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Feasibility of long-term cerebral and peripheral regional tissue oxygen saturation measurements

J Schmitz, G Pichler, B Schwaberger, B Urlesberger, N Baik and C Binder

Department of Paediatrics, Division of Neonatology, Medical University of Graz, Graz, Austria
E-mail: corinna.binder@medunigraz.at

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Abstract
The aim of this study was to analyse the feasibility of long-term measurements of cerebral (crSO2) and peripheral (prSO2) regional tissue oxygen saturation on the first day of life by determining the amount of artefacts and their influence on rSO2. Near infrared spectroscopy (NIRS) measurements were performed fronto-parietal left (crSO2) and on the right forearm (prSO2). Arterial oxygen saturation (SpO2) was measured by pulse oximetry on the right wrist. Three criteria (C) were defined to identify artefacts (C1: missing values, C2: rSO2 jumping >15%, C3: rSO2 ≥ SpO2). The number of artefacts as a percentage of measurement time and mean rSO2 was calculated after the introduction of each criterion. Measurements were performed in 40 neonates. The number of artefacts in crSO2 measurements was similar after introduction of C1 (7.37 ± 4.64%) and after introduction of all criteria (8.89 ± 4.59%). The number of artefacts in prSO2 measurements after introduction of C1 was 10.83 ± 4.21%, and after introduction of all criteria significantly higher with 17.78 ± 4.27%. After introduction of C1, further criteria did not significantly change rSO2: crSO2 (78.6 ± 1.3% versus 78.5 ± 1.2%) and prSO2 (83.7 ± 0.9% versus 83.5 ± 0.9%). In conclusion, long-term NIRS measurements of crSO2 and prSO2 are feasible, since most artefacts are due to missing values and therefore easy to recognize.

Keywords: near infrared spectroscopy, neonate, artefacts, peripheral, cerebral, feasibility
List of abbreviations
aEEG  amplitude-integrated electroencephalography
C criterion
cm centimetre
crSO2 cerebral regional tissue oxygen saturation
g gram
h hour
mm millimetre
n number
NIRS near infrared spectroscopy
nm nanometre
prSO2 peripheral regional tissue oxygen saturation
rSO2 regional tissue oxygen saturation
s seconds
SD standard deviation
SpO2 arterial oxygen saturation

1. Introduction

While advances in medical care have improved the survival of preterm neonates, neurodevelopmental problems still persist (Duerden et al 2013). In particular, preterm neonates are prone to primary brain injury and disturbances in brain maturation (Duerden et al 2013). A large number of neonates survive with neurodevelopmental disabilities, such as major cognitive deficits and motor disability (Volpe 2009). Some long-term consequences are still unclear and give cause for concern (Hack 2006).

Besides clinical observation, non-invasive monitoring including pulse oximetry, electrocardiograms, oscillometric blood pressure devices, electroencephalograms and transcutaneous pCO2 measurement sensors are routinely used in neonatal care units. Since the brain is such a vulnerable organ, additional monitoring of the brain might be beneficial. Near infrared spectroscopy (NIRS) enables monitoring of cerebral oxygenation and has the potential to become a routine diagnostic tool in the assessment of sick neonates (Wolf and Greisen 2009). It was first described by Jöbsis (1977) and is a continuous and non-invasive method to measure the regional tissue oxygen saturation (rSO2) in different regions such as cerebral tissue or peripheral muscle tissue. Most studies on cerebral oxygenation with NIRS were done in neonates with either the NIRO (Hamamatsu, Japan) (Dullenkopf et al 2005), INVOS (Somanetics, Troy, MI, USA) (Dullenkopf et al 2003) or FORE-SIGHT (CAS Medical Systems, Bradford, CT, USA) (Fenik and Rais-Bahrami 2009). Recently, we published several studies concerning peripheral muscle oxygenation in term and preterm neonates (Pichler et al 2012, Táx et al 2013).

An important question in long-term measurements (24 h and more) is the appearance of artefacts and their influence on the measurement results over time. No data are available until now with regard to the incidence of artefacts in NIRS measurements. Therefore, the aim of this study was to analyse the feasibility of long-term NIRS measurements of cerebral (crSO2) and peripheral (prSO2) regional tissue oxygen saturation on the first day of life in preterm and term neonates by determining the number of artefacts and their influence on rSO2.
2. Methods

2.1. Patients

This prospective study was conducted between August 2011 and August 2012 at the Department of Paediatrics, Medical University of Graz. All neonates were born at the Department of Obstetrics and Gynaecology and were admitted to the Neonatal Intensive Care Unit of the Department of Paediatrics, Medical University of Graz, Austria. Preterm neonates >33 weeks of gestation and term neonates were included in the study. Neonates with congenital malformations were excluded from the study. No other specific entry criteria were defined. Written parental informed consent was obtained before the start of the measurements. This study was approved by the regional Committee on Biomedical Research Ethics.

2.2. Instruments

The cerebral and peripheral NIRS measurements were performed with the INVOS 5100 Cerebral/Somatic Oximeter Monitor (Somanetics Corporation, Troy, MI, USA) using the Neonatal OxyAlert™ NIR Sensors. The INVOS 5100 uses a spatially resolved technique that enables non-invasive continuous measurement of regional tissue oxygen saturation (rSO₂), which is expressed as the percentage of oxygenated haemoglobin. The sensors consist of one light-emitting diode and two detectors, which are placed at two different distances from the light diode. The detectors are placed at distances of 30 and 40 mm from the emitting diode. The two wavelengths used are 730 and 810 nm. The sampling time for rSO₂ was 8 s. The arterial oxygen saturation (SpO₂) was measured by pulse oximetry using the IntellVue MP30/X2 monitor (Philips, Amsterdam, The Netherlands). The multichannel alpha-trace digital system (Alpha-Trace Medical Systems, Vienna, Austria) stored all variables for subsequent analysis.

2.3. Procedure

Measurements were performed while the neonate was lying in an incubator. Two NIRS sensors were attached to the infant, one on the left fronto-parietal forehead to monitor crSO₂ and the other on the right forearm to monitor prSO₂. The sensor on the forehead was secured with an elastic bandage and the sensor on the right forearm was attached with an adhesive tape, without applying circular pressure. The measurements started in the first 6 h after birth and were performed over a period of 24 h. The sensors were replaced every 6 h to prevent any possible damage to the skin. Furthermore a pulse oximeter probe was placed around the neonates’ ipsilateral wrist to measure SpO₂.

2.4. Data analysis

After transferring NIRS and SpO₂ data into Excel 2007 (Microsoft Corporation, Redmond, CA, USA) the NIRS data were analysed for periods with artefacts. The following three criteria were defined to identify artefacts.

Criterion 1 (C1): missing rSO₂ values due to measurement failure because of movement artefacts or displacement of the sensors.

Criterion 2 (C2): abrupt changes in rSO₂ values exceeding a range of ±15% between two values (8 s) with abrupt jumping back to the original level within 1 min were defined as artefacts. As tissue oxygenation includes the arterial, capillary and venous compartment it seems unlikely that changes exceeding ±15% within seconds represent a physiological...
phenomenon, but are strongly suspected to be due to small dis- and replacement of sensors. Changes in a gradual manner over several values were not defined as artefacts.

Criterion 3 (C3): the rSO2 is made up of venous, arterial and capillary oxygen saturation (Watzman et al 2000). As a consequence the SpO2 value should always exceed the corresponding rSO2 value. All rSO2 values that were higher or equal to SpO2 were considered as not physiological and were thus defined as artefacts. In each minute mean rSO2 was compared to mean SpO2. If the rSO2 value exceeded the corresponding SpO2 value, all the following rSO2 values were considered to be artefacts, up to the next rSO2 value that was lower than the corresponding SpO2.

To analyse the number of artefacts and influence of artefacts on the mean rSO2 values, two NIRS datasets were generated. Dataset 1 included all measured data after the introduction of criterion 1. Dataset 2 also excluded rSO2 values due to criteria 2 and 3.

2.5. Statistical analysis

To analyse the number of artefacts, the percentage of time of artefacts after each criterion was calculated in each neonate. Mean crSO2 and prSO2 values were calculated for the 24 h measurement period.

ANOVA was used to compare rSO2 values and the number of artefacts between and within datasets. A \( p \)-value < 0.05 was considered to be statistically significant. Data are presented as mean ± SD. The statistical analysis was performed with IBM SPSS Statistics 20 (IBM, Armonk, NY, USA).

3. Results

Cerebral and peripheral measurements were performed in 31 preterm and 9 term neonates with a male/female ratio of 22:18. Demographic data of all neonates are presented in table 1.

In prSO2 measurements the number of artefacts was significantly higher than in crSO2 measurements (table 2). In total 8.89 ± 4.59% of all crSO2 values and 17.78 ± 4.27% of prSO2 values failed at least one of the criteria and had to be eliminated. Criterion 1 (C1) was responsible for the highest number of measurement failures. While the introduction of criteria 2 and 3 caused no significant further increase in the number of artefacts for cerebral NIRS measurements (\( p = 0.26 \)), in the peripheral NIRS measurements the number of artefacts increased significantly after the introduction of criteria 2 and 3 (\( p = < 0.01 \)). In particular, artefacts due to criterion 3 occurred more frequently in peripheral than cerebral measurements. Nevertheless, neither mean crSO2 nor mean prSO2 values changed significantly after the
Table 2. Mean number of artefacts (percentage of total measurement time) in cerebral and peripheral measurements.

<table>
<thead>
<tr>
<th>Artefacts (%)</th>
<th>crSO₂</th>
<th>prSO₂</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criterion 1 (missing measurement)</td>
<td>7.37 ± 4.64</td>
<td>10.83 ± 4.21</td>
<td>0.01</td>
</tr>
<tr>
<td>Criterion 2 (rSO₂ jumping)</td>
<td>0.03 ± 0.03</td>
<td>0.07 ± 0.05</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Criterion 3 (rSO₂ &gt; SpO₂)</td>
<td>1.50 ± 0.80</td>
<td>6.89 ± 1.65</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>All criteria</td>
<td>8.89 ± 4.59</td>
<td>17.78 ± 4.27</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Table 3. Mean NIRS data during the 24 h measurement period in preterm and term neonates after the introduction of the quality criteria.

<table>
<thead>
<tr>
<th></th>
<th>crSO₂</th>
<th>prSO₂</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criterion 1</td>
<td>78.6 ± 1.3</td>
<td>83.7 ± 0.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>All criteria</td>
<td>78.5 ± 1.2</td>
<td>83.5 ± 0.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>p-value</td>
<td>0.90</td>
<td>0.35</td>
<td></td>
</tr>
</tbody>
</table>

Introduction of criteria 2 and 3 (compared to criterion 1). Throughout the measurements, prSO₂ values were significantly higher than crSO₂ values. Mean rSO₂ data for all patients during the 24 h measurement period are presented in table 3.

4. Discussion

In the present study, we were able to demonstrate that, in neonates, up to 8.89 ± 4.59% of the cerebral measurements and up to 17.78 ± 4.27% of the peripheral measurements were corrupted by artefacts. To our knowledge this is the first study determining the number of artefacts in long-term cerebral and peripheral NIRS measurements.

Cerebral oxygen saturation has been evaluated in several studies in neonates (Dullenkopf et al 2003, Wijbenka et al 2011, Lemmers and Van Bel 2009). With 78.6 ± 1.3% our study showed similar crSO₂ values in comparison to other NIRS studies. Wijbenka et al (2011) described crSO₂ in preterm and term neonates on the first day of life around 80% (using the INVOS 5100 with the neonatal sensor). Dullenkopf et al (2003) reported mean values of 84.0 ± 7.4% in children (using the INVOS 5100 with the paediatric sensor). Lemmers and Van Bel (2009) observed a mean crSO₂ of 68 ± 9.2% on the left forehead of preterm neonates in the first three days of life (using the INVOS 5100 with the adult sensor). It has been shown that the INVOS 5100 paediatric sensor measures rSO₂ around 10% higher than the adult sensor under identical conditions (Dullenkopf et al 2003), whereas no difference could be seen between the neonatal and paediatric sensor (Morris et al 2012). Our peripheral measurements also showed similar values to the ones reported previously in other studies (Pocivalnik et al 2011, Hyttel-Sorensen et al 2011). Pocivalnik et al (2011) measured a prSO₂ of 82.7 ± 7.6% in term and preterm neonates. Hyttel-Sorensen et al (2011) measured a mean prSO₂ of 70.1 ± 6.7% on the forearm of adults.

There is a considerable amount of work published on the detection and removal of artefacts (Scholkmann et al 2010, Molavi and Dumont 2012). For example, Scholkmann et al (2010) developed a movement artefact reduction method based on moving standard deviation and spline interpolation, which, according to their studies, significantly reduces artefacts and increases the signal quality. As far as we know this is the first study to assess the incidence of artefacts in long-term NIRS measurements. It has been shown that other routinely used instruments in neonatal monitoring are also prone to artefacts. aEEG for example is routinely
used to monitor neonates with perinatal asphyxia (Hellstroem-Westas and Rosen 2006, Shany et al 2006) and diagnosis of seizure activity (Shah et al 2008). Hagman et al (2006) assessed the influence of artefacts in aEEG and observed that artefacts occurred in 12% of the recorded time. 55% of the artefacts were derived from electrical interference and 45% from movement interference. Pulse oximetry is also routinely used to monitor oxygen saturation in neonates. There are a few studies observing the performance of different pulse oximeters and their liability to artefacts. Barker (2002) compared old and newer pulse oximeters with regard to motion artefacts and found a wide range of oximeter performances in his study, with performance index values varying from 94% to 28%. He concluded that the more recent pulse oximeters outperform the older models in terms of accuracy and reliability during motion. Another study (Durbin and Rostow 2002) also compared a conventional pulse oximeter with an improved innovative pulse oximeter and collected the percentage of non-functional monitoring time, finding it to be 8.7% ± 16.4% for the conventional and 1.2% ± 3.3% for the improved pulse oximeter.

In our study, the largest number of artefacts was caused by missing values due to movement artefacts and displacement of the sensors. These artefacts are easy to recognize as artefacts. In cerebral measurements, only a small number of artefacts were recognized due to defined criteria, whereas peripheral measurements showed a significantly higher number of artefacts. This could be due to more movements in the extremities than in the head or due to the different method of attachment of the sensors. In addition, light interferences and the small diameter of the forearm may have influenced the rSO2 readings. The definition of the criteria raises some limitations. The first limitation is the missing gold-standard for measuring tissue oxygenation. Another limitation is the definition of the second criterion. It was introduced based on the observation that most changes occur due to small movements. Nevertheless, it cannot be ruled out that some of these artefacts were not artefacts but represent physiological changes. The second limitation is that criterion 3 was based on rSO2 and SpO2, so it was not possible to rule out which of these two parameters was affected by artefacts. In addition, the highest value of rSO2 the INVOS displays is 95%, whereas the pulse oximeter displays SpO2 values up to 100%, causing some limitations in higher oxygenation levels.

In conclusion, long-term NIRS measurements of crSO2 and prSO2 are feasible, since most artefacts were due to missing values and therefore easy to recognize. Artefacts other than missing values did not significantly influence the results of long-term NIRS measurements.

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