Letters to the editor

Oxygen monitoring

To the Editor: I read with interest the recent publication by Stippler et al. (Stippler M, Ortiz V, Adelson PD, et al: Brain tissue oxygen monitoring after severe traumatic brain injury in children: relationship to outcome and association with other clinical parameters. Clinical article. J Neurosurg Pediatr 10:383–391, November 2012). The study examines a 4-year experience with continuous brain tissue oxygen (PbtO₂) monitoring in managing 46 children with severe TBI. The authors are to be congratulated on the excellent outcomes achieved in their patients. As they point out, this does not necessarily mean that these outcomes are due to PbtO₂ monitoring per se; however, it does reflect what can be achieved in units committed to advanced neurocritical care and the benefits of enrolling patients in prospective studies, as was the case with the authors’ hypothermia trial. There are several aspects of their findings and approach to PbtO₂ monitoring that are similar to our experience and a few that are substantially different.

In 2009 we published our initial experience with PbtO₂ monitoring in 52 children with severe TBI. Similarly, we found complex relationships between PbtO₂ and other clinical variables. We then followed this up more recently with a detailed analysis of hourly and continuous data of PbtO₂ and intracranial pressure (ICP) in 75 children, along with several other variables, showing several examples of why these relationships are so complex. Knowing the pathophysiology of the injured brain, this is entirely expected. We now have experience with about 200 children whom we have monitored using PbtO₂ (mostly children who have sustained a traumatic brain injury), and this complexity is a consistent finding. Increased ICP is not a homogeneous phenomenon; in the diffusely injured brain ICP may be increased in association with cellular or vasogenic edema, hyperemia, impaired autoregulation (where increased blood pressure drives up the ICP), subclinical seizures, or spreading depression. All of these are physiologically different, vary between patients, and are dynamic in individual patients over time. Moreover, several interventions to decrease ICP may have variable and at times even contrasting effects on brain perfusion, and therefore, PbtO₂.

The findings in the study by Stippler et al. are based on hourly values for PbtO₂, which is a limitation in analyzing data, as was the case with our original study. Our understanding of the dynamics between PbtO₂ and other variables has vastly improved with continuous data recording, as has our ability to analyze the data. One of the criticisms of Stippler and colleagues’ study, therefore, is the use of summary values for much of their analysis. Clinical article. J Neurosurg Pediatr 10:383–391, November 2012. The study examines a 4-year experience with continuous brain tissue oxygen (PbtO₂) monitoring in managing 46 children with severe TBI. The authors are to be congratulated on the excellent outcomes achieved in their patients. As they point out, this does not necessarily mean that these outcomes are due to PbtO₂ monitoring per se; however, it does reflect what can be achieved in units committed to advanced neurocritical care and the benefits of enrolling patients in prospective studies, as was the case with the authors’ hypothermia trial. There are several aspects of their findings and approach to PbtO₂ monitoring that are similar to our experience and a few that are substantially different.

In 2009 we published our initial experience with PbtO₂ monitoring in 52 children with severe TBI. Similarly, we found complex relationships between PbtO₂ and other clinical variables. We then followed this up more recently with a detailed analysis of hourly and continuous data of PbtO₂ and intracranial pressure (ICP) in 75 children, along with several other variables, showing several examples of why these relationships are so complex. Knowing the pathophysiology of the injured brain, this is entirely expected. We now have experience with about 200 children whom we have monitored using PbtO₂ (mostly children who have sustained a traumatic brain injury), and this complexity is a consistent finding. Increased ICP is not a homogeneous phenomenon; in the diffusely injured brain ICP may be increased in association with cellular or vasogenic edema, hyperemia, impaired autoregulation (where increased blood pressure drives up the ICP), subclinical seizures, or spreading depression. All of these are physiologically different, vary between patients, and are dynamic in individual patients over time. Moreover, several interventions to decrease ICP may have variable and at times even contrasting effects on brain perfusion, and therefore, PbtO₂.

The findings in the study by Stippler et al. are based on hourly values for PbtO₂, which is a limitation in analyzing data, as was the case with our original study. Our understanding of the dynamics between PbtO₂ and other variables has vastly improved with continuous data recording, as has our ability to analyze the data. One of the criticisms of Stippler and colleagues’ study, therefore, is the use of summary values for much of their analysis. Acute episodes of tissue hypoxia/ischemia may have devastating consequences and may be followed by posts ischemic reperfusion events that dilute critically important results, especially when one averages this over 24 hours.

Therefore, we have found little use in the analysis of daily values for PbtO₂, as opposed to episodes of PbtO₂ below certain thresholds. It is a credit to their study that their episodes of reduced PbtO₂ (< 15 mm Hg) and occurrence of unfavorable outcomes were so low; however, this limited their ability to analyze meaningful thresholds.

This point is important because the authors report a particularly high threshold for possible treatment: their a priori decision was to maintain PbtO₂ above 25 mm Hg and found that 30 mm Hg appeared to best discriminate between favorable and unfavorable outcomes. This is quite different from our experience, which is similar to data in adult patients, in which episodes of PbtO₂ below 10 mm Hg were associated with unfavorable outcome, and episodes below 20 mm Hg showed only a trend. Lower thresholds are also in keeping with our more recent findings with microdialysis in traumatic brain injury in children, in which increased lactate/pyruvate levels only occur at lower PbtO₂ thresholds (unpublished data). This would be in keeping with outcome data in studies in adults (15–20 mm Hg) and experimental studies in which measures of metabolic compromise tend to increase when PbtO₂ is lower than 10 mm Hg. We have used a threshold of 20 mm Hg for treatment to maintain a buffer zone but increasingly are using more aggressive treatments only when PbtO₂ drops below 10–15 mm Hg. This would seem to be more in keeping with the accumulated data so far. There are possible reasons for the authors’ findings of such a high threshold. First, the most common intervention for PbtO₂ in their study appeared to be an increase in the fraction of inspired oxygen (FiO₂). This would be the only substantial difference from their normal ICP/cerebral perfusion pressure (CPP) strategy; treating ICP and CPP thresholds, avoidance of inadvertent hypoventilation, and transfusion of packed red blood cells if the hemoglobin concentration was less than 9 g/dl, as they describe in their Methods, are arguably interventions they would have performed anyway. My concern about increased FiO₂ as a primary intervention is based on the fact that PbtO₂ measures the partial pressure of O₂ in the tissues and is therefore subject to increased partial pressure of arterial O₂ (PaO₂). Consequently, when the FiO₂ is increased, the PaO₂ may increase substantially, without much change in O₂ content (and therefore O₂ delivery) when the patient has enough hemoglobin that is well saturated at the start. However, PbtO₂ will substantially increase in most patients even without substantially greater O₂ delivery, simply because the driving force of O₂ pressure from the capillary to the tissues is increased. In absence of any other maneuver to increase O₂ delivery, this may be the only alternative; however, it is likely not as good as interventions to improve delivery. Also, arguably it may mask potential ischemia, cause arteriolar vasoconstriction, and increase acute lung injury. In our recent experience with tissue cerebral blood flow monitoring in combination with PbtO₂, we have observed the decrease in cerebral blood flow that may occur at times with hyperoxia (unpublished data). Therefore, the
benefits of hyperoxia as a therapeutic strategy continue to be debated.

Second, the positioning of the probe is unclear; in the authors' Methods, probe placement is described to be in the cortex of the frontal lobe. Most institutions report PbtO2 thresholds based on white matter placement, which of course is below the cortex. This is important for 2 reasons: misplacement of these probes is easy and so confirmation of placement with imaging is essential, and gray matter and white matter have substantially different cerebral blood flow and oxygenation profiles. In our experience of probes misplaced either partially or wholly in gray matter, the PbtO2 values have been substantially higher. Targeting a higher PbtO2 threshold than is necessary may place patients at risk of adverse events associated with the treatment that may outweigh their benefit.

The authors also note that high PbtO2 values were sometimes documented in patients who experienced unfavorable outcomes. This is not unexpected and is similar to our experience. Presumably, these episodes reflect either a dysregulated brain (uncoupling between metabolic need and cerebral blood flow), postischemic reperfusion syndrome, or decreased extraction of interstitial sometimes because of mitochondrial dysfunction.

Lastly, the authors use, and analyze, a relatively high CPP threshold by our standards (55 mm Hg in children < 6 years and 60 mm Hg in children > 6 years). For a 3-year-old child at the 50th percentile for height and an ICP of 20 mm Hg, the mean arterial pressure would then be running close to the 95th percentile. Of course, there is much debate about the choice of CPP thresholds, as much in adults as in children. The guidelines for adults have downgraded the initial high CPP recommendations (now 60 mm Hg) in recognition of data from Europe suggesting tolerance of lower CPP values based on metabolic monitoring and the increased risks of targeting an unnecessarily high threshold. Of course, it makes little physiological sense to recommend one specific threshold given the variability of autoregulatory status in these patients, but our preference is to start with lower thresholds (45 mm Hg in children < 2 years and 50 mm Hg in those > 2 years) and adjust according to autoregulatory status and PbtO2 or microdialysis parameters. In our experience, lower CPP thresholds may be tolerated in children depending on prevailing dynamics. Again this is important because of the known risks of maintaining higher CPP levels.

We agree with the authors that it would be preferable to conduct multicenter studies to determine the benefit of PbtO2 monitoring (as it would be true for ICP monitoring). However, with increasing experience we have realized some of the substantial difficulties in this. For us, the value of additional monitoring (such as PbtO2) lies not so much in the targeting of another threshold for a new monitor, but rather the enhanced understanding of the pathophysiological disturbances in individual patients using additional monitoring that cannot be appreciated with ICP monitoring alone. The more one analyzes these data with high-frequency recording, the more obvious are the inter- and intrapatient physiological differences. After all, as important as ICP monitoring is, the number alone cannot reveal the underlying pathophysiological etiology.

Similarly, it cannot reveal how perfusion and metabolism of the brain respond to the commonly used treatment strategies. Comparing effectiveness of strategies between centers is a good idea, but it also has several limitations; reading the description of the patients of their study in comparison with ours reveals the substantial differences in patients presenting to our 2 centers.

In summary, therefore, I congratulate the authors on their study and their commitment to maintaining momentum in pediatric neurocritical care, while highlighting our different thinking about thresholds chosen and therapeutic approach to PbtO2 values.

ANTHONY A. FIGAJI, M.D., M.MED., F.C.S., Ph.D.
University of Cape Town
Cape Town, South Africa

Disclosure

The author reports no conflict of interest.

References


RESPONSE: No response was received from the authors of the original article.

Please include this information when citing this paper: published online November 1, 2013; DOI: 10.3171/2012.11.PEDS12486. ©AANS, 2014