 weeks → 30%
  – > 32 weeks → 21%
• SpO₂ targets (PREDUCTAL)
  – 3 min → 75-80%
  – 5 min → 85%-90%
  – 10 min → >90%
• Titration procedure should be evaluated.
• Initial FiO₂ should be included in Fup studies.

Thank you very much for your attention!

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