Cerebral Oximetry in Preterm Infants: Methods, Measurements and Evaluating Clinical Benefit

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Dr. Gorm Greisen is a Clinical Professor of Pediatrics at the Institute for Klinisk Medicine and consultant neonatologist at the Department of Neonatology at the Juliane Marie Centre, Rigshospitalet. Dr. Greisen’s program of research focuses on the causes of brain injury in preterm infants, cerebral blood flow and cerebral oxygenation as well as neurodevelopmental outcomes in preterm infants for thirty years. Recent publications have focused on the impact of vasopressors on cerebral oxygenation in the piglet model. He is currently engaged in an A phase II randomized clinical trial on cerebral near-infrared spectroscopy plus a treatment guideline versus treatment as usual, for extremely preterm infants during the first three days of life (SafeBoosC).

Annual Quality Congress Breakout Session, Saturday, October 3, 2015
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Objective: Discuss two risks and two potential benefits of bedside cerebral oximetry measurement in very preterm infants.
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Disclosures

I have

- no financial interest in any medical equipment
- a long-standing research interest in near-infrared spectroscopy and cerebral circulation and oxygenation in the preterm newborn infant
- coordinated of the SafeBoosC trial that was fully financed by the Danish Strategic Research Council

And I am clinical partner in the EU-financed BabyLux project, developing and testing a NIRS based prototype device combining measurement of tissue oxygenation and blood flow

What do we already do?

Acta Paediatrica Oct 2012:

Term MRI for small preterm babies: do parents really want to know and why has nobody asked them?

Acta Paediatrica Oct 2012:

Trying to predict the future of ex-preterm infants: who benefits from a brain MRI at term?
the ‘bias of knowledge’

vs

the right not to know

75% correctly predicted  \( (p = 0.02) \)

- the brain injury that will impair development has already happened – or at least started – by 24 hours of age

- aEEG may be used to select infants for interventions

- it cannot yet be said that aEEG improved outcome
Attempting to come in before damage happens

Inadvertent hyperventilation
- hypocapnia
- reduced CBF
- brain hypoxia-ischaemia
- brain injury
- psychomotor deficit

An example of a brain damaging process involving cerebral hypoxia-ischaemia

A way to intervene

Inadvertent hyperventilation
- hypocapnia
- reduced CBF
- brain hypoxia-ischaemia
- brain injury
- psychomotor deficit

respiratory volume control?

A way to individualise

Inadvertent hyperventilation
- hypocapnia
- reduced CBF
- brain hypoxia-ischaemia
- brain injury
- psychomotor deficit

transcutaneous pCO2?

Doppler ultrasound?

Individually at a deeper pathophysiological level

Inadvertent hyperventilation
- hypocapnia
- reduced CBF
- brain hypoxia-ischaemia
- brain injury
- psychomotor deficit

cerebral oximetry?

Getting even closer to the problem
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Inadvertent hyperventilation
hypocapnia
reduced CBF
brain hypoxia-ischaemia
low blood pressure
low cardiac output
persistent duct
brain injury
psychomotor deficit

- covering multiple pathways

Adult mouse cortex:
Hypoxia in the 'lethal corners'

Near infrared tissue oximetry:

△O2Hb, △HHb (μmol/l)
StO2 (0-100%)

A small animal model
But NIRS is possible
What will happen if we add nitrogen to the inspired air?

Measuring cerebro-venous oxygen saturation by NIRS

9 normal term babies (Buchvald et al. Biol Neonat 1999)
SvO2: ~65%

41 normal preterm babies (Wardle et al. JCBFM 2000)
SvO2: ~68%
(normal human adult: SvO2: ~65%)

\[ \text{VO}_2 = \text{CBF} \times (\text{Ca} - \text{Cv}) \]
\[ \text{Cv} = \text{Hb} \times \text{SvO2} \]
\[ \text{OEF} = \frac{(\text{SaO2} - \text{SvO2})}{\text{SaO2}} \]

Oxygen extraction and CBF are inversely related

(CMRO2 = CBF x OEF x Hb)

Oxygen extraction and CBF are inversely related

October 3, 2015
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Spatially Resolved Spectroscopy

\[ \text{StO2} = k \times \text{O2Hb} / k \times (\text{O2Hb} + \text{HHb}) \]

Repeatability (precision) = 5.2% 

(Sorensen J Biomed Opt 2006)

Cerebral oxygenation in term infants after CS from min 3 to 10 min


- but SRS oximeters are CE-marked and marketed
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Time-resolved near-infrared spectroscopy

The effect of source-detector distance

The effect of scattering

The effect of absorption

Real life

Putting NIRS TRS (oxygenation) and flow (DCS) into one device
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The phase-II randomised controlled trial

- cerebral oximetry (visible screen)
  + treatment guideline
  + standard care
- vs
- cerebral oximetry (black screen)
  + standard care

In extremely preterm infants during the first 72 hours of life
Infants enrolled from June 2012 to Dec 2013
Clinical trials number: NCT01590316

Case 1
Twins, GA 27 wks, both <500 g
No surfactant
CPAP, a bit of oxygen
ECHO: ductus < 1 mm
Moving, taking 1-2 ml milk, diuresis
MABP good (30-45 mmHg)
CRT fine
cStO2 in twin A 75% in twin B 60%
Now at 30 hrs of age cStO2 has dropped to 50% in twin B
Do something?

Case 2
GA 26 wks, 850 g
INSURE
CPAP, a bit of oxygen
Apneas
Murmur
Moving, diuresis
MABP 36 mmHg
CRT OK
cStO2 is low, some of the time below 55%
Born on a Friday, ECHO Monday showed ductus 3 mm

Case 3
GA 25 wks, 780 g
No surfactant
CPAP, in air
cStO2 been 60-70%, now at 60 hrs 85-90%
BS = 3.1 mmol/l
Do something?

Critical questions for phase-II:
- Will clinical staff use the treatment guideline?
- Do we possess the means to influence StO2?
- Will parents / staff accept the blind screen? (yes)

SafeBoosC-II

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

N = 86
GA = 26.6 wks
P < 0.001

N = 80
GA = 26.6 wks

(BMJ. Jan 5 2015)
Well, it may work – but does it help?

It may reduce the burden of hypo- and hyperoxia – but does it improve neurodevelopmental outcome?

(the concept of clinically relevant outcomes)