Slow Blood Sampling From an Umbilical Artery Catheter Prevents a Decrease in Cerebral Oxygenation in the Preterm Newborn

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ABSTRACT. *Objective.* **Blood sampling from an umbilical artery catheter (UAC) placed in a high position (thoracal 6–9) has the potential to produce clinically significant changes in cerebral blood flow and, thereby, in cerebral oxygenation. This may contribute to cerebral impairment in preterm newborn infants. Therefore, we set up a study to determine the effects of different sampling speeds through a UAC on cerebral oxygenation in preterm infants.**

Methods. **Thirty pairs of measurements were conducted on 20 preterm infants (median gestational age: 30.14 weeks; median birth weight: 1170 g). For each infant, 2 blood samplings (both 2.3 mL, including flush volume) through the UAC in high position were taken at 2 different speeds (20 and 40 seconds) in alternating sequence. Cerebral oxygenation was measured noninvasively by near-infrared spectroscopy. Concentration changes in cerebral oxygenated hemoglobin (O_2Hb) and deoxygenated hemoglobin (HHb), along with the tissue oxygenation index (TOI; $O_2Hb/[O_2Hb + HHb] \times 100$), were recorded while blood was withdrawn and subsequently reinfused.**

Results. **A significant decrease in O_2Hb and TOI occurred during blood sampling within 20 seconds (median ΔO_2Hb: −1.5 μmol/L; range: −4.1–2.3; median ΔTOI: −0.6%; range: −6.3–2.3), whereas HHb increased (median ΔHHb: 0.4 μmol/L, range: −1.1–3.9). No significant change was found in O_2Hb, HHb, and TOI when sampling time was extended to 40 seconds.**

Conclusion. **Our results show that blood withdrawal over 20 seconds from a UAC in high position significantly decreases cerebral O_2Hb and TOI in preterm infants. Prolonging sampling time to 40 seconds can prevent this phenomenon.** *Pediatrics* **2003;111:e73–e76. URL: http://www.pediatrics.org/cgi/content/full/111/1/e73;** ***near-infrared spectroscopy, cerebral tissue oxygenation, neonate, tissue oxygenation index.***

ABBREVIATIONS. UAC, umbilical artery catheter; NIRS, near-infrared spectroscopy; TOI, tissue oxygenation index; O_2Hb, oxygenated hemoglobin concentration; HHb, deoxygenated hemoglobin concentration.

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Neonatal mortality has markedly decreased in the past decades because of better prenatal fetal care and, postnatally, because of the ever-expanding diagnostic and therapeutic means available to neonatologists. The limit of viability, which was approximately 28 weeks' gestation 10 years ago, has been constantly lowered to below 26 weeks, with a current 52% survival rate for liveborn infants who are born at 25 weeks.[1] Unfortunately, the decrease in mortality has not been accompanied by a decrease in mid- and long-term morbidity affecting especially the neurodevelopmental outcome. If prenatal damage to the central nervous system can frequently not be prevented, then everything needs to be done to decrease further all possible risks of postnatal cerebral lesions in infants who undergo intensive care, the most vulnerable among these being preterm infants.

The vast majority of very preterm and severely ill newborn infants are monitored using an umbilical artery catheter (UAC). This allows for continuous blood pressure monitoring, convenient arterial blood gas measurements, and painless blood sampling, with only little disturbance to the infant. However, UACs have been associated with complications such as local vascular (blanching or cyanosis of feet or toes)[2–4] or more extensive ischemic compromise,[4,5] aortic thrombi,[2,5–7] necrotizing enterocolitis,[5] arterial hypertension,[2] hematuria,[5] and hyperglycemia.[8–13] As high-placed UACs have been shown to be safer with regard to clinical vascular complications, many institutions prefer the high-positioned (thoracal 6–9) UAC. A recent Cochrane Review concluded that there seems to be no evidence to support the use of low-placed UACs, and, therefore, high catheters should be used exclusively.[14] In our institution, UACs are pulled back to a low position only in the presence of persistent hyperglycemia with a high-placed UAC.

Recently, it has been shown that sampling blood from a high-positioned UAC may potentially decrease cerebral blood volume and cerebral oxygenation in very low birth weight infants.[15] It is unknown whether this is caused by the volume of withdrawn blood or by the blood sampling rate. To determine whether different speeds of blood sampling via a UAC might affect or influence changes in cerebral oxygenation in sick preterm newborns who undergo intensive care, we set up this study to determine whether the sampling speed per se could

influence cerebral tissue oxygenation. We hypothesized that by extending the sampling time, it would be possible to avoid significant alterations in cerebral oxygenation. We explored this issue by using near-infrared spectroscopy (NIRS), a noninvasive method to evaluate changes in cerebral tissue oxygenation, while a fixed amount of blood was withdrawn from a high-positioned UAC.

METHODS

After obtaining approval from the local ethical committee and written parental consent, we enrolled 20 neonates who were admitted to the neonatal intensive care unit of the University Hospital (Zurich, Switzerland). Only preterm infants (<37 completed weeks' gestation) with a UAC (3.5 Ch, filling volume 0.15 mL; Sherwood Medical, Tullamore, Ireland) in high position were included in this study. The position (thoracal 6–9) was confirmed by radiograph. To exclude measurement effects as a result of hemodynamic instability or of changes in vasoactive dosing, we excluded infants who were in an unstable hemodynamic situation or needed vasoactive drugs. Hemodynamic stability was defined by a stable arterial blood pressure as continuously measured and displayed on screen, by a normal heart rate without any arrhythmia, by normal capillary refilling, and by normal urine production.

A NIRS optode (Hamamatsu Photonics, Hamamatsu City, Japan), consisting of an emitter and a receiver of near-infrared light with an interoptode distance of 50 mm, was placed on the skin overlaying the temple of the newborn, taking care to avoid the region over the sagittal sinus. Interference from light was prevented by shielding the optode. The light emitter optode carried 4 laser diodes operating at 775, 810, 847, and 919 nm, and the detector optode had 3 photodiodes, mounted in parallel with increasing distances, which permitted the calculation of an absolute tissue oxygenation index (TOI) value. The underlying technical principles of spatially resolved spectroscopy has been previously described in detail by Matcher and Suzuki.[16,17] The NIRS probe was connected to a precalibrated measuring unit (NIRO-300, Hamamatsu Photonics).

NIRS measurements were performed without interruption at a sampling rate of 0.5 Hz during the whole procedure of blood withdrawing and reinfusing, the same being true for transcutaneous arterial oxygen saturation (Nellcor 395, Nellcor Inc, Hayward, CA). Because a single lumen UAC was used, mean arterial pressure was recorded immediately before and after the blood sampling and catheter flushing procedure. After steady-state conditions were obtained for approximately 10 minutes, blood samples were withdrawn from the UAC at 2 different speeds, with the sampling speed order following an alternating sequence. For the 20-second sampling, 2 mL was aspirated in 15 seconds to fill the catheter with blood, and an additional 0.3 mL was taken in 5 seconds for the laboratory test. The surplus blood volume (2 mL) was then reinfused into the infant before the system was flushed with 2 mL of saline. For the 40-second sample, a similar procedure was undertaken, except that the first 2 mL was withdrawn over 30 seconds, and the blood sample itself (0.3 mL) was withdrawn over another 10 seconds. Both blood samples of the second sampling procedure were then returned to the infant, and the catheter afterward was flushed as usual. Between each sampling procedure, at least 10 minutes was allowed to elapse to permit all parameters to return to baseline conditions. Changes in the therapeutic and ventilator settings were avoided during the whole measurement, including the baseline and the 2 withdrawal recordings. Demographic and physiologic data were also recorded.

Data Analysis

All continuously measured data were simultaneously shown on the optical display and recorded onto a computer and subsequently analyzed off-line. For each analysis, a baseline sequence of 2 minutes was used. The time of blood withdrawal used for calculation was defined as the time between the 2 digital markers set at the beginning and at the end of the sampling procedure. The 10th and 90th percentile values of oxygenated hemoglobin concentration (O_2Hb), deoxygenated hemoglobin concentration (HHb), TOI, arterial oxygen saturation, and mean arterial pressure and their median values were calculated for the baseline condition. During withdrawal, the 90th percentile of the data set in case of an increase and the 10th percentile of the measurements in case of a decrease and their median values were used for calculation. This method was chosen to obtain more robust data by avoiding the determination of only 1 single incidentally extreme measured value as the lowest or highest point of the whole procedure. The Wilcoxon signed rank test was used to detect significant changes in O_2Hb, HHb, or TOI during the rapid or during the slow sampling procedure. For decreasing parameters such as O_2Hb and TOI, the 10th percentile values of the baseline and of the maximal decrease were compared. For the observed increase in HHb, the difference between the 90th percentile values of the baseline and of the maximum increase were compared. For the reasons already mentioned, the data beyond the 10th and 90th percentiles were not included in the analysis. $P < .05$ was considered as statistically significant. Calculations were performed using StatView (version 5.01 for Windows, SAS Inc, Cary, NC).

RESULTS

A total of 30 pairs of measurements were performed on 20 preterm infants. Five pairs of measurements had to be omitted because of artifacts caused by the movements of the infant, leaving 25 pairs of measurements for analysis in 20 preterm infants. Five newborns contributed to a second set of data. All preterm infants included were under stable clinical conditions during the measurements. The clinical data are shown in Table 1.

Figure 1 depicts the changes in O_2Hb, HHb, and TOI during a 20-second withdrawal and subsequent reinfusion and the changes when withdrawal time was extended to 40 seconds in 1 infant studied. Table 2 summarizes these results by reporting the median and range values of the changes in O_2Hb, HHb, and TOI during the rapid and during the slow blood sampling procedure. O_2Hb and TOI decreased significantly when blood was sampled over 20 seconds while, simultaneously, HHb increased. No such significant differences were found for O_2Hb, HHb, or TOI at the 40-second withdrawal time (Table 2). Moreover, there were no significant changes in cerebral O_2Hb, HHb, and TOI during reinfusion of the withdrawn volume and the flushing volume.

DISCUSSION

The present study shows that in preterm infants, withdrawing blood over 20 seconds from a high-positioned UAC significantly decreases cerebral O_2Hb and TOI, with a simultaneous increase in HHb. These phenomenon could be prevented when sampling time was prolonged to 40 seconds.

These results suggest that rapidly withdrawing blood from a catheter in a high aortic position induces a significant fall in oxygenated blood supply to the central nervous system, the potential mechanism acting via a rapid steal of blood that cannot be com-

TABLE 1. Patient Characteristics

	Median	Range	Number
Gestational age (wk)	30⅐	25⅗–35⅗	
Birth weight (g)	1170	650–2540	
Gender (male/female)			16/9
Assisted ventilation			4
Nasal CPAP			17
Spontaneous breathing			4

CPAP indicates continuous positive airway pressure.

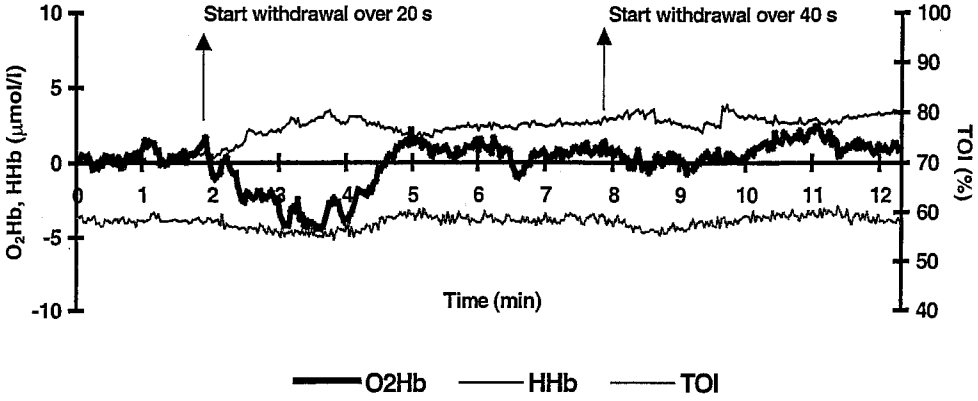

Fig 1. Original NIRS tracing during blood sampling at 2 different speeds (20 and 40 seconds) in 1 infant studied.

TABLE 2. Changes During the Rapid and the Slow Sampling Procedure

	Withdrawal Over 20 s		*P* Value	Withdrawal Over 40 s		*P* Value
	Median	Range		Median	Range	
Δ O_2HB (μmol/l)	−1.5	−4.1 to 2.3	.002	−0.5	−2.1 to 4.4	.113
Δ HHb (μmol/l)	0.4	−1.1 to 3.9	.018	−0.1	−1.5 to 2.4	.946
Δ TOI (%)	−0.6	−6.3 to 2.3	.030	−0.5	−4.2 to 1.5	.055

pensated for in time. The observed effect may well be age dependent, as the relationship between the withdrawn blood volume and the circulating blood volume will certainly change with gestational and postnatal age. Although our study did not include term infants, it may well be that the observed decrease in cerebral O_2Hb would not occur in term infants with a higher circulating blood volume, as the withdrawn 2.3 mL of blood would represent only a small fraction of their total circulating blood volume. As depicted in Fig 1, the rapid withdrawal over 20 seconds was followed by a fall in O_2Hb that lasted for 2.5 minutes. Although this was not consistently observed throughout our study, this nevertheless demonstrates that even short alterations in cerebral blood supply may be followed by lasting effects in cerebral oxygenation.

Alterations in cerebral hemodynamics during sampling blood from UACs have been shown by some investigators, primarily with the intention to study the differences between sampling from umbilical catheters in high or in low positions.[14,18] None of the these studies, however, investigated the influence that the duration of blood sampling may have on cerebral oxygenation. Lott et al[18] described the impact of blood sampling procedure over 20 seconds from high UAC on cerebral blood flow velocity, as measured by cerebral ultrasound. Using NIRS, Roll et al[15] also investigated the effect of blood sampling from high UAC and found a significant decrease in cerebral blood volume and cerebral oxygenation. Their sampling procedure, however, was not performed within a set time but rather done "as usual." As a consequence, their blood sampling durations spread over a wide range, between 26 and 75 seconds, with a median of 40 seconds. This may explain why our results are not in keeping with their findings, as we did not observe a significant decrease in O_2Hb when sampling time was extended to 40 seconds. This discrepancy may also be related to several other methodological differences. For example, the volume of blood withdrawn was not standardized in their study, showing a range between 0.4 and 3.0 mL. In our study, not only were the sampling times set at 2 fixed values, namely at 20 and 40 seconds, but also the sampling volumes were kept identical over the whole study, with each infant being its own control. Importantly, we did not observe any significant changes in cerebral O_2Hb, HHb, and TOI during reinfusion of the withdrawn volume and of the subsequent flushing volume. The reinfusion time was not fixed, but our recordings show that reinfusion was not accompanied by an alteration in oxy- or deoxyhemoglobin. The explanation for this could be that the reinfusion of these small flush volumes encounters a strong opposite aortic flow that, with perhaps the exception of a very quick bolus injection or a greater flush volume, tends to dampen the hemodynamic effects on cerebral perfusion.

To our knowledge, this is the first study performed in preterm infants to evaluate the impact of various durations of the blood sampling procedure from high UAC on cerebral oxygenation under controlled conditions of withdrawal time and volume. Although the clinical importance of a short decrease in cerebral oxygenation, as observed during fast blood sampling, is not quite clear, our results add an additional means of further reducing potential risk factors for cerebral impairment in tiny infants already at high risk of mid- and long-term neurologic disabilities. As our constant aim should be to reduce every potential harm that our various interventions may have on these very premature and sick infants, these findings may be of clinical importance considering that these sampling procedures are routinely and repetitively performed on preterm infants who undergo neonatal intensive care. Furthermore, prolonging sampling time is an easy alteration to make to

routine practices, and because it has the potential to improve further the daily care of these fragile infants, it will certainly be well understood and taken up by the nursing staff.

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