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REGULAR ARTICLE

Blood sampling via umbilical vein catheters decreases cerebral oxygenation and blood volume in preterm infants

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Abstract

Aim: We have shown previously that blood sampling via umbilical artery catheters decreases cerebral oxygenation and cerebral blood volume in preterm infants. To evaluate alternative methods, we assessed the effects of blood sampling via umbilical vein catheters in a cohort of preterm infants.

Methods: Twenty neonates (median birth weight 900 g [range 410–1900 g], median gestational age 27 weeks [24–31 weeks]) were studied during routine blood sampling via umbilical vein catheters by near-infrared spectroscopy. Tissue oxygenation index and changes in concentrations of cerebral oxygenated and deoxygenated haemoglobin were measured and changes in cerebral oxygenation and cerebral blood volume were calculated. Oxygen saturation and heart rate were recorded simultaneously.

Results: There was a significant drop of cerebral oxygenation (−2.135 ± 0.532 μmol/L) and cerebral blood volume (−0.037 ± 0.019 mL/100 g tissue) during umbilical vein blood sampling. Although peripheral arterial oxygen saturation remained unchanged, cerebral tissue oxygenation index decreased from 64.8 ± 2.5% to 62.4 ± 2.6% ($p < 0.01$), accompanied by a slight increase in heart rate (from 140 ± 2.9 to 144 ± 2.9 beats/min, $p < 0.01$).

Conclusions: Umbilical vein blood sampling reduces cerebral oxygenation and cerebral blood volume. The magnitude of the effects is similar to those during umbilical artery blood sampling.

INTRODUCTION

Acute changes of cerebral oxygenation and cerebral blood volume (CBV) are potentially harmful to extremely preterm infants prone to cerebral lesions such as intraventricular haemorrhage and periventricular leucomalacia (1). Low cerebral blood flow during the first days of life, as detected by near-infrared spectroscopy (NIRS; 1) or assessed by ultrasound measurements of superior vena cava blood flow (2,3) have been associated with intraventricular haemorrhage and poor neurodevelopmental outcome in preterm infants. Therefore all interventions that alter cerebral oxygenation and CBV should be avoided or, if this is not possible, should be performed using the least harmful method. In two previous studies, we demonstrated that blood sampling via umbilical artery catheters, a common and repetitively performed procedure in the sick premature infant, induces significant decreases in cerebral oxygenation and CBV (4,5). Assuming that the observed changes relate to the fact that the blood is withdrawn directly from the descending aorta, we hypothesized that these effects can be blunted by sampling blood via an umbilical vein catheter. Therefore, the aim of the present study was to assess the effects of blood sampling via umbilical vein catheters according to a time-structured protocol on cerebral oxygenation and CBV in preterm infants.

PATIENTS AND METHODS

Patients

Between February 1999 and November 2000, 20 preterm infants treated in the neonatal intensive care unit at University Children's Hospital, Essen, Germany, with a gestational age <32 weeks and with an umbilical vein catheter placed for clinical reasons (14 male, 6 female, median birth weight 900 g (range 410–1900 g), gestational age median 27 weeks (range 24–31) weeks) were studied at a median age of 23 h of life (range 9–90 h). All but one infant had received surfactant for respiratory distress syndrome in the first hours of life. At the time of blood sampling, 16 infants were mechanically ventilated, and two infants were supported by nasal continuous positive airway pressure. One infant was treated with dopamine for arterial hypotension. Thirteen infants had received phenobarbitone for sedation between birth and the time measurements were performed. None of the infants exhibited severe intraventricular haemorrhage or parenchymal haemorrhagic infarction.

The study was approved by the ethical committee of the Medical Faculty of the University of Essen. Informed consent was obtained from all parents for infants included in the study.

Monitoring

Near-infrared spectroscopy (NIRS)

The principle of NIRS is based on the characteristic absorption of near-infrared light by haemoglobin depending on its oxygenation state. NIRS enables continuous, noninvasive measurement of changes in concentrations of oxygenated haemoglobin (O_2Hb) and deoxygenated haemoglobin (HHb). The sum of O_2Hb and HHb is described as total haemoglobin (tHb). tHb corresponds to the CBV provided that the haematocrit remains constant (6). Changes in CBV were calculated using the formula: 0.89 × tHb/large vessel haemoglobin concentration in g/dL. Changes in cerebral oxygenation were described by calculating the cerebral oxygenation index (HbD) from a change in O_2Hb minus a change in HHb (6). Tissue oxygenation index (TOI) as an absolute value of cerebral oxygenation reflecting primary oxygenation of cerebral venous blood was measured by spatially resolving oximetry (7).

In the present study the NIRO 300® (Hamamatsu Photonics, Herrsching, Germany) was used. The instrument uses laser-emitting diodes to generate light of four different wavelengths (775, 810, 850, 910 nm). Using an optode holder a 5-cm interoptode distance was chosen. Sampling frequency was 2/sec. The optodes were fixed in the frontotemporal region by an elastic bandage. The pathlength factor was 4.4. Quantified changes in chromophores are presented in micromoles per litre of tissue.

Arterial oxygen saturation and heart rate were monitored continuously using a standard monitoring system (CMS M1167A, Hewlett Packard GmbH, Böblingen, Germany).

Umbilical vein catheters

Umbilical catheters were inserted in infants exhibiting severe respiratory distress syndrome or blood pressure instability. The umbilical artery catheter was the preferred central line, but an umbilical vein catheter was inserted if placement of the umbilical artery catheter failed or when both catheters were considered necessary. The tip of the umbilical vein catheter was placed in the vena cava inferior slightly below the diaphragm. The catheter was used for blood sampling, application of medications as a bolus, or short infusion and infusion of nutrition fluids. Blood products were not given via the catheter. Medications given as a bolus or short infusion were not applied 1 h before and during NIRS measurements.

Blood sampling

Blood sampling via the umbilical vein catheter was performed according to the following protocol:

- disconnection of the catheter with the check-valve (dead space of the system: 0.3 mL),
- aspiration of the draw-up volume (mixture of blood and infusion solution: 1.6 mL) within 20 sec,
- aspiration the sample volume (1.7 mL) within 20 sec,
- reinjection of the draw-up volume (1.6 mL) within 30 sec,
- flushing with 0.9% saline solution (0.6 mL) within 6 sec,
- reconnection of the catheter.

The protocol was identical to that used in our previous study on umbilical arterial blood sampling (5).

Statistical analysis

All continuously recorded data were transferred to a computer and stored 2 times per second for later analysis. Optical analysis of all tracings to exclude movement artefacts was performed before further statistical analysis.

Mean values of O_2Hb, HHb, CBV, HbD, TOI, peripheral arterial oxygen saturation and heart rate were calculated over the following time periods:

- baseline of 2 min,
- last 10 sec of aspiration period,
- last 10 sec of replacement of draw-up volume,
- 6 sec of flushing period,
- 0–5 min after the end of the sampling procedure.

Data are reported as mean values ± standard deviations (SD).

Differences of measurements at the specified time points during blood sampling were assessed by the Friedman test as a nonparametric two-way ANOVA for repeated measurements, followed by post hoc matched-pair Wilcoxon signed rank tests comparing data to baseline. In all tests, the level of significance was set to 0.05.

RESULTS

Umbilical vein blood sampling was associated with significant changes of O_2Hb ($p < 0.001$), HbD ($p < 0.01$), CBV ($p < 0.01$), TOI ($p < 0.01$), and heart rate ($p < 0.01$), whereas HHb ($p = 0.07$) and oxygen saturation ($p = 0.1$) remained stable. Results are presented in Table 1, with post hoc comparisons to baseline.

DISCUSSION

The present study demonstrates that blood sampling via umbilical vein catheters induces significant decreases in cerebral oxygenation and CBV in preterm infants. These changes are not mirrored in changes of peripheral arterial oxygen saturation monitored simultaneously.

The quantity of the decrease is comparable to the decrease observed during blood sampling via umbilical artery catheters (Fig. 1; 4,5,8). This disproves our hypothesis that blood sampling via umbilical vein catheters is less harmful than via umbilical artery catheters. Our findings suggest that the crucial point causing the drop of cerebral oxygenation and CBV is the acute loss of intravascular volume, irrespective of whether it is withdrawn via umbilical artery or umbilical vein catheters.

There are few studies published assessing cerebral oxygenation and blood supply in preterm infants following blood withdrawal. One study by Bray et al. with a similar design, but different patient characteristics, involving more

Table 1 Mean and SD of changes in the NIRS variables O_2Hb (oxygenated haemoglobin), HHb (deoxygenated haemoglobin), CBV (cerebral blood volume), HbD (haemoglobin difference), TOI (tissue oxygenation index), and in arterial oxygen saturation and heart rate during different periods of blood sampling*

Period of blood sampling	Mean	SD	p-value
O_2 Hb (μmol/L)			
Aspiration	−1.114	±0.380	0.01
Reinjection	−1.416	±0.364	0.002
Flushing	−1.033	±0.378	0.007
0–5 min after sampling	−0.555	±0.379	0.04
HHb (μmol/L)			
Aspiration	0.475	±0.229	
Reinjection	0.719	±0.253	
Flushing	0.425	±0.195	
0–5 min after sampling	0.450	±0.347	
CBV (mL/100 g tissue)			
Aspiration	−0.037	±0.021	0.1
Reinjection	−0.037	±0.019	0.02
Flushing	−0.033	±0.018	0.04
0–5 min after sampling	−0.003	±0.022	0.3
HbD (μmol/L)			
Aspiration	−1.589	±0.509	0.006
Reinjection	−2.135	±0.532	0.002
Flushing	−1.458	±0.513	0.01
0–5 min after sampling	−1.005	±0.627	0.04
TOI (%)			
Baseline	64.8	±2.5	
Aspiration	63.2	±2.5	0.007
Reinjection	62.4	±2.6	0.002
Flushing	63.6	±2.6	0.015
0–5 min after sampling	63.2	±2.4	0.006
Arterial oxygen saturation (%)			
Baseline	94	±0.7	
Aspiration	93	±0.95	
Reinjection	93	±0.94	
Flushing	93	±0.83	
0–5 min after sampling	93	±0.76	
Heart rate (beats/min)			
Baseline	140	±2.9	
Aspiration	144	±2.9	0.003
Reinjection	144	±2.9	0.001
Flushing	144	±2.9	0.01
0–5 min after sampling	143	±2.9	0.04

*In variables showing significant changes during sampling [O_2Hb, CBV, HbD, TOI and heart rate], post hoc comparison to baseline p-values are listed.

mature (median gestational age 31 weeks) and heavier (median birth weight 1100 g) preterm infants also found a significant decrease in cerebral oxygenation and CBV during rapid blood sampling (30 sec) via umbilical vein and umbilical artery catheters (9). Interestingly, the changes observed were even more pronounced during blood sampling via umbilical vein, as compared to blood sampling via umbilical artery catheters. We could not reproduce this finding. However, in Bray's study blood sampling was performed more rapidly (30 sec vs. 40 sec in our study), the procedure was repeated three times in sequence each, first via the umbilical artery and then via the umbilical vein catheter, and the volume withdrawn was completely replaced. Furthermore, most infants received dobutamine and dopamine, which might have altered the cardiovascular response in these infants. In our study only one infant received dopamine. These variations in study design and patient characteristics might explain the different findings.

The maximum effects of blood sampling on CBV and HbD were observed beyond the time point of maximum volume loss, when reinjection of the draw-up volume was actually nearing completion. Directly reduced myocardial preload (blood being diverted from the right atrium into the syringe) might become evident after pulmonary passage within a few heartbeats. However, an even more prolonged effect on HbD and CBV was seen after blood sampling via the umbilical artery catheter (Fig. 1). Thus, more complex reactive mechanisms involving an increase in heart rate and perhaps an increase in cerebral vascular tone might play a role in explaining this prolonged effect. Blood was withdrawn slowly over a period of 40 sec, equivalent to at least 80 heart cycles, and the total amount of blood withdrawn during this time was similar to the stroke volume of a single heart action. Very rapid aspiration of blood via the umbilical vein catheter might indeed carry a risk to negatively affect cardiac filling by exerting a steel phenomenon from the superior vena cava, especially when the tip of the catheter is placed in the right atrium. In addition, this might impede venous drainage of the brain, which has been considered an important factor guaranteeing normal brain function (10).

Our data strongly suggest that the actual loss of intravascular blood volume is the crucial point adversely affecting cerebral oxygenation and CBV. This hypothesis is supported by a study by van de Bor et al. (11). Investigating the effects of exchange transfusions via umbilical vein catheters on cerebral oxygenation and CBV, they found a decrease of CBV and mean arterial blood pressure during withdrawal and an increase of both parameters during infusion. In contrast to that, in two-way exchange transfusions where the blood withdrawn via an umbilical artery catheter is replaced simultaneously via an umbilical vein catheter and therefore no actual blood loss occurs, cerebral oxygenation and CBV actually increased in the majority of infants studied (12).

It is unclear at present whether the decrease in cerebral oxygenation and in CBV observed during umbilical vein catheter blood sampling is of clinical importance. However, a decrease in HbD is a strong indicator of a decrease in cerebral blood flow (13), and low cerebral blood flow, as detected by NIRS (1) or assessed by ultrasound measurements of superior vena cava blood flow (2,3) has been associated with intraventricular haemorrhage and poor neurodevelopmental outcome in preterm infants. Withdrawing 3.3 mL from a 900-g infant in 40 sec is roughly equivalent to withdrawing 250 mL of blood from an adult male in the same time. As any blood sampling from umbilical catheters induces a significant decrease in cerebral oxygenation and

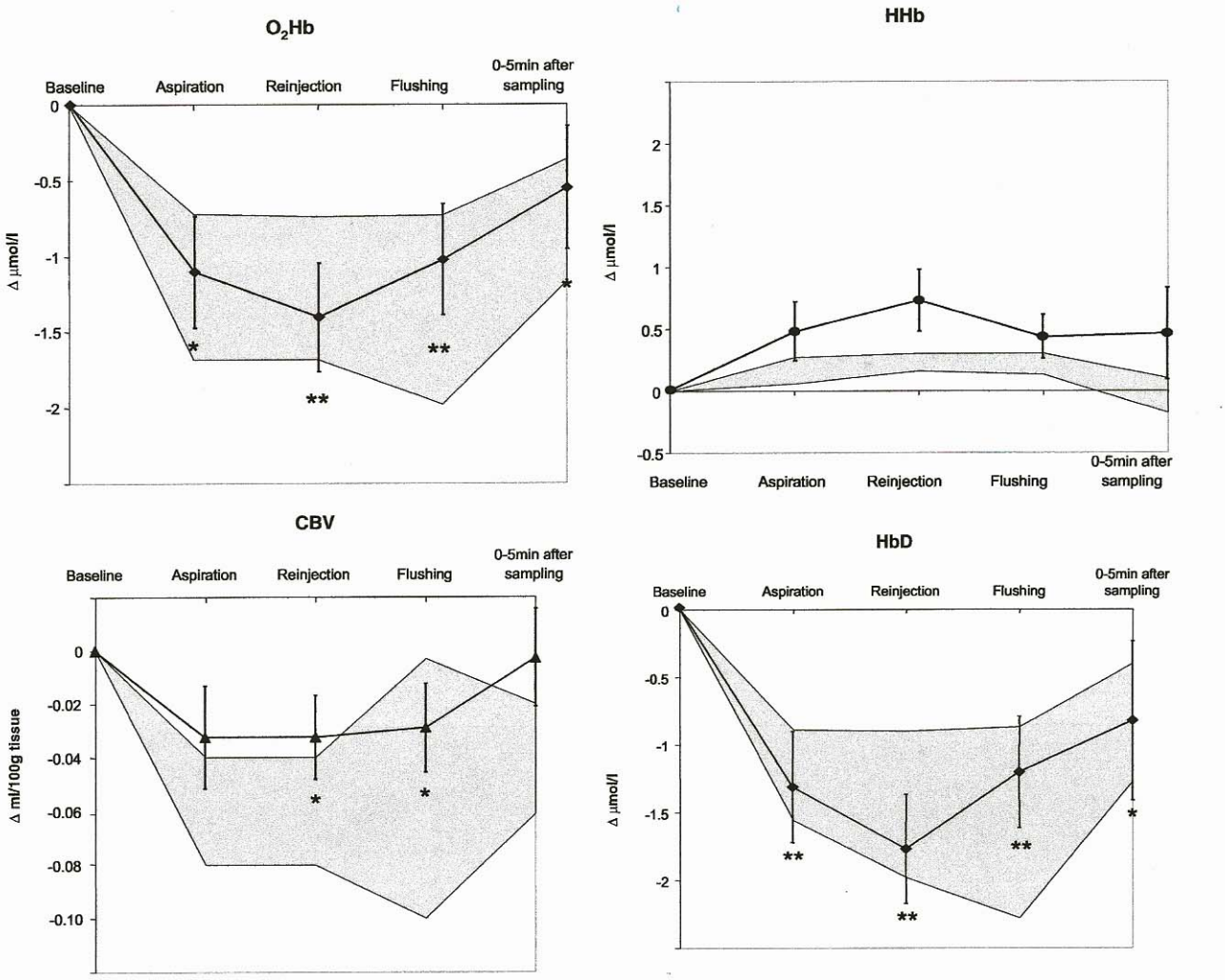

Figure 1 Changes in NIRS variables O_2Hb (oxygenated haemoglobin), HHb (deoxygenated haemoglobin), CBV (cerebral blood volume) and HbD (haemoglobin difference) from baseline during different periods of blood sampling. Black lines show mean values and SE during blood sampling from umbilical veins catheters. P indicates significance levels compared to baseline before sampling (*$p < 0.05$; **$p < 0.01$). Grey areas represent range of mean values during different sampling procedures from umbilical artery catheters from previous studies (4,5).

CBV in these infants, these procedures should be carried out with caution, and efforts to reduce the number of blood sampling procedures itself as well as the amount of blood withdrawn in extremely preterm infants are of up most importance.

In summary, the present study demonstrates that blood sampling via umbilical vein catheters induces significant decreases in cerebral oxygenation and CBV in preterm infants. It underlines preexisting concerns about the cerebral effects of blood sampling in preterm infants and therefore the necessity to restrict blood sampling in preterm infants as much as possible.

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Abstract

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METHODS: Twenty neonates (median birth weight 900 g [range 410-1900 g], median gestational age 27 weeks [24-31 weeks]) were studied during routine blood sampling via umbilical vein catheters by near-infrared spectroscopy. Tissue oxygenation index and changes in concentrations of cerebral oxygenated and deoxygenated haemoglobin were measured and changes in cerebral oxygenation and cerebral blood volume were calculated. Oxygen saturation and heart rate were recorded simultaneously.

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