Impaired cerebral autoregulation in preoperative newborn infants with congenital heart disease

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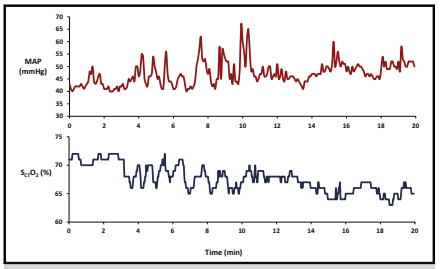
ABSTRACT

Objectives: To characterize cerebral autoregulation (CA) in preoperative newborn infants with congenital heart disease (CHD).

Methods: This was a prospective, pilot study of term newborns with CHD who required intensive care. Continuous mean arterial blood pressure (MAP), cerebral tissue oxygen saturation ($S_{CT}O_2$) via near-infrared spectroscopy, and arterial oxygen saturation (SaO_2) were collected. Significant low-frequency coherence between MAP and $S_{CT}O_2$ was used to define impaired CA in 20-minute epochs. Cerebral fractional tissue oxygen extraction (FTOE) = $(SaO_2 - S_{CT}O_2)/SaO_2$ was calculated. Spearman's and rank bi-serial correlations and logistic linear models accounting for multiple measures were used to identify associations with impaired CA and coherence.

Results: Twenty-four term neonates were evaluated for 23.4 ± 1.8 hours starting the first day of life. Periods of SaO_2 variability >5% were excluded, leaving 63 ± 10 epochs per subject, 1515 total for analysis. All subjects demonstrated periods of abnormal CA, mean 15.3% ± 12.8% of time studied. Significant associations with impaired CA per epoch included greater FTOE ($P = .02$) and lack of sedation ($P = .02$), and associations with coherence included greater FTOE ($P = .03$), lack of sedation ($P = .03$), lower MAP ($P = .006$), and lower hemoglobin ($P = .02$).

Conclusions: Term newborns with CHD display time-varying CA abnormalities. Associations seen between abnormal CA and greater FTOE, lack of sedation, and lower hemoglobin suggest that impaired oxygen delivery and increased cerebral metabolic demand may overwhelm autoregulatory capacity in these infants. Further studies are needed to determine the significance of impaired CA in this population. (J Thorac Cardiovasc Surg 2017;154:1038-44)



Impaired cerebral autoregulation: arterial pressure and cerebral blood flow vary together.

Central Message

Full-term newborn infants with severe forms of congenital heart disease display pressure passive cerebral perfusion in a spectrum similar to what has been described in premature newborns.

Perspective

This prospective pilot study found impaired cerebral autoregulation in preoperative infants with full-term congenital heart disease. Our findings highlight the importance of preoperative hemodynamic monitoring in a population of neonates known to have abnormalities of brain maturation and cerebral oxygen delivery, who are highly vulnerable to cerebral insult and neurodevelopmental impairment.

See Editorial Commentary page 1045.

Cerebral autoregulation (CA) is the body's normal process of regulating constant blood flow to the brain despite changing perfusion pressure. When CA is impaired, a change in blood pressure results in a parallel change in cerebral blood flow. Abnormalities of CA have been found in sick premature infants,[1-5] a group at high risk for brain injury, and have been found to correlate with development of intracranial hemorrhage and mortality.[2,6,7] Abnormal CA also has been linked adverse neurologic outcomes in newborns with hypoxic-ischemic encephalopathy and children with traumatic brain injury.[8,9] Cerebral oximetry via transcranial near-infrared spectroscopy (NIRS), which measures the tissue oxygen saturation of the brain, provides

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Abbreviations and Acronyms

CA = cerebral autoregulation
CHD = congenital heart disease
CI = confidence interval
$ETCO_2$ = end-tidal carbon dioxide
FTOE = cerebral fractional tissue oxygen extraction
MAP = mean arterial pressure
NIRS = near-infrared spectroscopy
OR = odds ratio
SaO_2 = systemic arterial oxygen saturation
$S_{CT}O_2$ = cerebral tissue oxygen saturation

a noninvasive surrogate of cerebral blood flow,[10-13] and correlations between changes in continuous cerebral oximetry measurements during spontaneous fluctuations of blood pressure can be used to evaluate CA on a dynamic basis.[2-4] Soul and colleagues[3] studied low birth weight premature newborns using this technique and found that 97% of subjects had periods of impaired CA, with abnormalities seen during 20% ± 10% of the time studied.

Full-term infants with congenital heart disease (CHD) have been shown to display findings of brain immaturity similar to those of premature infants, as well as patterns of preoperative brain injury and ischemia thought to be secondary to increased vulnerability of immature white matter,[14-17] and may display neurologic abnormalities even before undergoing cardiac surgery.[18] The reasons for neurologic insult in the CHD population are likely multifactorial, involving in utero fetoplacental circulation and genetic factors, as well as postnatal and perioperative insults secondary to unstable hemodynamics and medical interventions. Fetuses with severe forms of CHD have circulatory disturbances that alter oxygen and substrate delivery to the developing brain.[19] Midgestation fetuses with CHD frequently demonstrate abnormal patterns of cerebral blood flow, including lower cerebrovascular resistance, which suggests an active process of CA to redirect blood flow towards the brain.[20-22] Abnormalities of cerebral blood flow[23-25] and cerebral oxygen delivery[26] in neonates with CHD also have been found. Bassan and colleagues[27] evaluated CA in infants less than 7 months of age with CHD after cardiac surgery and found disturbed CA in 51% of subjects on a fluctuating basis, with abnormalities seen during about 15% of the time studied. CA has not been studied in preoperative newborns with CHD. The aim of this study was to characterize CA in full-term newborn infants with unpalliated complex CHD and examine what factors are associated with disturbed CA. We hypothesized that full-term newborn infants with CHD would display impaired CA.

METHODS

This was a prospective, observational pilot study to evaluate CA in full-term newborns with CHD. Eligibility criteria included infants with severe CHD, defined as defects requiring admission to the Cardiovascular Intensive Care Unit at Cincinnati Children's Hospital Medical Center within the first 24 hours of postnatal life, between October 2011 and December 2012. Subjects were excluded if less than 36 weeks' gestational age, if major chromosomal abnormalities were found, and if they did not require a clinically indicated indwelling arterial catheter for continuous measurement of blood pressure. The study was approved by the Institutional Review Board at Cincinnati Children's Hospital Medical Center (#2011-1868), and informed consent was obtained.

Mean arterial pressure (MAP), measured via pressure transducer connected to an indwelling arterial catheter, and preductal systemic arterial saturation (SaO_2), measured from a pulse oximeter, were obtained as part of routine clinical care and were recorded continuously with a sampling frequency of 0.2 Hz with BedMasterEx software (Excel Medical Electronics, Jupiter, Fla). Cerebral oximetry was recorded with a FORE-SIGHT Absolute Oximeter with Small Dual Sensor (CAS Medical Systems, Inc, Branford, Conn). The FORE-SIGHT monitor uses laser light to project 4 wavelengths into the brain to calculate the absolute cerebral tissue oxygen saturation ($S_{CT}O_2$) with the ratio of oxygenated to total hemoglobin. The sensor was applied unilaterally to the forehead of the neonate and recorded continuously with a sampling frequency of 0.5 Hz, time-synced to BedMasterEx file. Data were collected for up to 24 hours starting within the first 24 hours of life. Data were filtered for artifact and separated into 20-minute epochs of uninterrupted recordings for coherence analysis. Clinical care of the infants continued under the direction of the primary cardiovascular intensive care unit team without modification by investigators. Additional variables collected included continuous end-tidal carbon dioxide ($ETCO_2$), which was available only for intubated subjects, values of arterial blood gas and hemoglobin measurements obtained clinically during the study period, medications administered, presence and type of respiratory support, cardiac procedures which took place during the study period, cardiac and extracardiac diagnoses, results of preoperative brain imaging, chromosomal and microarray analysis when available, gestational age, delivery characteristics, Apgar scores, anthropomorphic data including height, weight, and head circumference.

Continuous data for each epoch were analyzed with custom software written in MatLab (MathWorks, Natick, Mass). $S_{CT}O_2$ and MAP signals were detrended and normalized to remove DC signal. The $S_{CT}O_2$ data were downsampled to 0.2 Hz. Correlation was measured for each 20-minute epoch using 10-minute windows and 50% overlap using Welch's periodogram method,[28] with coherence integrated for the very low-frequency range of 0.003 to 0.04 Hz with a 1024 sample fast Fourier transform, and a coherence score was generated for each epoch. The coherence score describes the degree of correlation between the waveforms at a given frequency range. Minor fluctuations in blood pressure are expected even if the patient is stable, and with these fluctuations the $S_{CT}O_2$ should not vary with MAP if CA is intact. Thus, coherence between $S_{CT}O_2$ and MAP indicates impaired CA. Coherence of 1.0 indicates perfect correlation, and coherence of 0 indicates a complete lack of correlation.

By the use of an F test and the aforementioned parameters, the threshold for significant coherence for $P = .05$ was determined to be 0.58.[29] Therefore, very low-frequency coherence >0.58 defined abnormal CA for our analysis. Examples of waveforms demonstrating high and low coherence are given in Figures 1 and 2. Cerebral fractional tissue oxygen extraction (FTOE) was calculated with the equation: $FTOE = (SaO_2 - S_{CT}O_2)/SaO_2$. For each epoch the mean and standard deviation of MAP, $S_{CT}O_2$, SaO_2, FTOE, and $ETCO_2$ when available were calculated. Epochs with SaO_2 variability >5% were excluded from analysis to minimize the effect of varying SaO_2 on $S_{CT}O_2$. Percentage of epochs with abnormal CA (coherence > 0.58) was calculated per patient.