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Perspective

Monitoring cerebral ischemia using cerebral oximetry: pros and cons

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Introduction

The high metabolic rate of oxygen in the human brain accounts for its extreme susceptibility to ischemic-hypoxic conditions[1]. Ischemic brain injury such as stroke is a potential neurologic complication in a variety of surgeries, including cardiac surgery, neurosurgery, and vascular surgery, particularly in patients at high risk for ischemic stroke[2]. In addition, ischemic brain injury accounts for most cases of perioperative strokes in noncardiac and non-neurosurgical surgeries[3]. Intraoperative cerebral ischemic-hypoxic events are not only related to an increased risk of stroke, but may also cause other neurologic complications such as postoperative cognitive dysfunction (POCD), mortality, major organ morbidity, and prolonged hospital lengths of stay[4-5]. One of the most important physiological consequences of cerebral ischemia is a reduction in oxygen delivery to the brain, leading to an imbalance in cerebral oxygen supply/demand. Cerebral hypoxia is a destructive physiological disturbance that should be avoided by all means. However, cerebral ischemia is not the sole cause of hypoxia. Other pathological conditions such as acute and severe systemic arterial blood desaturation and anemia can lead to an inadequate oxygen supply to the brain and subsequent cerebral hypoxia.

The successful treatment of perioperative cerebral ischemia-hypoxia depends on early and reliable diagnosis[3]. Cerebral tissue oxygenation monitoring is promising in its ability to facilitate the early diagnosis of cerebral ischemic-hypoxic conditions during surgery[6]. The near-infrared light with wavelengths of 700 to 1000 nm can penetrate the scalp and skull, and light up brain tissue in both adults and children. Near-infrared spectroscopy (NIRS) based cerebral oximetry measures the ratio of oxygenated hemoglobin over the total hemoglobin (sum of oxygenated and deoxygenated hemoglobin) at a depth of around 2 cm below the scalp in the part of the brain being illuminated, assuming the distance between the light emitter and detector is 4 cm. It is believed that venous blood contributes on average 70% to 75% of the volume of the total blood in the measured brain tissue in the frontal lobe. However, different individuals may have different percentages of venous blood in the frontal lobe, which explains why regional cerebral tissue oxygen saturation ($rScO_2$) as measured using cerebral oximetry shows inter-individual variability[7]. The two essential determinants of regional cerebral tissue oxygen saturation ($rScO_2$) are the cerebral metabolic rate of oxygen ($CMRO_2$) (consumption) and the oxygen delivery to the brain (supply)[7]. The cerebral oximetry devices that are currently being used in patients are based on continuous-wave technology, which differs from frequency-domain and time-domain technology[8-9].

Clinical application and encouraging results

In the present day, noninvasive cerebral NIRS monitoring is used in a variety of clinical settings, including cardiac or great vessel surgery, carotid endarterectomy, surgery in

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the sitting position, and aneurysmal subarachnoid hemorrhage[10-12]. Recently, cerebral oximetry based on NIRS has also been used to evaluate the balance between cerebral oxygen supply and demand in patients undergoing neurointerventional radiological procedures[13]. In pediatric patients, perioperative cerebral oxygenation as assessed by cerebral oximetry helps to identify cerebral ischemia-hypoxia in children with congenital heart disease[14,15]. The detection and treatment of perioperative cerebral ischemia-hypoxia are likely to decrease the risk of neurologic injury and improve neurodevelopmental performance after pediatric cardiac surgery[15]. However, a recently published study demonstrated that there was no significant association between new postoperative ischemic lesions and intraoperative cerebral desaturation as assessed using cerebral oximetry[16]. Zheng *et al.* performed a systematic review evaluating cerebral oximetry monitoring and postoperative neurologic outcomes in adult patients undergoing cardiac surgery, concluding that there was insufficient evidence to support the hypothesis that interventions that improve $rScO_2$ prevent stroke or other neurologic injuries[17].

Denault *et al.* developed an algorithm for the application of cerebral oximetry in cardiac surgery. This algorithm is based on interventions to optimize factors that may affect cerebral oxygen supply/demand[18] and involves adjusting for physiological variables such as the patient's head position, mean arterial pressure, oxygen saturation of the systemic arterial blood, partial pressure of carbon dioxide in the arterial blood, hemoglobin concentration, cardiac output, cerebral tissue oxygen consumption, and intracranial pressure[18]. A number of randomized controlled trials (RCTs) have been conducted to evaluate whether the use of cerebral oximetry and subsequent treatment strategies could prevent perioperative ischemic brain injury and improve postoperative outcomes.

Murkin *et al.* randomized 200 patients undergoing coronary artery bypass grafting (CABG) to either treatment (intervention) or blinded (control) groups with $rScO_2$ monitoring using NIRS-based cerebral oximetry. The authors demonstrated that the treatment of intraoperative cerebral desaturation (defined as a decrease in $rScO_2$ below 70% of the baseline value for 1 minute or longer) could shorten the length of ICU stay and reduce the incidence of perioperative major organ morbidity and mortality[4]. In a recently published RCT, $rScO_2$ was continuously monitored using cerebral oximetry in CABG patients and a standardized interventional protocol was used when $rScO_2$ fell below 80% of the baseline value or the absolute value was below 50% in the intervention group. The results showed that postoperative cognitive outcomes were significantly improved in patients with interventions based on continuous rSO_2 monitoring[19]. Two RCTs with small sample sizes also investigated whether interventions based on rSO_2 monitoring could reduce adverse postoperative neurological outcomes. In these two studies, the study teams concluded that the optimization of intraoperative $rScO_2$ during CABG significantly decreased a biomarker of neurological injury (S100B) and lowered the incidence of postoperative neurocognitive impairment[6,20]. At present, a Cochrane systematic review regarding the effect of perioperative cerebral oximetry monitoring on postoperative neurological and non-neurological outcomes in children and adults is being conducted[21].

The algorithm proposed by Denault *et al.* for cardiac patients was modified by Zogogiannis *et al.* for patients undergoing carotid endarterectomy[18,22]. In Zogogiannis's study, a 20% drop from baseline in $rScO_2$ was considered to be a cutoff value indicating cerebral ischemia, and the authors concluded that a modified algorithm based on cerebral NIRS monitoring could be helpful in the decision for intraoperative shunt placement. Pennekamp's team conducted a cohort study of carotid endarterectomy under general anesthesia and found that cerebral NIRS monitoring could independently reduce unnecessary shunt use. A nested RCT performed by Ballard *et al.* indicated that NIRS-based cerebral oximetry monitoring together with a standardized protocol for rectifying cerebral tissue desaturation could reduce postoperative cognitive decline in elderly patients scheduled for elective orthopedic or abdominal surgery[23].

In summary, ample studies have shown encouraging results with the use of cerebral oximetry in detecting cerebral ischemia-hypoxia events during surgery. However, the threshold and protocol used to define and treat cerebral tissue desaturation vary among different studies and different surgeries.

Contrasting observations and technical limitations

Despite encouraging results, there have been findings from other RCTs and reviews that have suggested that cerebral oximetry does not help early detection of cerebral ischemia or improve outcomes. Verborgh *et al.* performed a small RCT in patients undergoing off-pump CABG and found that continuous $rScO_2$ monitoring to maintain $rScO_2$ above 80% of the baseline value did not reduce the length of hospital or ICU stay as compared to conventional hemodynamic monitoring[24]. Cowie and colleagues prospectively evaluated elderly patients scheduled for colorectal or orthopedic surgery and found that cerebral tissue oxygenation monitoring and interventions to treat cerebral desaturation (defined as $rScO_2$ below 75% of the baseline value) did not seem to decrease the incidence of postoperative complications[25]. Although cerebral oximetry based on NIRS technology has the potential to aid anesthetic management of patients undergoing heart surgery, Gregory and colleagues claimed that there are many limitations to its clinical application as a standard monitor[7]. Specifically, how to incorporate the results of current studies into a standardized decision-making protocol remains uncertain[7]. A previous study claimed that cerebral oximetry based on NIRS technology has moderate sensitivity (60%) and low specificity (25%) in predicting clinically symptomatic cerebral ischemia in patients undergoing carotid endarterectomy[26].

The technical limitations of the NIRS-based cerebral oximetry should be recognized. As reported by Bickler *et al.*, variations in NIRS-measured $rScO_2$ exist among different individuals and devices likely due to differences in skin color, gender, and the volume ratio of arterial blood over venous blood in the frontal lobe[27]. The cerebral NIRS monitor based on continuous-wave technology is a trend monitor. Consequently, clinical decision-making should be based on the change from baseline together with the clinical situation instead of the absolute value observed[28].

The threshold value of clinically significant cerebral tissue desaturation based on cerebral oximetry remains undefined and the treatment protocols have varied. Different studies have used different thresholds of $rScO_2$ for interventions. Some authors have defined cerebral tissue desaturation as an absolute $rScO_2$ below 50%, or more than a 20% reduction from baseline[19-20]. Other investigators have used a decline of over 20% of the baseline value as the cutoff value for cerebral ischemia-hypoxia[5,22]. A number of RCTs have considered $rScO_2$ below 75% of the baseline value to represent cerebral tissue desaturation. Additional case reports have suggested that some patients with normal $rScO_2$ values actually suffer from hypoperfusion while others with low rSO_2 values are in normal states of cerebral perfusion[29].

It is important to note that cerebral oximetry is primarily applied to the upper forehead, unless the patient is bald, in which case the monitor can be applied on other parts of the head as well. Therefore, it is regarded as a regional monitor. However, evidence shows that cerebral oximetry can be sensitive to acute changes in blood flow in the middle cerebral artery when the monitor is applied to the upper forehead and the parietal regions of the head (unpublished data). This implies that cerebral oximetry primarily monitors the brain territory perfused by the anterior circulation or the internal carotid artery. Contamination of the cerebral oximetry signal by the extra-cerebral layers such as the scalp is another technical limitation of this type of monitoring, which should be taken into consideration during data interpretation and clinical decision-making.

Summary

Taking together, cerebral oximetry based on NIRS technology has the potential to facilitate timely diagnosis of cerebral ischemia-hypoxia events during surgery and may be effective in reducing postoperative complications related to intraoperative cerebral ischemia-hypoxia. However, the threshold for intervention on cerebral tissue desaturation based on cerebral oximetry monitoring seems to be patient population- and surgery-dependent, and needs to be better defined by further research. Moreover, the technical limitations of NIRS-based cerebral oximetry need to be recognized during its clinical application.

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