Near-infrared spectroscopic cerebral oxygenation reading in neonates and infants is associated with central venous oxygen saturation

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Summary

Background: The aim of the study was to elucidate easily determinable laboratory and vital parameters in clinical practice to explain variability of near-infrared spectroscopic cerebral oxygenation readings in critically ill newborns and infants using the NIRO 300 spectrometer.

Methods: Near-infrared spectroscopy (NIRS) cerebral tissue oxygenation index (cTOI) was measured on the forehead of critically ill neonates and infants with existing arterial and/or central venous access. We recorded patient characteristics and simultaneously determined sedation state, hemodynamic, respiratory and laboratory data, such as arterial blood gas analysis, electrolytes, hemoglobin and arterial lactate concentration, blood glucose and central venous oxygen saturation. Data were compared using linear, multiple and forward stepwise regression analysis (P < 0.05).

Results: A total of 155 neonates and infants aged from 0 to 365 days (median 12 days) were studied. Cerebral tissue oxygenation index (cTOI) values ranged from 32.1 to 91.0% (60.5 ± 11.5%). Simple linear regression analysis revealed significant associations between cTOI and arterial oxygen saturation (r = 0.254, P = 0.001), transcutaneously measured arterial oxygen saturation (r = 0.320, P £ 0.0001), central venous oxygen saturation (r = 0.489, P < 0.0001), arteriovenous oxygen extraction (r = 0.445, P < 0.0001) and presence of a cardiac shunt (r = 0.250, P = 0.024). Multiple regression analysis and forward stepwise regression revealed two independent, significant predictors for cTOI, namely SvO2 (P < 0.0001) and presence or absence of a cardiac shunt (P = 0.003). SvO2 alone explained 23.9% of the variability of cTOI. The addition of the variable ‘cardiac shunt’ improved the model to 33%.

Conclusions: Based on our study results cerebral tissue oxygenation readings by the NIRO 300 near-infrared spectrometer is influenced by central venous oxygen saturation, which partially explains intersubject variability of NIRS cerebral oxygenation readings.

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Introduction

Near-infrared spectroscopy (NIRS) is a well described, noninvasive technique which allows indirect monitoring of tissue oxygenation (1,2). The technique depends on the transparency of biological tissue to light in the near-infrared region and also on the fact that the main chromophores, oxygenated and deoxygenated hemoglobin, absorb near-infrared light depending on the oxygenation state and changes in hemoglobin oxygenation and can be quantified using the modified Lambert-Beer Law (2). Cerebral near-infrared spectroscopy has been extensively evaluated in preterm and term neonates, cardiac surgery, neurosurgery and head trauma regarding cerebral perfusion and is generally believed to be a cerebral oxygenation monitor (3–10). Most studies report on relative changes of the infrared signal due to unknown tissue specific absorption characteristics.

Newer generations of cerebral oximeters, such as the INVOS 5100 (INVOS 5100; Somanetics, Troy, MI, USA) or the NIRO 300 (NIRO 300; Hamamatsu Photonics, Hamamatsu City, Japan), allow additional measurement of a quantitative value of cerebral tissue oxygenation (11).

However, some doubts arise concerning the accuracy of the measured values, since a large variability in cerebral tissue oxygenation reading has been found in otherwise well oxygenated and hemodynamic stable normal adults, children and neonates, not correlating with SpO2 or other variables (8,11–13). Several technical and methodological factors influencing NIRS cerebral tissue oxygenation reading have been suggested such as changes in extracranial blood flow, intraindividual absorption differences and positioning of the probes (11,14,15).

The aim of the present investigation was to elucidate easily determinable clinical and laboratory factors in clinical practice to explain variability of near-infrared spectroscopic oxygenation readings in critically ill newborns and infants using the NIRO 300 spectrometer.

Material and methods

With approval of the Hospital Ethical Committee and informed parental consent, we investigated in a prospective, observational, clinical study newborns and infants up to 1 year of age admitted to the intensive care unit of the University Children’s Hospital of Zurich. Patients with hypoxic, metabolic or traumatic brain injury were excluded from the study in order to avoid any alteration in cerebral oxygenation reading caused by locally compromised cerebral perfusion or oxygenation (cerebral edema, hematoma, increased intracranial pressure).

The NIRO 300 (Hamamatsu Photonics) is a two-channel, four wavelength near-infrared photometer based on spatially resolved spectroscopy (16,17). The NIRO 300 light emitter optode provides laser light operating at 775, 810, 847 and 919 nm and the detector optode placed several centimeters from the emitter probe, carries three spatially separated detectors (three-segment photodiode chip) within one detector probe (11). Multidistance measurement of light attenuation by the three-segment photodiode chip allows the calculation of a quantitative tissue oxygenation index (TOI) representing the ratio of oxygenated hemoglobin (HbO2) to total hemoglobin (HbO2 + HHb). Emitter and receiver optodes were inserted into a commercially available nontransparent, soft probe holder (Hamamatsu Photonics; Probe Holder S: A 7928) to provide a constant interoptode distance of 50 mm and to shield the optodes from ambient light. In each patient, the light emitter optode was applied to the skin of the scalp on a line 1 cm above the supraorbital ridge and 1 cm lateral to the mid-sagittal plane on either the right or left forehead and the receiver optode was placed 50 mm lateral to the transmitting optode. This placement ensures measurement of cerebral TOI (cTOI) from frontoparietal brain tissue and avoids the sagittal sinus. The optodes were secured to the head with a flexible, self-adhesive bandage wrapped around the head. The NIRS emitter and receiver
probes were connected to a precalibrated measuring unit which was attached to the NIRO 300 device. After confirming proper signal quality by means of the initialization (probe check) procedure, NIRS measurements were performed at a sample rate of every 2 s. After obtaining steady-state cTOI values for 10 min, cerebral TOI values were recorded. The cTOI values were calculated as the median value of 30 measurements (1 min) during the blood sampling for blood gas analysis and recording the patient’s hemodynamic, respiratory and sedation data.

Patient characteristics such as age, weight, length, head circumference, hemodynamic data [heart rate (HR), mean arterial pressure (MAP), CVP] and respiratory parameters (pulse-oximetric arterial oxygen saturation (SpO₂), fractional inspiratory oxygen concentration (FiO₂), respiratory rate (RR), peak inspiratory pressure (PIP), positive endexpiratory pressure (PEEP) were recorded from bedside monitoring (Solar 8000M; Marquette, Milwaukee, WI, USA) and respirator (EVITA 4; Neo-Flow, Dräger, Lubeck, Germany). In addition, sedation state [deeply sedated (1), slightly sedated, tired (2), awake and calm (3), agitation (4)] was assessed and noted. Arterial blood was simultaneously taken and analysed for pH, PaCO₂, arterial oxygen saturation (SaO₂), arterial base excess (aBE), PaO₂, sodium, potassium, ionized calcium, blood glucose and lactate concentration (ABL-700; Radiometer, Copenhagen, Denmark). Central venous oxygen saturation (SvO₂) was measured oximetrically (Oximeter OSM 3; Radiometer or ABL-700; Radiometer). The position of the central venous catheter tip (right atrium, superior caval vein, inferior caval vein) was determined by chest radiography. Presence of an intracardiac left to right shunt was recorded from echocardiographic findings.

Statistical analysis

Data are presented as mean ± SD and/or median (range and interquartile range) as appropriate. Pearson’s correlation coefficients and P-values from linear regression analysis were calculated between cTOI values and patient characteristics (age, weight, length, head circumference), sedation state and hemodynamic, respiratory and laboratory data (continuous and categorical variables). Variables which correlated reasonably well with cTOI in the simple regression analyses (P < 0.1) were incorporated in a multiple regression equation with cTOI as the dependent variable. The effects of these potentially explanatory variables were also tested by forward stepwise regression. Potential confounding of the possible relations between cTOI values and continuous variables by categorical parameters [sex, sedation state, side of measurement (left or right), sensor 1 or sensor 2, mechanical ventilation or spontaneous ventilation, high frequency oscillation ventilation, and presence or absence of an intracardiac shunt] were checked by analysis of covariance. A P-value of <0.05 was considered to be statistically significant.

Results

A total of 155 critically ill neonates and infants (64 girls, 91 boys), aged from 0 to 365 days (median 12 days) were studied. A total of 123 patients were intubated and received mechanical ventilation. Demographic data are presented in Table 1.

The cTOI values ranged from 32.1 to 91.0% (60.5 ± 11.5%) in a group of neonates and infants with large ranges in hemodynamic, respiratory, and laboratory parameters (Table 2). Simple linear regression analysis revealed significant associations between cTOI and arterial oxygen saturation (r = 0.254, P = 0.001), central venous oxygen saturation (r = 0.489, P ≤ 0.0001), transcutaneously measured arterial oxygen saturation (r = 0.32, P ≤ 0.0001), arteriovenous oxygen extraction (r = 0.445, P < 0.0001) (Figure 1) and presence or absence of an intracardiac shunt (r = 0.250, P = 0.024). Correlation between cTOI and SvO₂ values was higher

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (range)</th>
<th>Interquartile range</th>
<th>Pearson r</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (days)</td>
<td>12.0 (0–365)</td>
<td>3–109</td>
<td>0.042</td>
<td>0.605</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>38.4 (27.0–42.0)</td>
<td>36.9–39.9</td>
<td>0.092</td>
<td>0.269</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>3.5 (1.3–12.0)</td>
<td>2.9–4.7</td>
<td>0.006</td>
<td>0.942</td>
</tr>
<tr>
<td>Body length (cm)</td>
<td>51.0 (37.0–82.0)</td>
<td>47.5–55.0</td>
<td>0.049</td>
<td>0.591</td>
</tr>
<tr>
<td>Head circumference (cm)</td>
<td>35.0 (28.0–52.0)</td>
<td>33.5–38.0</td>
<td>0.107</td>
<td>0.255</td>
</tr>
</tbody>
</table>

Table 1

Patient characteristics (n = 155) and their relation to cerebral tissue oxygenation index.
Table 2
Laboratory, hemodynamic and respiratory parameters (n = 155 Patients)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Units</th>
<th>Mean ± SD</th>
<th>Median (range; IQR)</th>
<th>r</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>cTOI</td>
<td>%</td>
<td>60.5 ± 11.5</td>
<td>60 (32.1–91.0; 52.1–66.3)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Temperature</td>
<td>°C</td>
<td>37.2 ± 0.6</td>
<td>37.1 (34.4–39.1; 36.8–37.5)</td>
<td>0.122</td>
<td>0.174</td>
</tr>
<tr>
<td>SpO2</td>
<td>%</td>
<td>91.8 ± 6.4</td>
<td>94 (66–100; 90–66)</td>
<td>0.320</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>apH</td>
<td>Units</td>
<td>7.39 ± 0.1</td>
<td>7.39 (7.22–7.58; 7.35–7.43)</td>
<td>0.133</td>
<td>0.121</td>
</tr>
<tr>
<td>PaCO2</td>
<td>kPa</td>
<td>5.7 ± 1.2</td>
<td>5.9 (2.0–12.5; 5.0–6.3)</td>
<td>0.046</td>
<td>0.588</td>
</tr>
<tr>
<td>Arterial base excess</td>
<td>mmol⁻¹</td>
<td>0.8 ± 4.3</td>
<td>0.7 (–15.1–14.2; –23–33.3)</td>
<td>0.076</td>
<td>0.378</td>
</tr>
<tr>
<td>PaO2</td>
<td>kPa</td>
<td>8.2 ± 2.8</td>
<td>7.5 (3.1–17.9; 6–9.3)</td>
<td>0.112</td>
<td>0.215</td>
</tr>
<tr>
<td>SaO2</td>
<td>%</td>
<td>91.3 ± 7.2</td>
<td>93.1 (58.4–98.4; 96–88.4)</td>
<td>0.254</td>
<td>0.001</td>
</tr>
<tr>
<td>Hemoglobin concentration</td>
<td>g⁻¹</td>
<td>130.1 ± 27.8</td>
<td>127.0 (53–218; 110–149)</td>
<td>0.087</td>
<td>0.280</td>
</tr>
<tr>
<td>SvO2 (n = 85)</td>
<td>%</td>
<td>68.8 ± 9.4</td>
<td>69.0 (40.0–85.4; 63–75.8)</td>
<td>0.489</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SvO2 right atrium (n = 42)</td>
<td>%</td>
<td>69.9 ± 10.1</td>
<td>70.0 (40.0–85.4; 63.3–78.9)</td>
<td>0.284</td>
<td>0.084</td>
</tr>
<tr>
<td>SvO2 vena cava inferior (n = 15)</td>
<td>%</td>
<td>66.5 ± 12.7</td>
<td>65.0 (49.0–83.0; 56.0–79.1)</td>
<td>0.814</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SvO2 vena cava superior (n = 28)</td>
<td>%</td>
<td>68.3 ± 6.2</td>
<td>68.5 (57.0–81.9; 63.5–72.7)</td>
<td>0.640</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arteriovenous oxygen extraction (n = 85)</td>
<td>%</td>
<td>23.5 ± 13.1</td>
<td>24.9 (10.9–67.0; 17.4–30.0)</td>
<td>0.445</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sodium</td>
<td>mmol⁻¹</td>
<td>138.0 ± 4.3</td>
<td>138.0 (120–150; 135–141.0)</td>
<td>0.078</td>
<td>0.390</td>
</tr>
<tr>
<td>Potassium</td>
<td>mmol⁻¹</td>
<td>4.0 ± 0.7</td>
<td>3.9 (3.1–6.1; 3.6–4.3)</td>
<td>0.096</td>
<td>0.294</td>
</tr>
<tr>
<td>Ionised calcium</td>
<td>mmol⁻¹</td>
<td>1.2 ± 0.1</td>
<td>1.2 (0.9–1.5; 1.1–1.3)</td>
<td>0.102</td>
<td>0.262</td>
</tr>
<tr>
<td>Blood glucose</td>
<td>mmol⁻¹</td>
<td>4.9 ± 1.3</td>
<td>4.7 (2.9–4.9; 4.1–5.6)</td>
<td>0.124</td>
<td>0.240</td>
</tr>
<tr>
<td>Arterial lactate concentration</td>
<td>mmol⁻¹</td>
<td>2.6 ± 2.0</td>
<td>2.1 (0.6–12.1; 1.6–2.8)</td>
<td>0.014</td>
<td>0.902</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>mmHg</td>
<td>52.5 ± 9.9</td>
<td>51.0 (28–84; 45–59)</td>
<td>0.017</td>
<td>0.831</td>
</tr>
<tr>
<td>Heart rate</td>
<td>b⁻¹</td>
<td>142.0 ± 20.1</td>
<td>140 (99–195; 129–157)</td>
<td>0.004</td>
<td>0.962</td>
</tr>
<tr>
<td>Central venous pressure (n = 85)</td>
<td>mmHg</td>
<td>7.5 ± 4.1</td>
<td>7.0 (1–24; 4–9)</td>
<td>0.120</td>
<td>0.258</td>
</tr>
<tr>
<td>FiO2 (n = 123)</td>
<td>%</td>
<td>31.7 ± 14.6</td>
<td>28 (21–100; 21–36)</td>
<td>0.003</td>
<td>0.968</td>
</tr>
<tr>
<td>Peak inspiratory pressure (n = 123)</td>
<td>cmH2O</td>
<td>21.0 ± 3.0</td>
<td>20 (16–32; 19.0–22.5)</td>
<td>0.026</td>
<td>0.785</td>
</tr>
<tr>
<td>PEEP (n = 123)</td>
<td>cmH2O</td>
<td>5.4 ± 3.0</td>
<td>4.0 (3–22; 4–6)</td>
<td>0.014</td>
<td>0.880</td>
</tr>
</tbody>
</table>

P-values and Pearson correlation coefficients are given for the relation between the respective variable and cerebral tissue oxygenation index (cTOI).

Discussion

This study evaluated factors, easily determinable in clinical practice, which influence cTOI values in neonates and infants without known cerebral disease or trauma. The main finding was that central venous oxygen saturation and the presence or absence of an intracardiac shunt explained one-third of intersubject variation of cTOI values measured by the NICO 300 spectrometer.

Near-infrared spectroscopy measures oxygenation state in the underlying tissue and reflects a mixture of intravascular oxygenated/deoxygenated venous, arterial and capillary hemoglobin in a proportion of approximately 75 : 20 : 5 (9,18,19). Because the venous portion predominantly determines near-infrared spectroscopic measurement of cerebral oxygenation, cTOI represents a balance between oxygen delivery and oxygen consumption rather than a reflection of tissue oxygenation itself. This has been demonstrated by different authors reporting on a close intraindividual relation between changes in cerebral blood flow and jugular venous O₂ saturation and changes in cTOI (10,20,21). Even more, cerebral near-infrared spectroscopy has been used to estimate jugular venous oxygen saturation (22,23).

when the central venous catheter was placed with the tip in the inferior (n = 15; r = 0.814, P < 0.001) or superior caval vein (n = 28; r = 0.640, P < 0.001) and lower when catheters were placed with the tip in the right atrium (n = 42; r = 0.284, P = 0.084) (Figure 2).

Further categorical parameters [sex, sedation state, side of measurement (left or right), sensor 1 or sensor 2, mechanical ventilation or spontaneous ventilation, high frequency oscillation ventilation] did not reveal statistically significant influence on cTOI values.

Multiple regression analysis and forward stepwise regression revealed two independent, significant predictors for cTOI, namely SvO₂ (P < 0.0001) and presence or absence of an intracardiac shunt (P = 0.003). SvO₂ explained 23.9% of the variability of cTOI. The addition of the variable ‘intracardiac shunt’ improved the model to 33%.

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Our results indicate that cTOI is associated with global hemodynamic function, as indicated by central venous oxygen saturation and the presence of intracardiac left-to-right shunt resulting in reduced systemic outflow. Potential explanation for the better correlation between cTOI and venous oxygen saturation in the superior and the inferior vena cava compared with those obtained from the right atrium are left-to-right shunt through a patent foramen ovale in neonates, patients with cardiac shunts and admixture of coronary sinus venous blood into the right atrium. Our results are similar to the findings with a NIRS optode placed over the palpable liver in infants and children, in whom the observed variance of single point transcutaneously measured near-infrared spectroscopic liver tissue oxygenation was explained mainly by central venous oxygen saturation (51%) (24). Similarly, Bay-Hansen et al. reported on a close relation between peripheral TOI values and cooximetry of central venous blood in neonates, implicating that NIRS oxygenation reading is associated with central venous oxygen saturation (25).

Central venous saturations are a result of cardiac output and thus correlate with the cerebral NIRS values since a large portion of the cardiac output is directed to the cerebral circulation. It has also been suggested, that venous oxygen saturation in the extracerebral tissue affects cTOI measurement (17). Extracerebral tissues (bone, scalp) have a profound influence on NIRS light transmission. They may act as an optical ‘channel’ distorting the behavior of NIR light in the human head (26,27). The NIRS signal penetrates deeper when the interoptode distance is widened, thereby reducing extracranial influences on cerebral oximetry. Germon et al. recommended a

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Figure 1
Linear regression plots are presented for the comparison of pulse-oximetric arterial oxygen saturation (SpO₂), oximetrically measured arterial (SaO₂) and central venous (SvO₂) oxygen saturation and arteriovenous oxygenation extraction (ERO₂) (x-axis) with near-infrared spectroscopic measured cerebral tissue oxygenation index (cTOI) measured on the forehead of neonates and infants (y-axis).
distance of at least 48 mm, as used in our study (50 mm) (28).

The influence of central venous oxygen saturation on NIRS cerebral tissue oxygenation readings partially explains the constant finding of large ranges of cTOI values reported in humans with normal arterial oxygen saturation. Using the INVOS 3100 Misra et al. found an average rSO2 of 67.2 ± 8.4% as did Yoshitani et al. (INVOS 4100: rSO2 of 66 ± 8% and NIRO 300 cTOI of 66 ± 7%) (8,12). In newborn premature infants cTOI confidence intervals of 54–65.7, 61.9–82.3 and 67.8–80.1% were found during the first 3 days of life, not correlating to SpO2 and other physiological variables (10). The latter finding can be explained by decreasing cardiac shunts in this life period with rise of systemic cardiac output and central venous oxygen saturation respectively.

Variance of cTOI values in our study was explained only by one-third by hemodynamic parameters. The varying cTOI – SvO2 differences are likely to be caused by interindividual differences in absorption properties and probe placement (8,11,26,27). Since these factors can be suggested to remain constant during continuous NIRS cerebral tissue oxygenation reading in a single patient, cTOI may become helpful to detect changes from an individual base line for SvO2 trend monitoring, which has to be investigated by further clinical studies.

Our findings further implicate that tissue oxygenation monitoring by near-infrared spectrometers in any organ of interest (brain, splanchnic, liver, muscle, heart) should include a second site of measurement, in order to exclude the contribution of changing global hemodynamic function. This has recently been applied by Fortune et al., who reported

Figure 2
Linear regression plots for the comparison of central venous oxygen saturation (x-axis) taken from all central venous catheters and samples taken from central venous lines with tip in the right atrium, in the superior vena cava and in the inferior vena cava with near-infrared spectroscopic measured cerebral tissue oxygenation index (cTOI) measured on the forehead of neonates and infants (y-axis).
on the cerebrospinalin oxygenation ratio (CSOR),
concerning the relation between NIRS measurement
over the forehead and below the umbilicus (29).
They demonstrated that CSOR was highly sensitive
for splanchnic ischemia in neonates. Falls and rises
in regional perfusion can be distinguished from
systemic hemodynamic fluctuations using the TOI
ratio between the two sites of measurements.

A limitation of this study is the lack of simultaneous
jugular venous oxygen saturation measurement in the
newborns and infants studied. However, in critically
ill new-borns and infants jugular venous oxygen
saturation monitoring is not easily determinable in
clinical practice. Second, this study investigated only
interindividual single point measurements of cTOI
and clinical and laboratory parameters. Further
clinical investigations focusing on the usefulness of
NIRS cerebral oxygenation reading as a SvO2 trend
monitor should include intraindividual repeated or
continuous measurements of cTOI, SvO2 and other
hemodynamic variables.

In conclusion, based on our study results cerebral
tissue oxygenation reading by the NIRO 300 near-
infrared spectrometer is influenced by central
venous oxygen saturation, which partially explains
the intersubject variability of NIRS cerebral oxygenation
reading. Actually, the presented NIRS technique cannot be used in clinical practice to predict
SvO2 from a single point assessment. Further clinical
studies are required to explore if NIRS cerebral oxygenation reading may become a useful tool to
detect changes from an individual base line for SvO2
trend monitoring.

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References


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