Taylor & Francis
Taylor & Francis Group

Umbilical artery catheter blood sampling volume and velocity: Impact on cerebral blood volume and oxygenation in very-low-birthweight infants

CLAUDIA ROLL, BRITTA HÜNING, MATTHIAS KÄUNICKE, JENS KRUG & SANDRA HORSCH

Department of Paediatrics, University Hospital, Essen, Germany

Abstract

Aim: Blood sampling from umbilical artery catheters decreases cerebral blood volume and cerebral oxygenation. The aim of this study was to assess the impact of sampling volume and velocity. *Methods:* Forty-eight infants, median birthweight 965 g (480–1500 g), median gestational age 27 wk (23–34 wk), were studied during routine blood sampling from umbilical artery catheters. The sampling procedure was performed following a strict protocol for draw-up volume (1.6 ml), sampling volume (1.7 ml or 0.2 ml), re-injection volume (1.6 ml) and flushing volume (0.6 ml), time of aspiration (40 s or 80 s), re-injection (30 s) and flushing (6 s). In each infant, sampling volume and aspiration time were subject to sequential variation in a randomized fashion (1.7 ml/40 s, 1.7 ml/80 s, 0.2 ml/30 s). Using near-infrared spectroscopy, changes in concentrations of cerebral oxygenated and deoxygenated haemoglobin were measured, and changes in cerebral blood volume and cerebral oxygenation were calculated. *Results:* During all three sampling procedures, oxygenated haemoglobin decreased significantly from baseline, whereas deoxygenated haemoglobin did not change. Correspondingly, a decrease in cerebral blood volume and cerebral oxygenation occurred. This decrease was not affected significantly by extending the sampling time from 40 s to 80 s, whereas it was blunted by reducing the amount of blood withdrawn.

Conclusion: Blood sampling from umbilical artery catheters induces a decrease in cerebral blood volume and cerebral oxygenation. The magnitude of the decrease depends on the blood volume withdrawn but not on sampling velocity.

Key Words: *Blood sampling, near-infrared spectroscopy, premature infant, umbilical artery catheter*

Introduction

Changes in cerebral haemodynamics and oxygenation are thought to be major causes of intracranial haemorrhage and periventricular leukomalacia in premature infants [1]. Therefore, changes in cerebral haemodynamics and oxygenation should be avoided during the first days of life when the premature infant's brain is most vulnerable to the development of brain lesions. On the other hand, blood sampling constitutes a necessity during this crucial time period, especially in the most critically ill infants who bear the highest risk of brain damage.

While venipuncture or heel-lance sampling cause pain [2,3]), thereby inducing hypoxaemia and blood pressure instability, blood sampling via an umbilical artery catheter (UAC) can be easily performed without disturbing the infant. However, we have shown previously that UAC blood sampling in VLBW infants significantly decreases cerebral blood volume (CBV)

and cerebral oxygenation, as measured by near-infrared spectroscopy (NIRS) [4]. In the present study, we investigated whether these changes can be ameliorated by performing UAC blood sampling in a slower manner, or by reducing the amount of blood withdrawn from the UAC.

Patients and methods

Patients

Preterm infants born from 1 August 1999 to 1 August 2001 with a birthweight ≤1500 g and a UAC placed for clinical reasons were included. Forty-eight infants (23 female, 25 male), median birthweight 965 g (range 480–1500 g), median gestation age 27 wk (range 23–34 wk), were studied during the first 72 h of life.

Forty-four of 48 infants were delivered by caesarean; 34 were singletons. Reasons for preterm birth

were premature rupture of membranes (10), premature labour (14), pathological heart rate or Doppler tracings (13), growth retardation (2), pregnancy-induced hypertension (5), and a combination of factors in some cases. Forty women had received betamethasone prior to delivery. Only two infants were outborn.

Forty-four infants were intubated in the delivery room, and 22 received surfactant there. In 32 infants, the UAC was placed the delivery room, in the other 16 infants during the first hours of life. All but three infants were mechanically ventilated during the NIRS measurements. Three infants were on high-frequency oscillatory ventilation, the remaining on synchronized intermittent mandatory ventilation (Babylog 8000, Dräger, Lübeck, Germany; HFO or SIMV mode).

Twelve of 48 infants were treated with inotropes for arterial hypotension during the first 48 h of life. Forty-one were given phenobarbitone during the time period between birth and NIRS measurement for sedation. Ultrasound of the brain exhibited intracranial haemorrhage in nine infants during their neonatal period (subependymal haemorrhage was present in one infant, a grade II intraventricular haemorrhage in seven infants and a parenchymal haemorrhage in one infant). In four infants, low grade haemorrhage was present at the time of the study. Three infants died before discharge (one from complications of necrotizing enterocolitis, one with oesophageal atresia, one from sepsis).

The study was approved by the Institutional Review Board of the Medical Faculty of the University of Essen. Parental informed consent was obtained in all cases.

Monitoring

The principle of NIRS is based on the characteristic absorption of near-infrared light by haemoglobin depending on the oxygenation state. NIRS enables non-invasive continuous measurement of changes in the concentrations of oxygenated haemoglobin (O_2Hb) and deoxygenated haemoglobin (HHb). The sum of O_2Hb and HHb is calculated and described as total haemoglobin (tHb). THb corresponds to CBV provided that the haematocrit remains constant [5]. Changes in CBV were calculated using the formula $0.89 \times tHb$/large-vessel haemoglobin concentration in g/dl. Changes in cerebral oxygenation were described by calculating the oxygenation index or haemoglobin difference (HbD) from a change in O_2Hb minus a change in HHb [5].

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

Heart rate, arterial oxygen saturation and arterial blood pressure were monitored continuously using a standard monitoring system (CMS M1167A, Hewlett-Packard GmbH, Böblingen, Germany). Transcutaneous pCO_2 (tc-pCO_2) was measured using the MicroGas 7650 (Kontron, Neufahrn, Germany). Arterial blood pressure was measured continuously via the UAC before and after the end of blood sampling, because disconnection of the system during sampling did not allow continuous measurement during the sampling procedure.

Umbilical artery catheters

UACs were routinely inserted in infants exhibiting severe respiratory distress syndrome and in infants with blood pressure instability. Catheters were placed in the high position above the diaphragm.

Blood sampling

The arterial blood sampling technique from the UAC was defined in detail: disconnections of the catheter with the check-valve (dead space of the system: 0.3 ml), withdrawal of the draw-up volume (mixture of blood and infusion solution), withdrawal of the sample volume, re-injection of the draw-up volume, flushing with saline solution, reconnection. In contrast to our first study, where nurses were asked to do the blood sampling procedure "as usual", resulting in different time intervals for the different steps of sampling and different volumes withdrawn, the time periods for the different steps of sampling were specified, as were the draw-up volume and the volume of saline solution used for flushing. Prior to the sample being taken, a draw-up volume of 1.6 ml was withdrawn to assure accurate measurements [6]. Flushing with 0.6 ml saline was performed at the end of the procedure. Velocity of flushing was set at 0.1 ml/s to avoid retrograde flow and blood pressure changes induced by faster flushing [7]. Re-injection of the draw-up volume was performed over 30 s. The sample volume corresponded to the minimal needs for the laboratory analysis: 1.7 ml for blood count, C-reactive protein, creatinine, sodium, potassium, chloride, calcium, glucose, and blood gas analysis in the morning of days 1 and 2, and 0.2 ml in the afternoon for glucose and blood gas analysis.

The first variable parameter of interest was the time of aspiration of the blood volume: an aspiration period of 40 s (median of the first study [4]) was compared

with 80 s. An aspiration time of longer than 80 s was not chosen, because blood was replaced and clotting had to be avoided. The sequence of sampling (aspiration time of 40 s in the morning of day 1 of life and 80 s in the morning of day 2 or vice versa) was randomized (closed envelops).

The second variable parameter of interest was the sample volume. A volume of 1.7 ml was compared to 0.2 ml. The small volume was always taken in the afternoon of day 1 of life.

The protocol is shown in Figure 1.

Calculations and statistical analysis

Planning this study, we calculated that a study population size of at least 34 infants was required to detect a 50% decrease in changes in NIRS parameters by changing sampling velocity with 80% power at the 0.05 level.

All continuously recorded data were transferred to a computer via the MacLab 16s ADInstruments and stored with a frequency of 2/s for later analysis. Optical analysis of all tracings was performed before further analysis to exclude artefacts.

Mean values of O_2Hb, HHb, HbD, CBV, heart rate, oxygen saturation and transcutaneous pCO_2 were calculated over the following periods:

- baseline of 2 min;
- last 10 s of aspiration for 40-s sampling;
- last 20 s of aspiration for 80-s sampling;
- last 5 s of aspiration for small-volume sampling;
- last 10 s of re-injection;
- whole flushing period of 6 s;
- 5 min after the end of the sampling procedure

Mean values over 10 s, 20 s and 5 s for the 40-s, 80-s and small-volume sampling periods, respectively, were calculated to make data comparable as the relative amount of volume aspirated before that period was the same.

Mean arterial blood pressure was calculated over a baseline period from 2 min to 30 s before sampling. After the end of the procedure, mean values were calculated over the time period 30 s to 5 min.

To assess differences from baseline, the paired t-test was performed between baseline and the periods of sampling for all parameters measured. Bonferroni Dunn procedure was used to correct for multiple testing. To compare between different modes of sampling, ANOVA was performed. P-values of <0.05 were considered significant.

Results

NIRS measurements were performed in 48 preterm infants. Before further analysis of the NIRS data, the tracings were plotted and visual analysis was performed to exclude artefacts. Analysis of 40-s sampling was possible in 42 infants, 80-s sampling in 43 infants, and smaller-volume sampling in 40 infants. This resulted in the possibility of paired comparison for
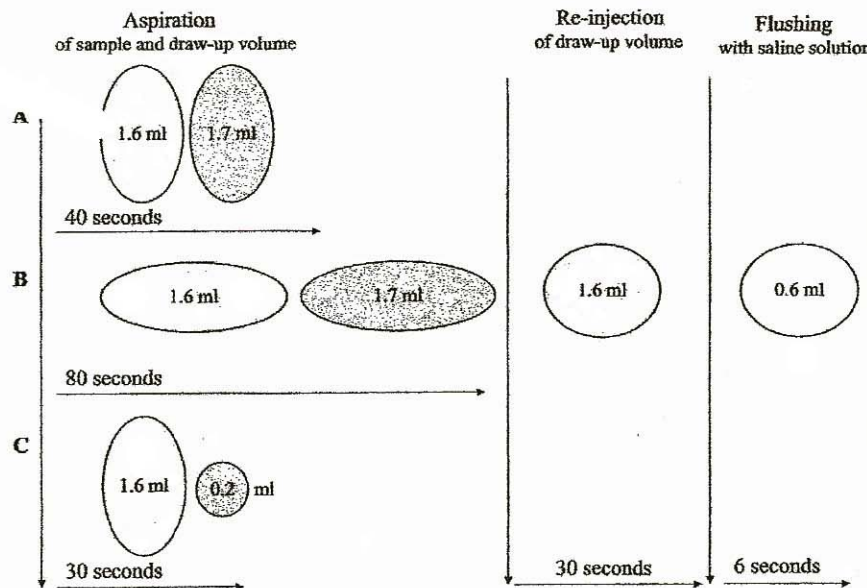

Figure 1. Protocol for the three different blood sampling procedures. The variable parameters are the time of aspiration and the sample volume. A) 40-s sampling with 1.7-ml sampling volume; B) 80-s sampling with 1.7-ml sampling volume; C) small-volume sampling with 0.2-ml sampling volume.

39 cases of 40-s versus 80-s sampling, 38 cases of 40-s versus smaller-volume sampling, and 37 cases of 80-s versus smaller-volume sampling.

Monitoring data could not be obtained during the full time of the measurement period in 23 measurements of pCO_2 values and in five measurements of arterial blood pressure.

O_2Hb

O_2Hb decreased significantly from baseline levels during aspiration, re-injection of the draw-up volume, and flushing with saline during all three procedures (Figure 2). O_2Hb was still significantly below baseline during the first 5 min after the end of the procedure in 40-s and 80-s sampling.

HHb

No significant changes in HHb occurred during any procedure (Figure 2).

CBV

CBV decreased significantly from baseline levels during all three types of sampling (Figure 2).

HbD

There was a highly significant decrease in HbD during all three types of sampling and all time periods of sampling (Figure 2).

Comparison of NIRS data between blood sampling procedures

Comparison between the different blood sampling procedures showed overall significant differences between the effects of taking a large or a small volume of blood, but no significant difference between 40-s and 80-s sampling (Figure 2).

Monitoring data

Heart rate. Heart rate increased slightly but significantly from baseline during all three blood sampling procedures (Table I).

Arterial oxygen saturation. Arterial oxygen saturation values, as measured by pulsoxymetry, did not change during the measurement period.

Tc-pCO₂. No changes occurred in tc-pCO_2 values during and after blood sampling.

Mean arterial blood pressure. Mean arterial blood pressure calculated over the time period from 30 s to 5 min after the end of blood sampling was not significantly different from baseline after 40-s sampling (before: mean 36.4 mmHg, SE 0.8; after: mean 37.3 mmHg, SE 0.9; $p = 0.1$). Mean arterial blood pressure increased slightly but significantly after 80-s sampling (before: mean 36.4 mmHg, SE 1.0; after: mean 37.8 mmHg, SE 1.1; $p = 0.007$), and after small-volume sampling (before: mean 36.8 mmHg, SE 1.2; after: mean 38.3, SE 1.3; $p = 0.01$).
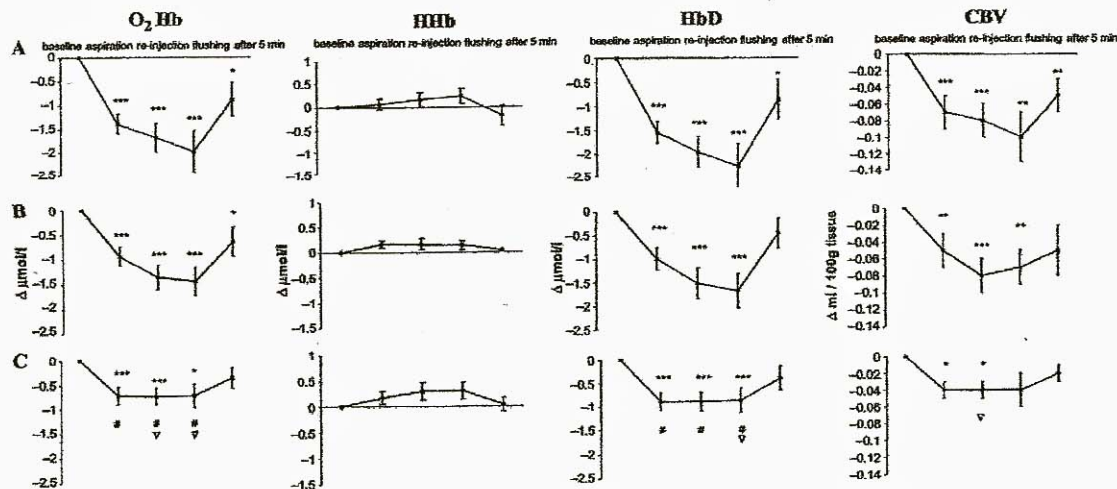

Figure 2. Changes in the NIRS parameters O_2Hb, HHb, HbD and CBV during 40-s sampling (A), 80-s sampling (B) and small-volume sampling (C) at the different time points of the sampling procedure. Significant changes as compared to baseline are marked by asterisks: ***$p < 0.001$; **$p < 0.01$; *$p < 0.05$. Significant differences between sampling procedures are marked by # (40-s sampling versus small-volume sampling) and V (80-s sampling versus small-volume sampling). There are no significant differences between 40-s sampling and 80-s sampling.

Table I. Heart rate (bpm, mean±SE) during blood sampling procedures.

	Baseline	Aspiration	Re-injection	Flushing	5 min after the procedure
40-s sampling	141.5±1.7	142.2±2.0 n.s.	143±1.9 $p=0.01$	141.1±2.5 n.s.	141.5±1.8 n.s.
80-s sampling	139.4±2.0	142.1±2.0 $p<0.0001$	142.1±1.9 $p<0.0001$	140.4±2.5 n.s.	140.5±2.0 n.s.
Small-volume sampling	142.1±1.7	143.5±1.7 $p=0.0005$	143.5±1.8 $p=0.0004$	143.2±1.9 $p=0.04$	142.9±1.9 n.s

Discussion

This study demonstrates that blood sampling from a UAC induces an inevitable decrease in CBV and cerebral oxygenation in preterm infants. In contrast to our expectations, reducing sampling velocity failed to prevent the reduction of oxygen supply to the preterm infant's brain associated with the blood withdrawal from a UAC. Sampling volume appears to be central in determining the magnitude of this decrease. Unfortunately, the draw-up volume constitutes a lower limit for efforts to reduce the total amount of blood withdrawn. Previous studies have shown that a minimum draw-up volume of 1.6 ml is required for accurate results [6]. Significant reductions of CBV and cerebral oxygenation were already observed at total volumes of 1.8 ml. Thus, decreasing the draw-up volume further would be necessary to prevent significant changes in cerebral oxygen supply associated with UAC sampling. This will require careful re-evaluation of the limits of the draw-up volume without compromising the quality of analysis. While there are limits to reducing draw-up volume, reducing the amount of blood necessary for laboratory analysis is more feasible. Both improved equipment and dedicated personnel are important to achieve this goal. While centralized analysis in large hospital laboratories may be more economical, technicians are not familiar with the small volumes of blood obtained from very-low-birthweight infants and may require special education. Following completion of this study, we have been able to cut the amount of blood necessary for standard determinations by more than 50%. We invited physicians and technical assistants from the laboratory to visit our unit and look at our unique patient population. Special care was then given to handling of the probes, tubes to ease rescue of as much serum as possible were introduced, and dilution of the serum is performed when the volume is insufficient.

CBV decreased significantly from baseline during all three types of sampling. In contrast to a previous study [4], where CBV decreased significantly during aspiration only, we have now been able to demonstrate a significant decrease from baseline until 5 min later (40-s sampling) and until flushing (80-s sam-

pling). However, as absolute values are in the same range, this effect might be explained by the higher number of infants included and the more stringent protocol causing less variance in data.

Changes in systemic haemodynamics during blood sampling were monitored by changes in heart rate and arterial blood pressure. As shown by the increase in heart rate during all three types of blood sampling, the loss of blood volume prompts counter-regulating mechanisms. While no significant changes in mean arterial blood pressure were recorded after 40-s sampling, mean arterial pressure increased significantly after 80-s sampling and after small-volume sampling. We speculate that counter-regulating mechanisms—the increase in heart rate and a hypothetical increase in vascular tone—might increase blood pressure so effectively that, after slower sampling or small-volume sampling, even the resulting blood pressure is above baseline.

There have been two other studies using NIRS, since our first study published in 2000 [4], to analyse the effects of UAC blood sampling on the preterm infant's brain [8,9]. Schulz et al. [9] assessed the effect of sampling velocity on changes in CBV and cerebral oxygenation. In contrast to the results of our present study, they demonstrated that slower blood sampling prevented a decrease in cerebral oxygenation in preterm infants. The study design differed from ours in several ways. Schulz et al. compared a sampling time of 20 s to a sampling time of 40 s. The slower sampling time corresponded to the faster sampling time in our study. While we have shown significant decreases in cerebral oxygenation and CBV during 40-s sampling as well as 80-s sampling, Schulz et al. only describe these changes during 20-s sampling. We assume that one reason for this discrepancy is the difference in main patient characteristics. Infants included in the study by Schulz et al. were more mature (median 30 vs 27 wk), their birthweight was higher (median 1170 g vs 965 g) and their clinical condition was described as stable. Only four of 20 were on mechanical ventilation as compared to 45 out of 48 in this study. Therefore, infants in our study might have been more prone to show alterations in cerebral haemodynamics and oxygenation. Bray et al. reported on the effects of withdrawal and

infusion via UACs in 16 preterm infants [8]. Infants were more mature and of higher birthweight than infants in our study, but they were all studied during a critical period of 24 h after birth, all were on mechanical ventilation, and 11 out of 16 were on inotropes. Withdrawal time for 3 ml of blood was 30 s. Re-infusion of the same blood volume was performed 4 min later over a 30-s period. CBV and cerebral oxygenation decreased significantly. Interestingly, the effect was blunted by ibuprofen. The substance was given for clinical purposes to 10 of the infants, and the study protocol repeated thereafter.

What are the conclusions of our study? Should we avoid blood sampling from UACs? The effect of sampling by radial artery catheters, which are used in some neonatal intensive care units as a first choice, has not been studied so far. As the total amount of blood withdrawn from circulation appears to be critical, strategies replacing UAC with umbilical venous catheter (UVC) sampling [8] or choosing a low-position UAC [10] have met with limited success. Bray et al. demonstrated that drawing blood from a UVC decreases CBV and HbD to an even more pronounced extent than sampling from a UAC [8]. Lott et al. used Doppler sonography to analyse the effects of blood withdrawal and infusion via a UAC [10]. Changes in blood flow velocities—a decrease during withdrawal and an increase during re-infusion—were less pronounced when performed from low-positioned UACs [10]. However, while UACs in the high position have been proven to be safe concerning intestinal blood supply [11,12], this has not been investigated for UACs in the low position, and other disadvantages of low-positioned UACs are obvious [13]. Heel lancing or venepuncture do not require draw-up volume but are fraught with pain, which itself carries the risk of derangement [2,3].

It is unclear at present whether the decrease in CBV and cerebral oxygenation observed during UAC blood sampling is of clinical importance. Remarkably, in the newborn beagle puppy, haemorrhagic hypotension preceding volume re-expansion is an adequate stimulus to produce intraventricular haemorrhage experimentally [14]. Blood sampling from UACs results in a similar sequence of events, but relatively smaller volumes are used. Furthermore, UAC blood sampling is a frequently performed procedure in sick infants, who are most prone to intraventricular haemorrhage.

In summary, we have demonstrated that sampling volume, not sampling velocity, determines drop in CBV and cerebral oxygenation induced by blood sampling from UACs. To avoid these potentially harmful effects, blood sampling should be restricted as much as possible.

References

[1] Volpe JJ. Neurology of the newborn, 4th ed. Philadelphia: WB Saunders; 2001.

[2] Upadhyay A, Aggarwal R, Narayan S, Joshi M, Paul VK, Deorari AK. Analgesic effect of expressed breast milk in procedural pain in term neonates: a randomized, placebo-controlled, double-blind trial. Acta Paediatr 2004;93: 518–22.

[3] Shah V, Ohlsson A. Venepuncture versus heel lance for blood sampling in term neonates. Cochrane Database Syst Rev 2004;18:CD001452.

[4] Roll C, Hüning B, Kaunicke M, Krug J, Horsch S. Umbilical artery catheter blood sampling decreases cerebral blood volume and oxygenation in very low birthweight infants. Acta Paediatr 2000;89:862–6.

[5] Wyatt J, Cope M, Delpy D, Wray S, Reynolds E. Quantification of cerebral oxygenation and haemodynamics in sick newborn infants by near infrared spectrophotometry. Lancet 1986;2:1063–7.

[6] Davies MW, Mehr S, Morley CJ. The effect of draw-up volume on the accuracy of electrolyte measurements from neonatal arterial lines. J Paediatr Child Health 2000;36: 122–4.

[7] Butt W, Gow R, Whyte H, Smallhorn J, Koren G. Complications resulting from use of arterial catheters: retrograde flow and rapid elevation in blood pressure. Pediatrics 1985;76: 250–4.

[8] Bray M, Stucchi I, Fumagalli M, Pugni L, Ramenghi L, Agosti M, et al. Blood withdrawal and infusion via umbilical catheters: effect on cerebral perfusion and influence of ibuprofen. Biol Neonate 2003;84:187–93.

[9] Schulz G, Keller E, Haensse D, Arlettaz R, Bucher HU, Fauchère JC. Slow blood sampling from an umbilical artery catheter prevents a decrease in cerebral oxygenation in the preterm newborn. Pediatrics 2003;111:e73–6.

[10] Lott JW, Conner GK, Phillips JB. Umbilical artery catheter blood sampling alters cerebral blood flow velocity in preterm infants. J Perinatol 1996;16:341–5.

[11] Roll C, Hanssler L. Effect of umbilical arterial catheters on intestinal blood supply. Acta Paediatr 1998;87:955–9.

[12] Shah JB, Bracero LA, Gewitz MH, Fish BG, Dweck HS. Umbilical artery catheters and blood flow velocities in the superior mesenteric artery: effect of insertion, removal, aspiration, and bolus infusion. J Clin Ultrasound 1998;26: 73–7.

[13] Barrington KJ. Umbilical artery catheters in the newborn: effects of position of the catheter tip. Cochrane Database Syst Rev 2000;2:CD000505.

[14] Godard-Finegold J, Armstrong D, Zeller R. Intraventricular haemorrhage following volume expansion after hypovolaemic hypotension in the newborn beagle. J Pediatr 1982; 100:796–9.

PubMed

Display Settings: Abstract

Umbilical artery catheter blood sampling volume and velocity: impact on cerebral blood volume and oxygenation in very-low-birthweight infants.

Roll C, Hüning B, Käunicke M, Krug J, Horsch S.

Department of Paediatrics, University Hospital, Essen, Germany. Cludia.Roll@kinderklinik-datteln.de

Abstract

AIM: Blood sampling from umbilical artery catheters decreases cerebral blood volume and cerebral oxygenation. The aim of this study was to assess the impact of sampling volume and velocity.

METHODS: Forty-eight infants, median birthweight 965 g (480-1500 g), median gestational age 27 wk (23-34 wk), were studied during routine blood sampling from umbilical artery catheters. The sampling procedure was performed following a strict protocol for draw-up volume (1.6 ml), sampling volume (1.7 ml or 0.2 ml), re-injection volume (1.6 ml) and flushing volume (0.6 ml), time of aspiration (40 s or 80 s), re-injection (30 s) and flushing (6 s). In each infant, sampling volume and aspiration time were subject to sequential variation in a randomized fashion (1.7 ml/40 s, 1.7 ml/80 s, 0.2 ml/30 s). Using near-infrared spectroscopy, changes in concentrations of cerebral oxygenated and deoxygenated haemoglobin were measured, and changes in cerebral blood volume and cerebral oxygenation were calculated.

RESULTS: During all three sampling procedures, oxygenated haemoglobin decreased significantly from baseline, whereas deoxygenated haemoglobin did not change. Correspondingly, a decrease in cerebral blood volume and cerebral oxygenation occurred. This decrease was not affected significantly by extending the sampling time from 40 s to 80 s, whereas it was blunted by reducing the amount of blood withdrawn.

CONCLUSION: Blood sampling from umbilical artery catheters induces a decrease in cerebral blood volume and cerebral oxygenation. The magnitude of the decrease depends on the blood volume withdrawn but not on sampling velocity.