Cerebral Tissue Oxygenation Index and SIDS

In this issue of Pediatrics, Fyfe et al present convincing evidence that cerebral tissue oxygenation index (TOI) is lower in habitually supine-sleeping preterm infants placed prone rather than supine, and that the cerebral TOI for preterm infants placed prone is lower than the TOI for term infants placed prone. Increased rates of sudden infant death syndrome (SIDS) among all infants sleeping prone, and even higher rates among preterm infants placed prone, provide the epidemiologic rationale for their physiologic studies.1,2

An established approach in attempting to understand sudden unexpected infant deaths (SUID), including SIDS, is the Triple Risk Model: a susceptible infant at a susceptible developmental stage is exposed to a stressor that cannot be overcome.3 The susceptible infants investigated by Fyfe et al were born before term and were studied at 2 to 4 weeks, 2 to 3 months, and 5 to 6 months post-term age, and compared with a group of infants born at term. Much recent study of SUID has focused on the interaction between sleep position and sleep microenvironment. This group from Australia has carried the torch in trying to understand infant susceptibility to sudden death that is affected by autonomic and motor development.

Fyfe et al report that decreases in cerebral TOI among prone infants, both term and preterm, occurred independent of changes in systemic mean arterial pressure and systemic oxyhemoglobin saturation measured by pulse oximetry. Impaired drainage when prone through veins draining the central nervous system is proposed as 1 reason for the apparent increase in cerebral oxygen extraction and presumed diminished cerebral perfusion. It is their hypothesis that neurobehavioral arousal and homeostatic responses to, for example, hypoxemia or hypotension, are impaired by changes in cerebral oxygenation.

Our comments on this study focus on potential intrasubject variability,4 as well as the “clinical significance” of the diminished cerebral oxygenation described and its potential causal association with sudden infant death.

As we understand their methods, TOI data recorded at 6 points over 6 to 12 minutes during sleep were averaged and pooled, and a single value for cerebral TOI was used for group data calculations, for prone or supine, active or quiet sleep, from each infant. But is a single TOI value sufficient? A figure in an earlier publication from this group (Fig 1)5 shows that the variability in cerebral TOI over longer periods of recording in a single infant may be on the order of 10% to 12%, a magnitude that is significant statistically when between-group and between-positions comparisons were made by Fyfe et al. If the authors had provided coefficients of variation for their time-weighted TOI averages to support the lack of variability in TOI measurement from infant to infant, that would have been reassuring, as would a clearer picture of how their data from 6 to 12 minutes of recordings
When attempting to explain the "clinical significance" of their cerebral TOI findings, the authors are appropriately circumspect. In studies in animals that are relevant to ICU and perioperative care, it has been shown that cerebral hypoxia below a normothermic threshold of 45% is associated with elevated lactate, depletion of adenosine triphosphate, electroencephalographic slowing, and, finally, EEG silence. But severe central nervous system injury is not the clinical issue this paper addresses. And unfortunately the impact of less severe degrees of cerebral ischemia is not known. Rather the "clinical" questions raised by their findings are whether and in what way decreases in cerebral TOI of the magnitude they describe are linked to failure to arouse during prone sleep to a standard stimulus (eg, soft jets of air to the face).

In anticipation of future publications using near infrared spectroscopy to study infant death through assessment of cerebral oxygenation and oxygen extraction, we suggest 2 caveats. First, infant deaths once said to be unexplained, and thus diagnosed as SIDS, are now often called "positional asphyxia" in the United States, sometimes in the absence of any quantitative estimate of the asphyxial threat posed by the sleep environment. Nevertheless, the physiologic mechanisms for these deaths, although perhaps not called SIDS, will be elucidated by studies like those of Fyfe et al. Second, maturation of respiratory control also leads to a more measured response to ventilatory perturbations rather than the frequently excessive response associated with arousal from sleep. We suggest that they should consider whether diminished cerebral oxygenation might also delay maturation of ventilatory control and favor a more vigorous response to a ventilatory perturbation that could further lead to perhaps lethal instability. We look forward to ongoing work by these authors and others for the advancement of such a hypothesis.

REFERENCES

5. Wong FY, Witcombe NB, Yiallourou SR, et al. Cerebral oxygenation is depressed during sleep in healthy term infants when they sleep prone. Pediatrics. 2011;127(3). Available at: www.pediatrics.org/cgi/content/full/127/3/e558
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Pediatrics; originally published online August 25, 2014;
DOI: 10.1542/peds.2014-1875

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