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The influence of perinatal asphyxia on peripheral oxygenation and perfusion in neonates

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ABSTRACT

Background: Perinatal asphyxia influences peripheral oxygenation and perfusion in neonates.
Objectives: The aim was to investigate the influence of perinatal asphyxia on peripheral oxygenation and perfusion in neonates by using near-infrared spectroscopy (NIRS).
Methods: Prospective observational study. Neonates with gestational age >34 weeks and birth weight >2000 g without infection or congenital malformations were included. Peripheral muscle NIRS measurements in combination with venous occlusion were performed once in the first 48 h of life. Tissue oxygenation index (TOI), mixed venous oxygenation (SvO2), fractional oxygen extraction (FOE), haemoglobin flow (Hbflow), oxygen delivery (DO2) and oxygen consumption (VO2) were assessed. Furthermore arterial oxygen saturation, heart rate, blood pressure and temperatures were measured. Neonates with a UapH ≤ 7.15 and an Apgar 5 ≤ 6 were compared to neonates with a UapH ≥ 7.15, an Apgar 5 ≥ 7 (control group) and a UapH was correlated to NIRS parameters.
Results: 8 asphyxiated neonates were compared to 30 neonates in the control group. TOI (67.7 ± 5.5%) and DO2 (29.0 ± 14.2 μmol/100 mL/min) were significantly lower in asphyxiated neonates compared to the controls (TOI 71.8 ± 4.9%, p = 0.045; DO2 43.9 ± 16.9 μmol/100 mL/min, p = 0.028) and FOE was significantly higher (0.33 ± 0.05) compared to the controls (0.28 ± 0.06, p = 0.028). Furthermore significant correlations between UapH and DO2 (r = 0.78, p = 0.022), VO2 (r = 0.80, p = 0.018) and FOE (r = −0.75, p = 0.034) in the asphyxiated group were found.
Conclusion: Peripheral oxygenation and perfusion measured with NIRS are compromised in neonates with perinatal asphyxia with worsening of parameters and degree of acidosis in the umbilical cord blood.

1. Introduction

The definition of perinatal asphyxia has evolved over the last 50 years from a single-indicator definition (e.g. umbilical artery pH (UapH), base deficit, Apgar score, fetal distress) to a multiple-indicator definition [1]. Strictly speaking perinatal asphyxia is a condition of impaired gas exchange that leads to progressive hypoxemia and hypercapnia [2]. Severe perinatal asphyxia is described by the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists as a combination of severe acidosis at birth (UapH < 7.0), a persistently depressed Apgar score at 5 min, neonatal neurologic sequelae (e.g. seizures, coma, hypotonia) and multiple organ system sequelae in the neonatal period [3]. In most NICUs an UapH of more than 7.2 is considered normal whereas an UapH of 7.0 to 7.2 is considered mild or moderate acidemia [4].

As a consequence fetuses who experience a significant asphyxial episode might develop shock with centralization, where perfusion/oxygenation of the central organs (e.g. heart or brain) is preferred to peripheral ones (e.g. muscle), or even uncompensated shock where centralisation fails. These neonates are at risk of developing hypoxic-ischemic encephalopathy or other end-organ sequelae [4]. Perinatal asphyxia is therefore one of the major causes of cerebral injury implicating later neurodevelopmental disabilities [5,6].

Recognition of disturbances in perfusion of peripheral tissue might help to recognize neonates with (compensated) shock to enable early intervention. Near-infrared spectroscopy (NIRS) is a noninvasive method, which enables measurement of tissue oxygenation and perfusion in "peripheral muscle" [7–11]. In adults several studies have already investigated the influence of shock and severity of shock on peripheral oxygenation and perfusion using NIRS [12–14].

Aim of the present study was therefore to investigate peripheral oxygenation and perfusion assessed by NIRS in asphyxiated neonates within the first 48 h after birth. We hypothesized that in asphyxiated neonates peripheral perfusion is impaired and peripheral tissue oxygenation is lower compared to non-asphyxiated neonates. Furthermore we hypothesized that the severity of impairment of peripheral

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oxygenation and circulation depends on the degree of acidosis in the umbilical cord blood.

2. Methods

2.1. Patients

A prospective observational cohort study was conducted from January 2006 to December 2010 at the Neonatal Unit of the Department of Paediatrics, Medical University of Graz. Neonates >34 weeks of gestation with either moderate or severe perinatal asphyxia were considered for inclusion during the first 48 h of life.

Since peripheral application of NIRS probes in neonates below 2000 g is difficult, study entry criterion was a body weight above 2000 g at time of measurement. No other specific entry criteria were defined. Peripheral muscle oxygenation and circulation were measured by NIRS. The study was approved by the ethic committee of the Medical University of Graz. In each subject informed consent was obtained from the parents before starting the measurements.

Perinatal asphyxia was defined as a UapH ≤ 7.15 and an Apgar 5 ≤ 6. Neonates with a UapH ≤ 7.15 and an Apgar 5 ≤ 6 were considered moderately asphyxiated, while neonates with a UapH ≤ 7.0 and an Apgar 5 ≤ 3 were considered severely asphyxiated. Neonates with asphyxia were compared to non-asphyxiated neonates with a UapH ≥ 7.15 and an Apgar 5 ≥ 7 (control group). Neonates were included for measurements in the control group, if they had no signs of asphyxia, infection/systemic inflammatory response or congenital malformations.

2.2. NIRS

NIRS measurements were carried out with the NIRO 300 (Hamamatsu Photonics, Japan). The optodes were placed on the left lateral calf with an interoptode distance of 3.0 cm. A differential path length factor of 5.51 was used [15]. The sampling rate was 2/s. The NIRO 300 uses the spatially resolved method, which enables the non-invasive continuous measurement of TOI and changes in the concentration of oxygenated haemoglobin (HbO2) and deoxygenated haemoglobin (Hb). Derived from the changes in HbO2 and Hb the changes in the concentration of total haemoglobin (HbT) can be calculated. HbO2, Hb and HbT were calculated in μmol units.

2.3. Venous occlusion

Venous occlusion was performed using a pneumatic cuff placed around the left thigh. Venous occlusion causes an increase in calf blood volume by undisturbed arterial (in)flow and interrupted venous (out)flow. Thus, changes in HbO2, Hb and HbT during venous occlusion are caused only by arterial inflow and oxygen consumption of tissue. Yoxall and Weindling [16] described this method in 1996 by performing venous occlusions around the upper arm in neonates and compared results to co-oximetry.

2.4. Protocol

Measurements were performed under standardized conditions during undisturbed daytime sleep after feeding [17]. The neonates were lying in a supine position, head tilted up 10° and the left calf with the NIRS optodes was positioned just above the level of mid sternum. Heart rate and arterial oxygen saturation (SaO2) were measured by pulse oximetry using the ipsilateral foot. A rectal sensor and a skin sensor placed on the ipsilateral thigh continuously measured core and peripheral temperatures. After positioning of the NIRS optodes, the pneumatic cuff, the temperature and pulse oximetry sensors, a calm-down period was introduced until there was at least a 3-minute resting period without any body movements. Afterwards, arterial blood pressure was measured oscillometrically with the pneumatic cuff on the lift thigh. After another resting period of 1 min, the pneumatic cuff was inflated within 0.5–1 s to a pressure below the diastolic arterial pressure and above the venous pressure (i.e. 20–30 mm Hg). The cuff remained inflated for 20 s and NIRS data were recorded. This procedure was repeated at least five times with a resting period of at least 40 s between inflations and/or until one measurement passed the first quality criterion published recently [18].

The changes of TOI, HbO2, Hb and HbT during these venous occlusions were collected in a polygraphic computer system (alpha-trace digitalMM, B.E.S.T. Medical Systems, Austria).

2.5. Calculations

"Haemoglobin-flow" (Hbflow/min) was calculated from the increase of HbT during venous occlusion projected to 1 min. "mixed venous oxygenation" (SvO2) was calculated as the ratio of oxygenated to total haemoglobin: HbO2/HbT. "oxygen delivery" (DO2) was calculated from (Hbflow/min) * 4 * (SaO2/100), "oxygen consumption" (VO2) from (Hbflow/min) * 4 * (SaO2 − SvO2) and finally "fractional oxygen extraction" (FOE) was calculated as the ratio of oxygen consumption to oxygen delivery: VO2/DO2.

2.6. Statistical analysis

Only data from measurements passing both recently published quality criteria were included for further analysis [18].

Differences in demographic characteristics and NIRS parameters between asphyxiated neonates and the control group were investigated using unpaired Student's *t*-test and Chi square test.

Correlations between UapH and NIRS parameters were shown using regression analysis. P-values of <0.05 were considered to indicate statistical significance.

The statistical analysis was performed using the statistical software of 'SPSS' Version 17.0.

3. Results

A total number of 780 neonates >34 weeks were admitted to the neonatal unit from January 2006 to December 2010. 22 neonates were diagnosed with asphyxia, 11 with severe and 11 neonates with moderate asphyxia. In eight asphyxiated neonates (two severely and six moderately asphyxiated neonates) informed consent was obtained and they were included for measurements. These asphyxiated neonates were compared to 30 neonates, in whom measurements were performed

Table 1
Demographic and clinical parameters of all 8 asphyxiated neonates and the control group.

	Asphyxiated neonates (2 severely and 6 moderately)	Control group	p-value
Patients (n)	8	30	
Females/males (n)	3/5	4/26	
Gestational age (week)	38.1 ± 1.2	39.2 ± 1.3	**0.044**
Postnatal age (h)	19.0 ± 13.0	20.6 ± 11.7	0.753
Birth weight (g)	3221 ± 475	3421 ± 600	0.391
Umbilical artery pH	7.0 ± 0.14	7.3 ± 0.07	<**0.001**
Apgar 5 min	3.8 ± 2.0	9.4 ± 0.8	<**0.001**
Haemoglobin (g/dL)	16.3 ± 3.5	18.4 ± 2.9	0.131
Heart rate (bpm)	131 ± 12.5	126 ± 14.2	0.439
Arterial oxygen saturation (%)	95.9 ± 3.9	96.3 ± 3.1	0.748
Mean arterial blood pressure (mm Hg)	43.9 ± 5.3	44.1 ± 6.0	0.924
Temperature rectal (°C)	35.8 ± 1.1	37.0 ± 0.3	<**0.001**
Temperature peripheral (°C)	33.2 ± 1.6	35.0 ± 1.0	<**0.001**