Monitoring cerebral ischemia using cerebral oximetry: pros and cons

Yun Yu¹, Yi Lu², Lingzhong Meng³, Ruquan Han¹,*

¹Department of Anesthesiology, Beijing Tian Tan Hospital, Capital Medical University, Beijing 100050, China; ¹²School of Medicine, University of California San Francisco, San Francisco, California 94143, USA; ³Department of Anesthesia and Perioperative Care, University of California San Francisco, San Francisco, California 94143, USA.

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 pathologic 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 (rScO2) as measured using cerebral oximetry shows inter-individual variability[7]. The two essential determinants of regional cerebral tissue oxygen saturation (rScO2) are the cerebral metabolic rate of oxygen (CMRO2) (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].

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...
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 neurological 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 rScO₂ 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 rScO₂ monitoring using NIRS-based cerebral oximetry. The authors demonstrated that the treatment of intraoperative cerebral desaturation (defined as a decrease in rScO₂ 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 \[^{[19]}\]. In a recently published RCT, rScO₂ was continuously monitored using cerebral oximetry in CABG patients and a standardized interventional protocol was used when rScO₂ 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 rSO₂ monitoring \[^{[19]}\].

Two RCTs with small sample sizes also investigated whether interventions based on rSO₂ monitoring could reduce adverse postoperative neurological outcomes. In these two studies, the study teams concluded that the optimization of intraoperative rScO₂ during CABG significantly decreased a biomarker of neurological injury ($100B) 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 \[^{[16,22]}\]. In Zogogiannis’ study, a 20% drop from baseline in rScO₂ 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 rScO₂ monitoring to maintain rScO₂ 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 rScO2 below 75% of the baseline value) did not seem to decrease the incidence of postoperative complications. 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. Specifically, how to incorporate the results of current studies into a standardized decision-making protocol remains uncertain. 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.

The technical limitations of the NIRS-based cerebral oximetry should be recognized. As reported by Bickler et al., variations in NIRS-measured rScO2 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. 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.

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 rScO2 for interventions. Some authors have defined cerebral tissue desaturation as an absolute rScO2 below 50%, or more than a 20% reduction from baseline.

Other investigators have used a decline of over 20% of the baseline value as the cutoff value for cerebral ischemia-hypoxia. A number of RCTs have considered rScO2 below 75% of the baseline value to represent cerebral tissue desaturation. Additional case reports have suggested that some patients with normal rSO2 values actually suffer from hypoperfusion while others with low rSO2 values are in normal states of cerebral perfusion.

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.

Acknowledgments

The work was supported by the Inaugural Anesthesia Department Awards for Seed Funding for Clinically-Oriented Research Projects from the Department of Anesthesia and Perioperative Care, University of California San Francisco, San Francisco, California, U.S.A. (to Dr. Meng).

References

[1] Gale SD, Hopkins RO. Effects of hypoxia on the brain: neuroimaging and neuropsychological findings following carbon monoxide poisoning and obstructive sleep apnea[J]. J Int Neuropsychol Soc, 2004,10(1):60-71.
[2] Bijker JB, Gelb AW. Review article: the role of hypotension in perioperative stroke[J]. Can J Anaesth, 2013, 60(2):159-167.
[3] Ng JL, Chan MT, Gelb AW. Perioperative stroke in non-cardiac, nonneurosurgical surgery[J]. Anesthesiology, 2011,115(4):879-890.
[4] Murkin JM, Adams SJ, Novick RJ, et al. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. Anesth Analg, 2007, 104(1):51-58.
[5] Slater JP, Guarino T, Stack J, et al. Cerebral Oxygen Desaturation Predicts Cognitive Decline and Longer Hospital Stay After Cardiac Surgery[J]. Ann Thorac Surg, 2009,87(1):36-45.
[6] Harilall Y, Adam JK, Biccard BM, Reddi A. The effect of optimising cerebral tissue oxygen saturation on markers of neurological injury during coronary artery bypass graft surgery. Heart Lung Circ, 2014,23(1):68-74.
[7] Gregory A, Kohl BA. Con: near-infrared spectroscopy has not proven its clinical utility as a standard monitor in cardiac surgery[J]. J Cardiothorac Vasc Anesth, 2013, 27(2):390-394.
Alassar A, Soppa G, Edsell M, et al. Incidence and Hoffman GM, Brosig CL, Mussatto KA, Tweddell JS, Kreeger RN, Ramamoorthy C, Nicolson SC, et al. A proposed algorithm for the intraoperative use of cerebral near-infrared spectroscopy [J]. Semin Cardiothorac Vasc Anesth, 2007, 11(4):274-281.

[8] Meng L, Gelb AW, Alexander BS, et al. Impact of phenylephrine administration on cerebral tissue oxygen saturation and blood volume is modulated by carbon dioxide in anaesthetized patients [J]. Br J Anaesth, 2012, 108(5): 815-822.

[9] Meng L, Cannesson M, Alexander BS, et al. Effect of phenylephrine and ephedrine bolus treatment on cerebral oxygenation in anaesthetized patients [J]. Br J Anaesth, 2011, 107(2): 209-217.

[10] Ono M, Zheng Y, Joshi B, Sigl JC, Hogue CW. Validation of a stand-alone near-infrared spectroscopy system for monitoring cerebral autoregulation during cardiac surgery [J]. Anesth Analg, 2013, 116(1): 190-204.

[11] Yoshitani K, Kuwajima K, Irie T, et al. Clinical validity of cerebral oxygen saturation measured by time-resolved spectroscopy during carotid endarterectomy [J]. J Neurosurg Anesthesiol, 2013, 25(3): 248-253.

[12] Mutoh T, Ishikawa T, Suzuki A, Yasui N. Continuous cardiac output and near-infrared spectroscopy monitoring to assist in management of symptomatic cerebral vasospasm after subarachnoid hemorrhage [J]. Neurocrit Care, 2010, 13(3): 331-338.

[13] Mazzeo AT, Di Pasquale R, Settineri N, et al. Usefulness and limits of near infrared spectroscopy monitoring during endovascular neuroradiologic procedures [J]. Minerva Anestesiol, 2012, 78(1): 34-45.

[14] Kreeger RN, Ramamoorthy C, Nicolson SC, et al. Evaluation of pediatric near-infrared cerebral oximeter for cardiac disease [J]. Ann Thorac Surg, 2012, 94(5): 1527-1533.

[15] Hoffman GM, Brosig CL, Mussatto KA, Tweddell JS, Ghanayem NS. Perioperative cerebral oxygen saturation in neonates with hypoplastic left heart syndrome and childhood neurodevelopmental outcome [J]. J Thorac Cardiovasc Surg, 2013, 146(5): 1153-1164.

[16] Allassar A, Soppa G, Edsell M, et al. Incidence and mechanisms of cerebral ischemia after transcatheter aortic valve implantation compared with surgical aortic valve replacement [J]. Ann Thorac Surg, 2015, 99(3): 802-808.

[17] Zheng F, Sheinberg R, Yee MS, Ono M, Zheng Y, Hogue CW. Cerebral near-infrared spectroscopy monitoring and neurologic outcomes in adult cardiac surgery patients: a systematic review [J]. Anesth Analg, 2013, 116(3): 663-676.

[18] Denault A, Deschamps A, Murkin JM. A proposed algorithm for the intraoperative use of cerebral near-infrared spectroscopy [J]. Semin Cardiothorac Vasc Anesth, 2007, 11(4): 274-281.

[19] Colak Z, Borojevic M, Bogovic A, Ivancan V, Biocina B, Majeric-Kogler V. Influence of intraoperative cerebral oximetry monitoring on neurocognitive function after coronary artery bypass surgery: a randomized, prospective study [J]. Eur J Cardiothorac Surg, 2015, 47(3): 447-454.

[20] Mohandas BS, Jagadeesh AM, Vikram SB. Impact of monitoring cerebral oxygen saturation on the outcome of patients undergoing open heart surgery. Ann Card Anaesth, 2013, 16(2): 102-106.

[21] Yu Y, Zhang K, Zhang L, Zong H, Meng L, Han R. Cerebral near-infrared spectroscopy (NIRS) for perioperative monitoring of brain oxygenation in children and adults (Protocol). Cochrane Db Syst Rev, 2014; Art. No.: CD010947.

[22] Zogogiannis ID, Iatrou CA, Lazarides MK, et al. Evaluation of an intraoperative algorithm based on near-infrared refracted spectroscopy monitoring, in the intraoperative decision for shunt placement, in patients undergoing carotid endarterectomy. Middle East J Anaesthesiol, 2011, 21(3): 367-373.

[23] Ballard C, Jones E, Gauge N, et al. Optimised anaesthesia to reduce post operative cognitive decline (POCD) in older patients undergoing elective surgery, a randomised controlled trial [J]. PLoS One, 2012, 7(6): e37410.

[24] Verbhorh C, Pregardien C, Oubaha D, Beckers S, Poelaert J. Continuous monitoring of regional cerebral oxygen saturation during and outcome after OPCAB surgery [J]. Eur J Anaesthesiol, 2009, 26(Supplement 45): 59-60.

[25] Cowie DA, Nazareth J, Story DA. Cerebral oximetry to reduce perioperative morbidity. Anesth Intensive Care, 2014, 42(3): 310-314.

[26] Stilo F, Spinelli F, Martelli E, et al. The sensibility and specificity of cerebral oximetry, measured by INVOS-4100, in patients undergoing carotid endarterectomy compared with awake testing [J]. Minerva Anestesiol, 2012, 78(10): 1126-1135.

[27] Bickler PE, Feiner JR, Rollins MD. Factors affecting the performance of 5 cerebral oximeters during hypoxia in healthy volunteers [J]. Anesth Analg, 2013, 117(4): 813-823.

[28] Fenton KN, Freeman K, Glogowski K, Fogg S, Duncan KF. The significance of baseline cerebral oxygen saturation in children undergoing congenital heart surgery [J]. Am J Surg, 2005, 190(2): 260-263.

[29] Durandy Y, Rubatti M, Couturier R. Near Infrared Spectroscopy during pediatric cardiac surgery: errors and pitfalls [J]. Perfusion, 2011, 26(5): 441-446.