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Near-infrared spectroscopy to detect absence of cerebrovascular autoregulation in preterm infants

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HIGHLIGHTS

- The absence of cerebrovascular autoregulation was found in 40% of the preterm infants studied, as suggested by a relevant negative correlation between mean arterial blood pressure (MABP) and fractional tissue oxygen extraction (FTOE).
- None of the clinical variables predicted the absence of cerebrovascular autoregulation.
- Near-infrared spectroscopy (NIRS) could be a helpful tool to assess the presence or absence of cerebrovascular autoregulation.

ABSTRACT

Objective: Our aim was to explore clinical parameters that might predict the absence of cerebrovascular autoregulation (CAR) assessed by a negative relationship between mean arterial blood pressure (MABP) and fractional tissue oxygen extraction (FTOE) as measured by near-infared spectroscopy (NIRS) in preterm infants.
Methods: We included preterm infants (gestational age (GA) <32 weeks). Within 72 h after birth, we recorded the infants' NIRS parameters and MABP for a 24-h period. Fractional tissue oxygen extraction (FTOE) was calculated. For each infant we calculated Spearman rank (rho) correlations. A statistically significant negative correlation between MABP and FTOE indicated the absent CAR. We related the absent CAR to clinical parameters.
Results: Ten (40%) out of 25 infants (median GA 29.1 weeks, range 25.4–31.7, birth weight 1245 g, 560–1780) had a statistically significant negative correlation between MABP and FTOE (rho −0.432 to −0.156), suggesting the absence of CAR. None of the clinical variables predicted the absence of CAR.
Conclusions: We were unable to predict the absence of CAR in terms of clinical variables. Nevertheless, we found a statistically significant negative correlation between MABP and FTOE using NIRS, suggesting the absence of CAR in almost half of the preterm infants studied.
Significance: NIRS could be a helpful tool to assess the presence or absence of CAR.

1. Introduction

Cerebrovascular autoregulation (CAR) is a protective mechanism of the brain. Within limits, cerebral vessels adapt to changes in blood pressure in order to maintain a constant cerebral blood flow (CBF) (Volpe, 2008). There is conflicting evidence on whether this mechanism is present in preterm infants from birth onwards or whether it develops during the first days after birth (Noone et al., 2003; Pryds et al., 1989; Kehrer et al., 2005; Weindling and Kissack, 2001; Boylan et al., 2000; Tyszczuk et al., 1998). Some studies suggested that the ability to effectively autoregulate may fluctuate over time (Soul et al., 2007; Gilmore et al., 2011). In the case of impaired CAR, changes in blood pressure cause changes in CBF, which in turn lead to either cerebral underperfusion (low blood pressure) or hyperperfusion (high blood pressure). This could pose a risk for the preterm infant of developing brain damage (O'Leary et al., 2009).

In the neonatal period, CBF can be estimated by near-infrared spectroscopy (NIRS). This measures regional cerebral tissue

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oxygenation saturation (r_cSO_2) (Lemmers et al., 2006; Verhagen et al., 2009). A study in newborn lambs reported that cerebral tissue oxygen saturation correlates well with changes in CBF (Wong et al., 2009a). Fractional tissue oxygen extraction (FTOE) is calculated by combining r_cSO_2 values with arterial oxygenation (SpO_2) values (Wardle et al., 2000; Naulaers et al., 2007). FTOE reflects the balance between oxygen supply and oxygen consumption. In baboons, oxygen extraction was measured invasively and found to be inversely correlated with CBF (Schumann et al., 1998). In the case of diminished CBF, more oxygen is extracted from the blood to meet the needs of cerebral metabolism. In the case of high CBF, less oxygen needs to be extracted from the blood. In case CAR is intact and CBF is not disturbed, FTOE will remain constant (Naulaers, 2003).

Our aim was to explore clinical parameters that might predict the absence of CAR assessed by a negative relationship between mean arterial blood pressure (MABP) and FTOE in preterm infants during 24 h within the first 3 days after birth. We assumed that a statistically significant negative correlation between MABP and FTOE reflects the absence of CAR, as the extraction of oxygen will be higher in the case of diminished CBF. We decided to determine the correlation between MABP and FTOE to eliminate the influence of changes in the arterial oxygen saturation. We also examined the correlation between MABP and r_cSO_2 as regional oxygen saturation was what we actually measured.

We hypothesised that we would find infants with and without CAR on the basis of their clinical situation, e.g., in younger, smaller and sicker infants (Soul et al., 2007; Wong et al., 2008; Verma et al., 2000).

2. Methods

We studied preterm infants born after <32 weeks' gestational age (GA) and admitted to our NICU. The attending neonatologist decided on NIRS monitoring on clinical grounds. Infants were included consecutively only if they were <72 h of age when NIRS measurements commenced. We only included infants with an indwelling arterial catheter for constant blood pressure measurements. Exclusion criteria were major chromosomal or major congenital malformations.

2.1. Near-infrared spectroscopy

We used an INVOS 4100-5100 near-infrared spectrometer (Somanetics Corporation, Troy, MI, USA) in combination with the paediatric SomaSensor to measure r_cSO_2 values. The SomaSensor was placed on the left frontoparietal side of the infant's head and kept in place by an elastic bandage. A more detailed description of the method was published previously (Verhagen et al., 2009).

At the same time as measuring r_cSO_2, we measured SpO_2 by pulse oximetry and we calculated FTOE with the equation $FTOE = (SpO_2 - r_cSO_2)/SpO_2$ (Wardle et al., 2000; Naulaers et al., 2007).

2.2. Study design

We performed a prospective clinical observational cohort study in preterm infants in whom r_cSO_2 and SpO_2 and invasive MABP measurements were performed simultaneously for 24 h during the first 72 h after birth. We measured MABP with an indwelling arterial catheter placed in the umbilical or radial artery. Clinical variables with probable or known associations with CAR such as birth weight (Soul et al., 2007; Wong et al., 2008), GA (Soul et al., 2007; Wong et al., 2008; Verma et al., 2000), haemoglobin concentration (Ramaekers et al., 1992), glucose concentration (Vanderhaegen et al., 2010), the presence of brain lesions (Pryds et al., 1989; O'Leary et al., 2009; Tsuji et al., 2000), clinical risk index for babies (CRIB) score (Wong et al., 2008; International Neonatal Network, 2000) mortality (Wong et al., 2008) and blood gas values (Pryds et al., 1989) were collected, as well as the infants' postnatal age in hours, Apgar scores at 1, 5 and 10 min after birth, treatment for hypotension during NIRS measurement, mechanical ventilation or the presence of a patent ductus arteriosus.

We determined haemoglobin concentration, glucose concentration and blood gas values just before or during the 24-h recording period. We defined hypotension as an MABP of less than the GA in weeks. In the case of hypotension, the attending neonatologist decided whether or not treatment was required. The presence of brain lesions, e.g., intraventricular haemorrhage (IVH), periventricular leucomalacia (PVL) or transient periventricular echodensities (TPEs), was diagnosed with cranial ultrasound using standard diagnostic criteria (Volpe, 2008).

2.3. Statistics

We used SPSS 18.0 software for Windows (SPSS Inc., Chicago, IL, USA) for the statistical analyses. NIRS data, as well as MABP measurements, were stored off-line for analysis. For further analyses, we used the r_cSO_2, SpO_2, FTOE and MABP values sampled every 5 min. Mean values for FTOE and MABP, along with the other variables, were calculated for the 24-h recording periods. The recording period entailed a complete 24-h period closest to the infant's birth. We determined the level of variability of MABP by calculating the coefficient of variation of MABP in each infant. We visually inspected the data for normality with Q–Q plots. In the case of a non-normal distribution, we used non-parametric exact tests.

We determined the correlation between MABP and FTOE values, sampled every 5 min for 24 h, in each individual infant with the Spearman rank correlation test. Correlations found between MABP and FTOE were categorised into two groups: those with a statistically significant negative correlation and those without a statistically significant negative correlation. Differences in FTOE and MABP values between these groups were analysed with the Mann–Whitney's test. We followed a similar procedure to determine the correlation coefficients between MABP and r_cSO_2. Again, the infants were categorised into two groups: those with a statistically significant positive correlation and those without a statistically significant positive correlation.

To test the possible association of FTOE values with clinical variables, we used the Spearman rank correlation test. Where appropriate, differences in proportions of categorical data were tested by Fisher's exact test or the χ^2-for-trend test.

We performed univariate logistic regression analyses to investigate the influence of clinical variables on the presence or absence of CAR. We calculated correlation coefficients (Spearman's rho) to investigate the influence of clinical variables on the extent to which CAR is impaired. A P value of <0.05 was considered significant.

3. Results

3.1. Patient characteristics

We included 25 preterm infants with a median GA of 29.1 weeks (range 25.4–31.7), median birth weight of 1245 g (range 560–1780), median postnatal age of 23.4 h (range 2.7–63.4) and median CRIB score of 1 (range 0–9). During the 24-h recording period, eight infants received treatment for circulatory failure or signs thereof, seven of whom were treated with volume expansion and/or dopamine ($n = 5$) and/or dobutamine ($n = 1$). Three infants received red blood cell transfusions during NIRS