THE UNIVERSITY OF ARIZONA
COLLEGE OF MEDICINE PHOENIX

Non-Invasive Regional Oxygen Saturation Measurement in the Preterm Neonate with Applications to the Study of PDA

Laura Marrs, 2012, University of Arizona College of Medicine Phoenix

ABSTRACT

This study describes the establishment of normative values for cerebral and renal regional tissue oxygenation in the preterm neonate. This is the first step for studying other relationships of regional oxygenation, such as any potential differences between cerebral and renal regional oxygenation in infants with patent ductus arteriosus (PDA), a hypothesized difference secondary to ductal steal.

INTRODUCTION

The dramatic change in circulation patterns following delivery may be problematic for preterm infants. Circulation in the fetus is successful because a large supply of the blood from the pulmonary artery is transferred to the aorta by the ductus arteriosus. Typically in the term infant, the ductus arteriosus gradually closes 10-15 hours after birth, which allows for the deoxygenated blood that is returned to the right side of the heart to pass properly into the pulmonary circulation to become oxygenated. In preterm neonates, this process takes a longer period of time. If the ductus arteriosus fails to close, pulmonary overcirculation may develop.(Welty 2009)

Regarding monitoring, a technology known as near infrared spectroscopy (NIRS) is allowing for measurement of a regional venous saturation of oxygen. With the use of this technology, regional perfusion may be inferred. (Somanetics 2005)

NIRS has been previously applied to PDAs, especially as a screening tool, but there has not been a study comparing the regional oxygen saturation to established normative values. This project sought to establish those values, and to find if the mean rSO2 readings followed a linear trend over a period of five days. It is hypothesized that the difference between cerebral and renal oxygen saturation would be greater in an infant with PDA due to the decrease in oxygenation of the kidney secondary to ductal steal from post-ductal organs.

METHODS

For the normative value study, the original goal was to enroll 25 premature infants between 28-32 weeks of gestation in order to collect 14 recordings of 24 hours of data from a cerebral and somatic regional oximeter after consent from their guardians. Subjects were to be excluded from the study if they had any major congenital anomaly, were withdrawn by their guardian, received vasopressor medication, experienced asphyxia, or if they had a five minute APGAR score less than seven. Following consent, infants were resuscitated and managed following the standard of care, regardless of participation status in the study. Then a regional oximeter was applied over the forehead and over the renal area, with the INVOS regional oximeter device blinded to the healthcare providers. Continuous data was collected and analyzed to establish normative values of regional oxygenation in the preterm neonate.

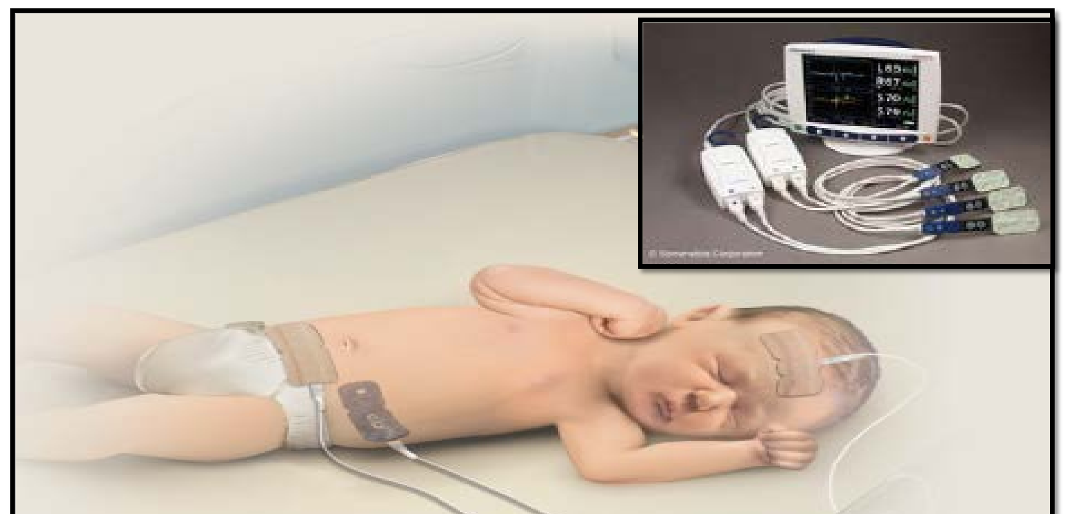

Figure 1: Example of INVOS Placement

RESULTS

The data consist of repeated rSO2 measurements on nine pre-term patients. Cerebral and somatic readings were taken every five seconds for days 2 through 6 of each patient's life. The patients represent a sample from the population of pre-term infants, suggesting that the patients should be treated as random effects. The correlation of observations must be taken into account to obtain valid standard errors.

Figure 2 presents cerebral readings at a rate of one measurement per hour. The mixed-model estimate for the mean cerebral reading is 77.5189 with a standard error of 1.9220 on 8 degrees of freedom, yielding a 95% confidence interval of (73.0868, 81.9510) for the population mean. The estimated variance component for the random patient-intercept (inter-subject variance) is 33.0636, and the estimated error variance (intra-subject variance) is 39.8614.

Figure 3 presents somatic readings at a rate of one measurement per hour. The mixed-model estimate for the mean somatic reading is 70.9105 with a standard error of 3.0838 on 8 degrees of freedom, yielding a 95% confidence interval of (63.8023, 78.0187). The estimated variance component for the random patient-intercept is 84.1705, showing patient to patient variability, and the estimated error variance is 220.24, showing within patient variability.

Figure 4 presents somatic readings at a rate of one. measurement per hour. The mixed-model estimate for the mean difference is 6.7178 with a standard error of 2.6217 on 8 degrees of freedom, yielding a 95% confidence interval of (0.672149, 12.76345), which shows that the mean cerebral reading is significantly higher than the mean somatic reading. A random-coefficient model did not detect a significant linear trend in any of the rSO2 readings.

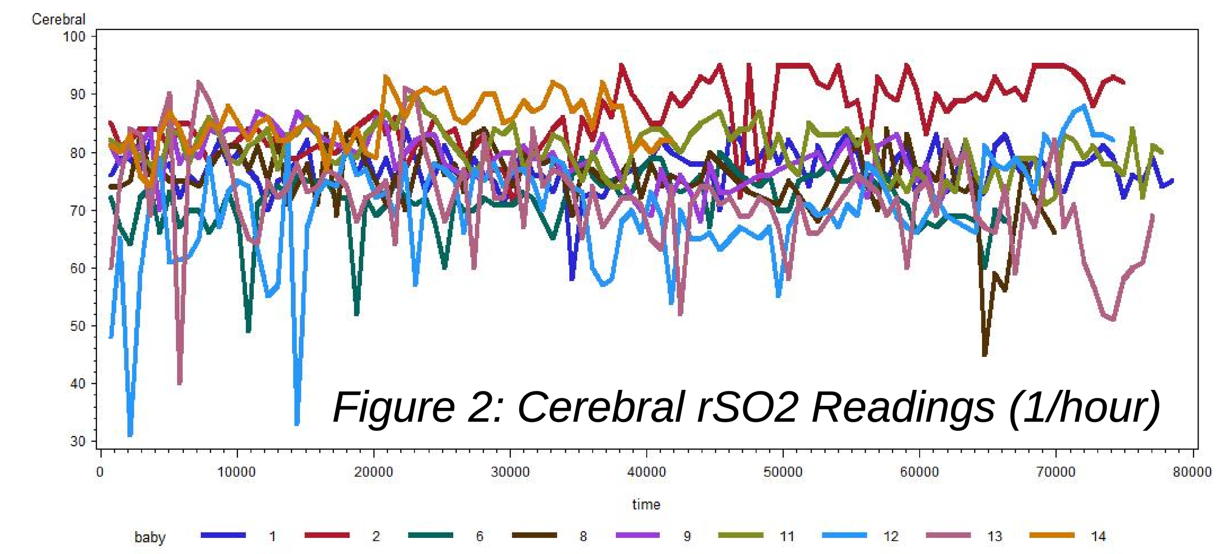

Figure 2: Cerebral rSO2 Readings (1/hour)

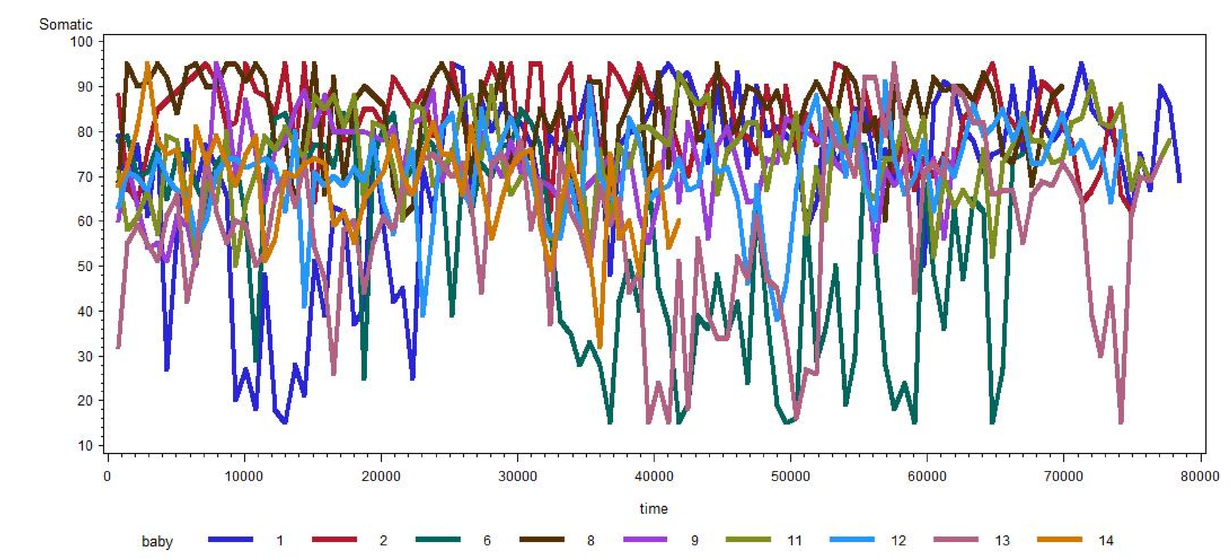

Figure 3: Somatic rSO2 Readings (1/hour)

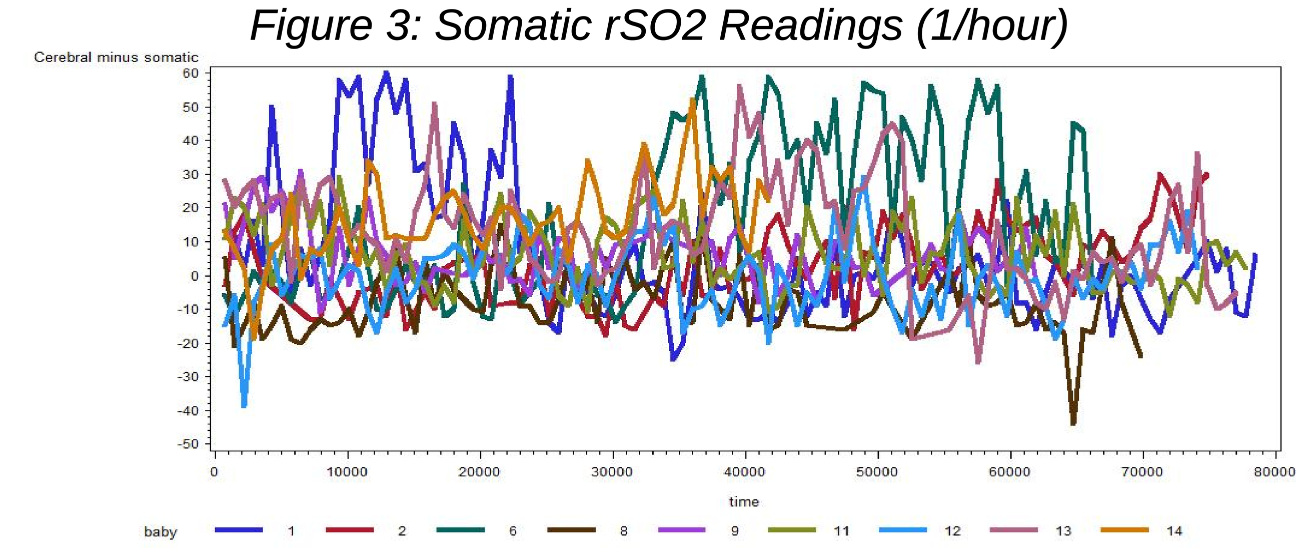

Figure 4: Difference Between Cerebral and Somatic Readings

DISCUSSION

Normative data for regional cerebral and renal oxygenation values has not been published. One larger-scale study has reported specific median normative values for preterm and term cerebral regional oxygenation based on gestational age in the first six hours of life. (Tina, et al. 2009) The article assumed independence and unlike the analysis described in this data, did not take into account the complex correlation structure in the data and some of their reported statistically significant differences are likely to be invalid.

In another study, normative values were given for premature babies for splanchnic tissue, as measured in the periumbilical region. They, similar to this analysis, reported no linear relationship in time for the regional oxygenation data outside of the confidence interval, but the interesting finding was a decrease in splanchnic tissue oxygenation in those preterm neonates with feeding intolerance when compared to those without intolerance. Cerebral and renal measurements were not recorded and therefore cannot be compared with the values in this data set. (Cortez, et al. 2011)

A large amount of variance was observed in our data. One possible explanation for this is changing the sensor caused a shift in the mean rSO2 readings. The readings for pre-term infants may be more sensitive to sensor placement than in adults due to the sensor being able to probe further into the tissue, secondary to anatomic differences in size between the two populations. (Adelson, et al. 1999)

Additionally, preterm infants are predisposed to a variety of medical issues, including respiratory issues, that may affect rSO2 readings. Thus, our estimate of normative rSO2 readings in pre-term infants is associated with large standard errors. It may be useful for future studies to look at more patients, spending less time on each patient. This study planned to collect 14 consecutive days of readings from each patient. After examining the data, it would be sufficient to collect data from each patient during a single 24 hour period. We did not observe any trends in the data that would require more than one day's worth of measurements. Furthermore, this would likely increase the number of patients willing to participate in the study. With only 9 subjects, we do not have enough degrees of freedom to test for the significance of covariates with several categories, such as race. Effects for birth weight, gender, one-minute APGAR, and method of delivery were tested one at a time, but none of the effects were significant.

We did not have adequate information on patients with PDA to draw a conclusion at this time regarding the possibility of ductal steal, as the test may be confounded with random subject effect. Future studies will need to be performed to elucidate characteristic regional oxygenation in a condition such as PDA that changes over time. The patients could be utilized as their own controls. This would greatly increase the sensitivity of the test by eliminating all of the patient-to-patient variation from the model, as well as likely decreasing the error variance.

WORKS CITED

Adelson PD, Nemoto E, Scheuer M, Painter M, Morgan J, Yonas H. Noninvasive continuous monitoring of cerebral oxygenation periictally using near-infrared spectroscopy: a preliminary report. *Epilepsia* 1999; 40(11):1484-9.

Cortez J, Gupta M, Amaram A, Pizzino J, Sawhney M, Sood BG. Noninvasive evaluation of splanchnic tissue oxygenation using near-infrared spectroscopy in preterm neonates. J Matern Fetal Neonatal Med. 2011; 24(4):574-82.

Somanetics. "The Invos System Pediatric Brochure." Somanetics Corporation (2005).

Tina LG, Frigiola A, Abella R, Artale B, Puleo G, D'Angelo S, Musmarra C, Tagliabue P, Li Volti G, Florio P, Gazzolo D. Near Infrared Spectroscopy in healthy preterm and term newborns: correlation with gestational age and standard monitoring parameters. *Curr Neurovasc Res.* 2009; 6 (3):148-54.

Welty SE. Patent Ductus Arteriosus in Premature Infants. UpToDate 2009.

ACKNOWLEDGMENTS

This project's formation and execution were possible thanks to Dr. Gregory Martin, MD. Explanation of the data collection process and organization of the data was provided by Irene Pacheco. Statistical analysis was provided by Andrew Karl.