Can targeting cerebral saturations improve survival and neurodevelopmental outcomes?

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5 Minute Friday
July 15, 2016
What is Near Infrared Spectroscopy (NIRS) ?

- NIRS can be used as a non-invasive monitoring technique for cerebral and somatic oxygenation and hemodynamics.
- Data is acquired from vascular beds (cerebral, renal, and splanchnic) with varied flows and extraction ratios.
- While pulse oximetry provides a measure of arterial oxygen saturation reflecting oxygen supply to the tissues, NIRS-measured regional oximetry measures the balance between local oxygen delivery and consumption beneath the sensor.
- It provides a non-invasive measure of end-organ oxygenation and perfusion.
How a NIRS sensor works

Placement of NIRS sensor on Forehead. The two black circles are the light source and detector.

Light passes from light source through the scalp, skull, and brain tissue then to the detector.

Cerebral saturation (rSO2) reflects a ratio of arterial to venous blood of 25%:75%
Normal NIRS values in newborns

<table>
<thead>
<tr>
<th>rSO2</th>
<th>Term</th>
<th>Preterm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral (%)</td>
<td>66-89</td>
<td>66-83</td>
</tr>
<tr>
<td>Renal (%)</td>
<td>75-97</td>
<td>64-87</td>
</tr>
<tr>
<td>Mesenteric (%)</td>
<td>63-87</td>
<td>32-66</td>
</tr>
</tbody>
</table>

Values differ by sensor type with neonatal sensors reading 10% higher

What rScO2 values injure the brain?

- Mitochondrial damage in CA1 region of hippocampus in newborn piglets subjected to graded anoxia. Hou X et al., Physiol Meas 2007
  
rScO2 <40%

- New or worse ischemia on MRI in infants with hypoplastic left heart syndrome (HLHS). Dent C et al., J Thorac Cardiovasc Surg 2002
  
rScO2 <45% for >180 minutes

  
rScO2 ranging 33-44%

- Abnormal high energy phosphates measured by MRI spectroscopy in brains of newborn piglets. (Kusaka T, Ped Res 2009)
  
rScO2 <40%
Target rScO2 ranges for newborns

Safeguarding the brain of our smallest children
SafeBoosC Trial

**Objective:** Can cerebral oxygenation be stabilized using NIRS

**Design:** 8 NICUs in EU randomizing newborns <28 weeks to NIRS algorithm or blinded NIRS monitor

**Primary outcome:** Time spent outside the target cerebral sat range 55-85%

**Secondary outcome:** Mortality and brain injury using HUS
SafeBoosC II: Phase 2 Study (Randomized)

<28 wks GA (n=166)

Avoid:
- Hyperoxia: $r\text{ScO}_2 > 85\%$
- Hypoxia: $r\text{ScO}_2 < 55\%$

Infants enrolled in:
- Lyon
- Madrid
- Copenhagen
- Cork
- Utrecht
- Graz
- Milan
- Cambridge

NIRS-monitored

Standard Treatment

Sample Size: n=86/80

(SafeboosC II Group, BMJ 2015)
What could be done?

When cerebral rScO₂ is low (<55%), consider:

- Low pCO₂ (Increase pCO₂)
- hsPDA (Close)
- Hypotension (treat)
- Anemia (Erytrocyte transfusion)
- Low arterial saturation (Increase FiO₂)

When cerebral rScO₂ is high (>85%), please consider:

- Supranormal Art Sat (Decrease FiO₂ if possible)
- Too high pCO₂ (Decrease pCO₂)
- Low glucose (Treat low blood glucose)
Intervention algorithm in SafeBoosC trial

**Cardiovascular status**
- Blood Pressure
- CRT
- Lactate
- Urine output

**Clinical assessment**
- Echocardiography
- Low CO/SVC flow
- PDA

**Oxygen transport**
- [Hb] low
- SaO2 low
- PCO2 low

**Respiratory status**
- SaO2 high
- PCO2 high

**rStO2 < 55%**
- Consider volume expansion, vasopressor/inotropes, decrease MAP
- On vasopressors?
  - Consider reducing vasopressor

**rStO2 > 85%**
- Consider volume expansion, inotropes, decrease MAP
- Consider treatment

**Blood Pressure**
- Consider reducing vasopressor

**On vasopressors?**
- Consider reducing vasopressor

**Low CO/SVC flow**
- Consider volume expansion, inotropes, decrease MAP

**PDA**
- Consider treatment

**[Hb] low**
- Consider RBC transfusion

**SaO2 low**
- Consider increase FiO2
- Consider decrease FiO2

**PCO2 low**
- Consider decrease MV
- Consider increase MV

**SaO2 high**
- Respiration status

**PCO2 high**
- Blood glucose level

**Low**
- Consider increase glucose intake

**Respiratory status**
- Blood glucose level

**Abbreviations:**
- rStO2: regional tissue oxygen saturation of haemoglobin
- CRT: capillary refill time
- CO: cardiac output
- SVC: superior vena cava
- MAP: mean airway pressure
- PDA: patent ductus arteriosus
- [Hb]: blood haemoglobin concentration
- RBC: red blood cells
- SaO2: arterial haemoglobin saturation
- FiO2: inspired oxygen fraction
- PCO2: partial pressure of carbon dioxide.
## SafeBoosC II Trial - Results

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>NIRS (n=86)</th>
<th>Blinded NIRS (control) (n=80)</th>
<th>Relative change in % (95% CI)</th>
<th>Adjusted relative risk (95% CI)</th>
<th>Adjusted P value (unadjusted)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (interquartile range) burden of hypoxia and hyperoxia (%hours)</td>
<td>36.1 (9.2-79.5)</td>
<td>81.3 (38.5-181.3) (n=78)</td>
<td>−58 (−35 to −74)</td>
<td>NA</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cause mortality at term</td>
<td>12/86 (14)</td>
<td>20/80 (25)</td>
<td>NA</td>
<td>0.50 (0.29 to 1.00)</td>
<td>0.10 (0.049)</td>
</tr>
<tr>
<td>Brain injury on cerebral ultrasonography:</td>
<td></td>
<td></td>
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<tr>
<td>None</td>
<td>21/80 (26)</td>
<td>26/77 (34)</td>
<td>NA</td>
<td>—</td>
<td>0.11 (0.053)</td>
</tr>
<tr>
<td>Mild-moderate</td>
<td>49/80 (61)</td>
<td>33/77 (43)</td>
<td>NA</td>
<td>—</td>
<td></td>
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<tr>
<td>Severe</td>
<td>10/80 (13)</td>
<td>18/77 (23)</td>
<td>NA</td>
<td>—</td>
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<tr>
<td><strong>Exploratory</strong></td>
<td></td>
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</tr>
<tr>
<td>Median (interquartile range) burden of hypoxia (%hours)</td>
<td>16.6 (5.4-68.1)</td>
<td>53.6 (17.4-171.3) (n=78)</td>
<td>−58 (−24 to −76)</td>
<td>NA</td>
<td>0.0012*</td>
</tr>
<tr>
<td>Mean (SD) burden of hyperoxia (%hours)</td>
<td>1.2 (0.3-9.6)</td>
<td>1.1 (0.1-23.4) (n=78)</td>
<td>1 (−35 to 194)</td>
<td>NA</td>
<td>0.98*</td>
</tr>
</tbody>
</table>
Infants enrolled in:
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SafeBoosC II

Hyperoxia: \( r\text{ScO}_2 > 85\% \)
Hypoxia: \( r\text{ScO}_2 < 55\% \)

\( p < 0.001 \)

81% hrs
36% hrs

Control
(No NIRS)

Intervention
(Yes NIRS)

N = 80
GA = 26.8 wks

N = 86
GA = 26.6 wks

(SafeboosC II Group, BMJ 2015)
SafeBoosC II Trial Conclusions

- The burden of cerebral hypoxia and hyperoxia was significantly reduced in ELBW infants monitored with NIRS.
- Larger trials are needed to determine if this management algorithm will improve long-term outcomes.