Umbilical Arterial Blood Sampling Alters Cerebral Tissue Oxygenation in Very Low Birth Weight Neonates

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Objective To evaluate the magnitude, consistency, and natural history of reductions in cerebral regional tissue oxygenation ($CrSO_2$) during umbilical arterial (UA) blood sampling in very low birth weight neonates.

Study design Data were collected during a prospective observational near-infrared spectroscopy survey conducted on a convenience sample of 500-1250 g neonates during the first 10 postnatal days. A before-after analysis of UA blood sampling effects on $CrSO_2$ absolute values and variability was performed. The present analysis was not designed a priori and was conducted following the bedside observation of $CrSO_2$ decrements contiguous with UA blood draws.

Results Fifteen very low birth weight neonates had 201 UA blood draws. Baseline $CrSO_2$ (mean ± SEM) decreased following UA blood sampling, from 70 ± 1% to a nadir of 63 ± 1% ($P < .001$) occurring 4 ± 3 (range 2-24) minutes following blood draws. $CrSO_2$ subsequently increased to 70 ± 1% ($P < .001$ compared with nadir) at 10 ± 4 (range 4-28) minutes following UA blood sampling. Coefficients of variation (mean ± SEM) increased from 0.02 ± 0.001 at baseline to 0.05 ± 0.004 ($P < .001$), followed by a decrease to 0.03 ± 0.003 ($P < .001$ for all comparisons), thus denoting increased $CrSO_2$ variability following UA blood sampling.

Conclusions UA blood sampling is associated with significant $CrSO_2$ decrements with increased variability over clinically significant intervals. Whether these changes impact complications of prematurity, including intraventricular hemorrhage and periventricular leukomalacia, remain unknown. *(J Pediatr 2015;167:1013-7).*

In very low birth weight (VLBW) neonates, umbilical arterial (UA) catheterization is a commonly performed procedure for the purposes of blood pressure monitoring, fluid and medication administration, and blood sampling procedures.[1-4] In the neonatal intensive care unit (NICU), the convenience of UA catheters has resulted in their ubiquitous usage, with UA blood sampling often performed multiple times daily during the first postnatal days among this patient population.[2-5]

Previous studies have evaluated the effects of variations in UA blood sampling techniques, including blood volume and sampling duration, on cerebral regional tissue oxygenation ($CrSO_2$) as measured using near-infrared spectroscopy (NIRS).[6-9] However, no reports describe the natural history of these changes in $CrSO_2$ in response to the routine undisturbed performance of UA blood draws in the NICU. Such information might have important implications for further understanding the pathophysiology and management of important neonatal adverse outcomes such as intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL). Though commonly performed, whether UA blood draws are associated with transient or prolonged changes in $CrSO_2$ remains unknown.

In this non-a priori analysis of prospectively collected NIRS data, we describe the magnitude, duration, and recovery characteristics of changes in $CrSO_2$ associated with UA blood sampling among VLBW neonates. We hypothesized that our data will replicate previously reported decrements in $CrSO_2$ and will additionally demonstrate substantial variability between individual UA blood sampling events.

Methods

This prospective, observational cohort study was approved by the Institutional Review Board of New York Medical College and the Maria Fareri Children's Hospital as posing minimal risk to subjects. $CrSO_2$ data were acquired during a normative survey of VLBW neonates by observing baseline values and changes occurring with routine clinical practices

$CrSO_2$	Cerebral regional tissue oxygenation
IVH	Intraventricular hemorrhage
NICU	Neonatal intensive care unit
NIRS	Near-infrared spectroscopy
PVL	Periventricular leukomalacia
UA	Umbilical arterial
VLBW	Very low birth weight

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Supported in part by Somanetics, Troy, MI (now Medtronic, Boulder, CO). The authors declare no conflicts of interest.

http://dx.doi.org/10.1016/j.jpeds.2015.08.016

over the first 10 postnatal days.[10-12] These data were then analyzed in a post hoc (non-a priori) fashion following the observation of diminished $CrSO_2$ contiguous with UA blood draws.

All neonates were admitted to the 50-bed, level IV Regional Perinatal Center at Maria Fareri Children's Hospital of Westchester Medical Center from a catchment area of 23 000 annual births. A convenience sample of VLBW neonates were enrolled within the first 72 postnatal hours and were monitored for 7 days each. Inclusion criteria restricted enrollment to patients with birth weights less than 1250 g. Newborns with birth weights less than 500 g, major congenital or chromosomal anomalies, congenital heart disease, 5-minute Apgar score <3, not expected to survive for the 7-day study duration, or showing evidence of extremely immature skin (eg, gelatinous, translucent, and/or poorly keratinized) were excluded. Written informed consent was obtained from parents prior to enrollment.

After delivery and initial stabilization, continuous $CrSO_2$ monitoring was started using the INVOS 5100C Cerebral/Somatic Oximeter with OxyAlert NIRSensors–Infant Model IS (neonatal) (Covidien, Mansfield, Massachusetts). This device assesses the regional oxygenation status of underlying venous, arterial, and capillary hemoglobin sources using a 75:20:5 respective ratio[10-16] at a manufacturer-reported signal depth of 1.5 cm beneath the monitoring probe.[11,12,17] Regional tissue oxygenation is then expressed as a proportion of oxygenated hemoglobin to total hemoglobin (oxyhemoglobin/[oxyhemoglobin + deoxyhemoglobin]).[10-16] Consistent with numerous previous studies, $CrSO_2$ monitoring leads were placed transversely across subjects' foreheads.[10-14,18-25]

In all subjects, NIRS monitoring leads were placed atop nonadhesive Mepitel gel-impregnated gauze strips (Mölnlycke Health Care, Göteborg, Sweden) to avoid adhesive contact with fragile neonatal skin. This technique was confirmed by the Somanetics (now Covidien) laboratories as having no effect on NIRS signal integrity.[10-12,21] During each 24-hour monitoring period, leads were removed for a 30-minute "skin resting period," and skin integrity was evaluated.

NICU Care

All NICU care, including decisions regarding UA blood sampling, was by the attending neonatologist. Neonates were managed according to predefined NICU ventilator, fluid and electrolyte management, and feeding protocols.[26-28] No prospective decisions were made based on NIRS results.

UA Catheterization and Blood Sampling Procedures

All UA catheters were placed per attending discretion shortly following birth as required based on clinical circumstances. UA catheter tips were maintained in the "high" position and confirmed as between the sixth and ninth thoracic vertebrae on chest radiograph. All UA blood draws were performed at the discretion of the NICU attending and clinical care team for a variety of clinical indications.

Individual UA blood draws were performed by NICU bedside nurses and consisted of several phases: (1) withdrawal of catheter dead space blood; (2) withdrawal of laboratory sample blood; (3) autotransfusion of catheter dead space blood; and (4) normal saline flush. Per NICU guidelines, UA blood draws are typically completed in approximately 1 minute, though this varies depending on the volume of blood required for testing. As this protocol was not designed a priori to evaluate $CrSO_2$ data with regard to UA blood sampling, these procedures were all performed as a "routine" component of bedside care, allowing for person-to-person practice variability in the varied UA blood sampling procedural components. Thus, specific elements of the UA blood sampling procedure, such as the volumes of catheter dead space and laboratory sample blood drawn and/or saline used, along with the duration of the individual procedural components, were not recorded in this study.

Data Collection and Analyses

Demographic, antenatal, and birth history data were abstracted from patient medical records. The dates and times of individual UA blood draws were from patient bedside flow sheets. $CrSO_2$ data were collected in a raw data format on the INVOS 5100C monitor (Covidien) every 6 seconds; the most frequent data sampling setting offered by this device.[10-12]

Given previously published $CrSO_2$ variability data, very short data averaging intervals were employed to minimize $CrSO_2$ signal variability as a potential confounder in our analysis.[12] Baseline $CrSO_2$ was analyzed over 2-minute intervals prior to each UA blood draw. $CrSO_2$ data were then averaged over 2-minute epochs throughout the UA sampling procedure and following completion of each blood draw until recovery to baseline or to the establishment of any oxygenation plateau lasting for 10 minutes. These data were then subdivided into $CrSO_2$ baseline, nadir, and recovery values for each UA blood draw. Time to nadir and recovery of baseline (or plateau) $CrSO_2$ following UA blood draws was also noted.

Statistical Analyses

Individual $CrSO_2$ baseline, nadir, and recovery data were compared in a before-after approach using repeated-measures ANOVA with Dunnett post hoc analyses referring to the baseline $CrSO_2$ in addition to Bonferroni correction to evaluate for persistent effects (eg, differences between nadir and recovery). Coefficients of variation (SD/mean) were calculated for the baseline, nadir, and recovery data sets and similarly compared. As a comparison between "first" and "repeat" UA blood draws demonstrated no differences in $CrSO_2$ baseline value, variability, and presence/degree of decrement, each UA blood draw was considered as an independent event for statistical analyses. Statistical significance was designated as a P value of <.05. All statistical analyses were performed using SigmaStat v 12.0 (Aspire Software International, Ashburn, Virginia).