Intensive Care Med (2022) 48:1463–1466
https://doi.org/10.1007/s00134-022-06788-w

SPECIAL ISSUE INSIGHT

Monitoring cerebral oxygenation in acute brain-injured patients

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Monitoring cerebral oxygenation may improve the understanding of brain dysfunction after an acute brain injury (ABI) [1]. Indeed, ABI leads to a cascade of events resulting in altered cerebral metabolism, reduced oxygen delivery, and increased oxygen consumption, further aggravating the severity of the initial damage and becoming a significant determinant of worse outcomes in this setting [1].

Although the cornerstone of the medical therapy in ABI patients is driven by the monitoring of intracranial pressure (ICP) [2], the implementation of cerebral oxygen monitoring has recently gained interest, as cerebral hypoxia can occur even in the absence of intracranial hypertension, and strategies to control ICP do not always guarantee optimal oxygen delivery. Recent clinical algorithms have therefore sought to incorporate both ICP- and brain oxygen-based targets and therapeutic algorithms into the management of ABI patients [3, 4], suggesting the possibility for an individualized approach to minimize the occurrence of secondary hypoxic brain events, especially in patients with traumatic brain injury (TBI).

Pathophysiology of cerebral oxygenation

Brain metabolism is aerobic, and cerebral oxygenation depends on oxygen supply and consumption equilibrium. It is directly correlated to cerebral blood flow (CBF) and the difference between arterial (CaO_2) and venous (CvO_2) oxygen contents, i.e., {CBF × (CaO_2 – CvO_2)} [5] (Fig. 1), and it represents the product of CBF and the cerebral arteriovenous oxygen tension difference rather than a direct measurement of total oxygen delivery or cerebral oxygen metabolism [5].

Arterial blood oxygen content (CaO_2) is a significant determinant of oxygen delivery, and it depends on the haemoglobin (Hb) levels, the percentage of haemoglobin saturation in oxygen (SaO_2), and, to a small extent, the partial pressure of oxygen in arterial blood (PaO_2). Consequently, respiratory failure with systemic hypoxemia can lead to cerebral hypoxia, especially if the cerebrovascular reserve (i.e., changes in vascular tone to regulate CBF) is impaired [6]. Optimizing Hb levels can also improve brain oxygenation in selected cases [7].

Oxygen delivery mainly depends on CBF, which has as main determinants cerebral perfusion pressure (CPP, the difference between mean arterial pressure and ICP), cerebral vasoreactivity and autoregulation, aimed to maintain CBF adequate to the metabolic needs. Oxygen delivery can also be limited by alterations in cerebral microcirculation, which would reduce the oxygen diffusion to the brain cells. Increased oxygen consumption can be observed in agitated patients, high body temperature, and seizures.

The technology of cerebral oxygen measurement

The most used cerebral blood oxygen monitoring methods in ABI patients include jugular venous oxygen saturation ($SjvO_2$) monitoring, near-infrared spectroscopy (NIRS) and brain tissue partial pressure of oxygen ($PbtO_2$). These tools are based on different principles and techniques and have advantages and pitfalls regarding invasiveness, accuracy, temporal and spatial resolution, cost, and noise artifacts (Fig. 1).

The most accepted and reliable method to assess and manage cerebral oxygenation in severe ABI patients is $PbtO_2$, developed with advances in electronics and

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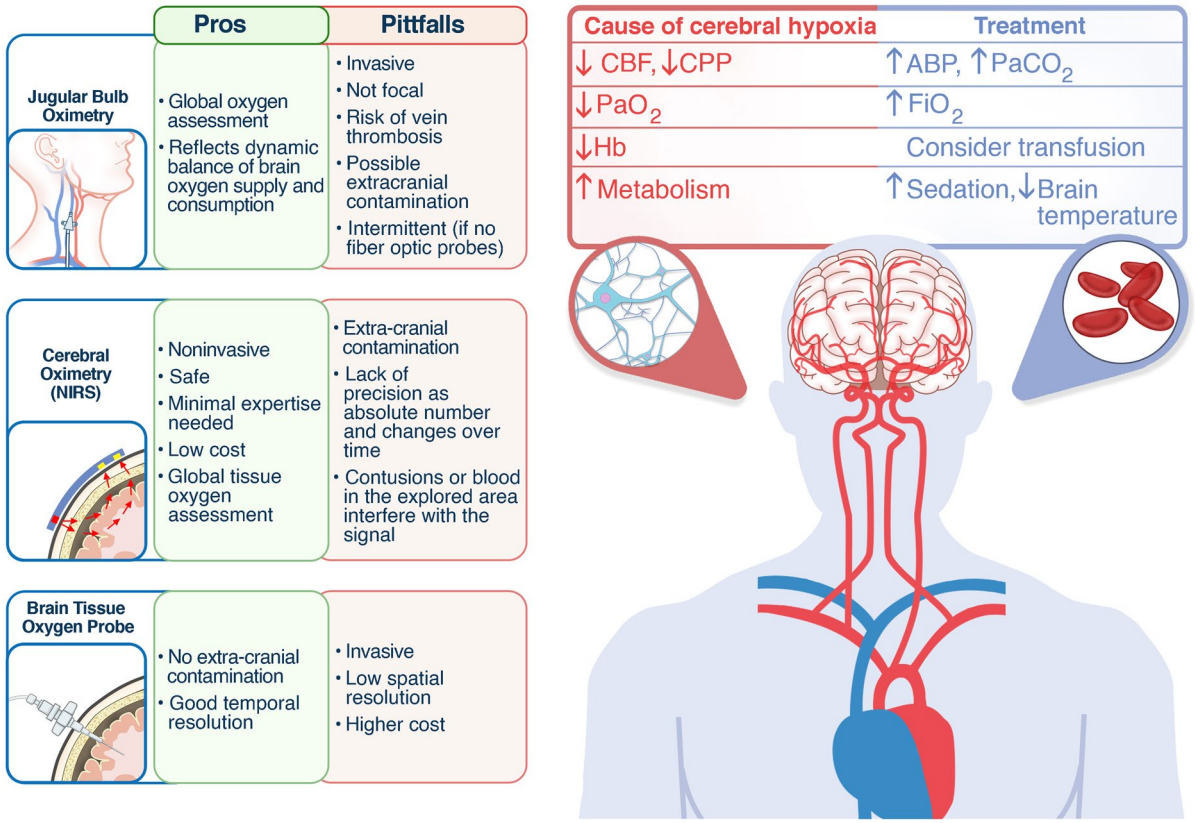

Fig. 1 Main determinants of brain oxygenation and most used devices currently used in clinical practice. *CPP* cerebral perfusion pressure, *CBF* cerebral blood flow, *PaO_2* arterial partial pressure of oxygen, *Hb* hemoglobin, *ABP* arterial blood pressure, *FiO_2* inspired fraction of oxygen

optical fiber technology. $PbtO_2$ measures the oxygenation of brain tissues at the interstitial level, which is dependent on the flux of oxygen through the extracellular compartment, which arises from a concentration gradient maintained by a balance between supply at the capillaries and consumption within the cells [8]. Different catheters are available for $PbtO_2$ monitoring, in particular the "Licox" and "Neurovent," which are directly inserted in the penumbra cerebral area, i.e. close to the contusional or hypoperfused area or at higher risk of secondary damage, through a burr hole. The placement of the probe is evaluated by brain imaging and an oxygen challenge (i.e. fraction of inspired oxygen, FiO_2 at 100% for 5 min) is generally performed to evaluate probe function. Despite being invasive, this technique is usually relatively safe; in a cohort of 123 patients, intracranial bleeding was observed in 14 placements (11%), of which only one required surgical drainage [9].

A $PbtO_2$ threshold of < 20 mmHg is considered a trigger for treatment and interventions, especially in patients with severe TBI [1].

Finally, $SjvO_2$ monitoring has seen a recent increase of interest, as vascular catheters, which can continuously report blood saturation, have been a significant advance over the historical approach of intermittent venous blood sampling and may provide more global cerebral oxygenation measurements.

Evidence and clinical applications

Several observational studies have reported a relationship between reduced $PbtO_2$ and poor outcomes after TBI [10, 11]. In the Brain Oxygen Optimization in Severe Traumatic Brain Injury Phase-II Randomized Trial (BOOST-II) [12], the primary aim was to assess whether a specific therapeutic algorithm based on ICP and $PbtO_2$ values could improve cerebral oxygenation in severe TBI when compared to ICP alone. The trial included 119 patients and demonstrated that using a management protocol based on both ICP and $PbtO_2$ significantly reduced the time spent within cerebral hypoxia (reduction of the total duration of hypoxia by 66% and an average depth of hypoxia by 72%). In addition, the trial demonstrated the safety (i.e., low incidence of complications)

and feasibility of the use of such monitoring in these patients. Although the trial was not powered for clinical outcomes, a non-significant trend towards a better neurological outcome was observed in the ICP/$PbtO_2$ group. Currently, three randomized controlled trials investigating the impact on clinical outcomes of $PbtO_2$-guided therapy in TBI patients are ongoing: the BOOST-III trial (NCT03754114) [13] and the Brain Oxygen Neuromonitoring in Australia and New Zealand Assessment Trial (BONANZA) (ACTRN12619001328167) [14], which will both assess the effects of this strategy on the long-term neurological outcome (i.e., Glasgow Outcome Scale-Extended, GOS-E, scale evaluated at 6 months) and the French OXY-TC trial (NCT02754063) [15], which will assess the impact of such approach on brain injury assessed by brain imaging (Table 1, Electronic Supplementary Material).

While awaiting the results of these trials, current recommendations and clinical algorithms for the management of TBI counsel that, when progression in the intensity of care would exceed the "Tier 1" for ICP treatment, additional $PbtO_2$ monitoring should be taken into consideration to individualize patients' treatment, i.e., CPP and haemoglobin targets [16, 17]. Whether such an approach might also help non-TBI patients with an acute brain injury remains to be demonstrated.

Monitoring invasive cerebral oxygenation has significant implications for individualizing the clinical management of ABI patients. Such tool should be part of the multimodal neuromonitoring methods and could drive specific interventions in this setting to minimize secondary brain injuries.

Supplementary Information
The online version contains supplementary material available at https://doi.org/10.1007/s00134-022-06788-w.

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Funding
None.

Declarations

Conflicts of interest
FST received lecture fees from INTEGRA and is Advisory Board Member from Neuroptics, all outside the submitted work. CR received lecture fees from Masimo and GE healthcare, outside the submitted work. GC reports grants and personal fees as Speaker Bureau Member and Advisory Board Member from INTEGRA and Neuroptics, all outside the submitted work.

Publisher's Note

Received: 24 May 2022 Accepted: 12 June 2022
Published: 7 July 2022

References

1. Taran S, Pelosi P, Robba C (2022) Optimizing oxygen delivery to the injured brain. Curr Opin Crit Care 28(2):145–156
2. Robba C, Graziano F, Rebora P, Elli F, Giussani C, Oddo M, Meyfroidt G, Helbok R, Taccone FS, Prisco L, Vincent JL, Suarez JI, Stocchetti N, Citerio G (2021) Intracranial pressure monitoring in patients with acute brain injury in the intensive care unit (SYNAPSE-ICU): an international, prospective observational cohort study. Lancet Neurol 20(7):548–558
3. Chesnut R, Aguilera S, Buki A, Bulger E, Citerio G, Cooper DJ, Arrastia RD, Diringer M, Figaji A, Gao G, Geocadin R, Ghajar J, Harris O, Hoffer A, Hutchinson P, Joseph M, Kitagawa R, Manley G, Mayer S, Menon DK, Meyfroidt G, Michael DB, Oddo M, Okonkwo D, Patel M, Robertson C, Rosenfeld JV, Rubiano AM, Sahuquillo J, Servadei F, Shutter L, Stein D, Stocchetti N, Taccone FS, Timmons S, Tsai E, Ullman JS, Vespa P, Videtta W, Wright DW, Zammit C, Hawryluk GWJ (2020) A management algorithm for adult patients with both brain oxygen and intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). Intensive Care Med 46:919–929
4. Hunt K, Bose G (2020) Clinical neuroprotection and secondary neuronal injury mechanisms. Anaesth Intensive Care Med 21:293–297
5. Rosenthal G, Hemphill SM, Martin C, Morabito D, Obrist WD, Manley GT (2008) Brain tissue oxygen tension is more indicative of oxygen diffusion than oxygen delivery and metabolism in patients with traumatic brain injury. Crit Care Med 36(6):1917–1924
6. Robba C, Poole D, McNett M, Asehnoune K, Bösel J, Bruder N, Chieregato A, Cinotti R, Duranteau J, Einav S, Ercole A, Ferguson N, Guerin C, Siempos II, Kurtz P, Juffermans NP, Mancebo J, Mascia L, McCredie V, Nin N, Oddo M, Pelosi P, Rabinstein AA, Neto AS, Seder DB, Skrifvars MB, Suarez JI, Taccone FS, van der Jagt M, Citerio G, Stevens RD (2020) Mechanical ventilation in patients with acute brain injury: recommendations of the European Society of Intensive Care Medicine consensus. Intensive Care Med 46:2397–2410
7. Bogossian EG, Rass V, Lindner A, Iaquaniello C, Miroz JP, Dos Santos E, Njimi H, Creteur J, Oddo M, Helbok R, Taccone FS (2022) Factors associated with brain tissue oxygenation changes after RBC transfusion in acute brain injury patients. Crit Care Med 50(6):e539–e547
8. Leach MR, Shutter LA (2021) How much oxygen for the injured brain—can invasive parenchymal catheters help? Curr Opin Crit Care 27:95–102
9. Al Barajraij M, Bogossian E, Dewitte O, Gaspard N, El Hadwe S, Minini A, Andre J, Taccone FS, Schuind S, Barrit S (2021) Safety profile of an intracranial multimodal monitoring bolt system for neurocritical care: a single-center experience. Acta Neurochir (Wien) 163(12):3259–3266
10. Stiefel MF, Spiotta A, Gracias VH, Garuffe AM, Guillamondegui O, Maloney-Wilensky E, Bloom S, Grady MS, LeRoux PD (2005) Reduced mortality rate in patients with severe traumatic brain injury treated with brain tissue oxygen monitoring. J Neurosurg 103(5):805–811
11. Spiotta AM, Stiefel MF, Gracias VH, Garuffe AM, Kofke WA, Maloney-Wilensky E, Troxel AB, Levine JM, Le Roux PD (2010) Brain tissue oxygen-directed management and outcome in patients with severe traumatic brain injury. J Neurosurg 113(3):571–580
12. Okonkwo D, Shutter L, Moore C, Temkin NR, Puccio AM, Madden C, Andaluz N, Chesnut R, Bullock MR, Grant G, McGregor J, Weaver M, Jallo J, LeRoux P, Moberg D, Barber J, Lazaridis C (2017) Brain oxygen optimization in severe traumatic brain injury phase-II: a phase II randomized trial. Crit Care Med 45(11):1907–1914

13. BOOST-3 | SIREN [Internet] (2021) https://siren.network/clinical-trials/boost-3. Accessed 23 June 2022
14. BONANZA-ANZICS [Internet] (2021) https://www.anzics.com.au/current-active-endorsed-research/bonanza/. Accessed 10 Dec 2021
15. Payen J-F, Richard M, Francony G, Audibert G, Barbier EL, Bruder N, Dahyot-Fizelier C, Geeraerts T, Gergele L, Puybasset L, Vigue B, Skaare K, Bosson JL, Bouzat P (2020) Comparison of strategies for monitoring and treating patients at the early phase of severe traumatic brain injury: the multicentre randomised controlled OXY-TC trial study protocol. BMJ Open 10:e040550
16. Hawryluk GWJ, Aguilera S, Buki A, Bulger E, Citerio G, Cooper DJ, Arrastia RD, Diringer M, Figaji A, Gao G, Geocadin R, Ghajar J, Harris O, Hoffer A, Hutchinson P, Joseph M, Kitagawa R, Manley G, Mayer S, Menon DK, Meyfroidt G, Michael DB, Oddo M, Okonkwo D, Patel M, Robertson C, Rosenfeld JV, Rubiano AM, Sahuquillo J, Servadei F, Shutter L, Stein D, Stocchetti N, Taccone FS, Timmons S, Tsai E, Ullman JS, Vespa P, Videtta W, Wright DW, Zammit C, Chesnut RM (2019) A management algorithm for patients with intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). Intensive Care Med 45:1783–1794
17. Meyfroidt G, Bouzat P, Casaer MP, Chesnut R, Hamada SR, Helbok R, Hutchinson P, Maas AIR, Manley G, Menon DK, Newcombe VFJ, Oddo M, Robba C, Shutter L, Smith M, Steyerberg EW, Stocchetti N, Taccone FS, Wilson L, Zanier ER, Citerio G (2022) Management of moderate to severe traumatic brain injury: an update for the intensivist. Intensive Care Med 48:649–666