

Monitoring Cerebral Perfusion and Oxygenation: An Elusive Goal

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ABSTRACT

The impetus for cerebral hemodynamic monitoring in neurotrauma first arose from the original “talk and die” studies which described the group of head injured patients “who talk and then subsequently died”. At necropsy, hypoxic or ischaemic brain damage was observed in a variable proportion of patients raising the possibility that systemic or cerebral hypoxia post trauma may have contributed to the poor neurological outcome. Improved understanding of the pathophysiology of neurotrauma influenced clinical practice in two ways: a) there was a plethora of monitoring modalities developed for evaluating cerebral hemodynamics and oxygenation and b) squeezing oxygenated blood through a swollen brain became the cornerstone of therapy in patients with head injury.

Whilst there appears to be some agreement on the principles of management of neurotrauma, opinion still remains divided on what provides the best assessment of cerebral perfusion and oxygenation. Although initial monitoring was largely confined to global indices of brain oxygenation, refinement in technology has made the measurement of oxygen tensions further down in the oxygen cascade at the level of the tissue possible and applicable by the bedside. Metabolic monitoring of the brain is now possible with the use of a variety of biochemical indices and with the availability of microdialysis. The purpose of this review is to examine the various modes of monitoring cerebral oxygenation, critically review the literature concerning their use in day to day intensive care practice, outline their limitations and define possible indications for their use. (Critical Care and Resuscitation 2005; 7: 195-199)

Key words: Cerebral perfusion, cerebral oxygenation, monitoring, resuscitation, review

The impetus for cerebral haemodynamic monitoring in neurotrauma first arose from the original “talk and die” studies which described the group of head injured patients “who talk and then subsequently died”.^{1,2} At necropsy, hypoxic or ischaemic brain damage was observed in a variable proportion of patients raising the possibility that systemic or cerebral hypoxia post trauma may have contributed to the poor neurological outcome. This conclusion was further supported by data from the studies of Bouma *et al*,³ and Jaggi *et al*,⁴ who demonstrated an inverse correlation between cerebral blood flow and neurological outcome in neurotrauma. The results from the Traumatic Coma Data Bank study confirmed the importance of hypoxia and hypotension in determining outcome from neurotrauma.⁵ Improved

understanding of the pathophysiology of neurotrauma influenced clinical practice in two ways: a) there was a plethora of monitoring modalities developed for evaluating cerebral hemodynamics and oxygenation and b) squeezing oxygenated blood through a swollen brain became the cornerstone of therapy in patients with head injury.

Whilst there appears to be some agreement on the principles of management of neurotrauma, opinion still remains divided on what provides the best assessment of cerebral perfusion and oxygenation. Although initial monitoring was largely confined to global indices of brain oxygenation, refinement in technology has made the measurement of oxygen tensions further down in the oxygen cascade at the level of the tissue possible and

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applicable by the bedside. Metabolic monitoring of the brain is now possible with the use of a variety of biochemical indices and with the availability of microdialysis. The clinician is now faced with both the choice and the dilemma of a large range of monitoring modalities to choose from, each of which has its own advantages and limitations.

The purpose of this review is to examine the various modes of monitoring cerebral oxygenation, critically review the literature concerning their use in day to day intensive care practice, outline their limitations and define possible indications for their use.

Factors determining cerebral oxygenation

The three main factors determining cerebral oxygenation are cerebral blood flow (CBF), arterial oxygen content (CaO_2) and cerebral metabolic rate of oxygen consumption (CMRO_2). In clinical practice, monitoring of arterial blood gas tensions is routine in most critically ill patients. CMRO_2 measurement is not commonplace in most intensive care units as it is technically cumbersome and is difficult to manipulate in clinical practice. Therefore, the predominant monitoring strategy in clinical practice has tended to focus on obtaining measurements of cerebral blood flow or its surrogates.⁶ Although a number of monitoring modalities are available, only few have reached clinical application and these will be reviewed in more detail.

Intracranial pressure (ICP) and cerebral perfusion pressure (CPP)

The ICP is currently the main parameter monitored in patients with TBI.⁷ Elevated ICP has been shown to be an independent predictor of outcome in patients with neurotrauma and averaged ICP exceeding 25 mmHg over the duration of monitoring doubles the risk of death. More sophisticated monitoring of ICP includes analysis of waveforms and assessment of compliance of the CSF compartment, both of which have been shown to have prognostic value in neurotrauma. The other benefits of measuring ICP include the ability to calculate CPP, titration of therapies such as CPP oriented and Lund protocols, and determination of need for decompressive craniectomy. To measure ICP reliably, an invasive monitoring system such as a fluid filled intraventricular catheter or a solid state fiberoptic device is required.

Fluid filled systems provide accurate data and facilitate CSF drainage to decompress the ventricular system. However, they have limited frequency response and present a risk of infection. Solid state fiberoptic devices produce highly accurate data initially, but are prone to signal drift, do not allow for CSF drainage and are expensive. Furthermore, the assumption that ICP is

uniformly distributed across the entire CSF space only holds true when there is unhindered circulation of CSF across all compartments and spaces. In the presence of brain swelling or if there is asymmetrical brain injury, this assumption may not be valid. Finally, there have been no randomised controlled trials to demonstrate that ICP monitoring improves overall outcome.

Although cerebral blood flow is an important determinant of cerebral oxygen delivery, its measurement with nitrous oxide or the Xenon 133 radiotracer is cumbersome and not practical in the ICU. The cerebral perfusion pressure is frequently used as an alternative for cerebral blood flow (CBF) measurements.

The era of CPP management in neurotrauma was ushered in by Rosner *et al.*⁸ Their data together with other studies demonstrating worse outcomes with low blood pressures formed the basis of the 1995 Brain Trauma Foundation guidelines of a CPP of 70 mmHg in neurotrauma. However subsequent studies have challenged this approach based on several lines of evidence: a) the demonstration of a plateau in brain tissue PO_2 at a CPP of 60 mmHg, b) the higher risk of ARDS in patients who are treated with pressors to achieve target CPP and c) the demonstration of elevations in ICP with a CPP targeted approach. These have led to a revision of BTF guidelines in 2003 to a CPP of 60 mmHg. Despite an improved understanding of cerebral hemodynamics in neurotrauma and development of mathematical indices to quantify derangement in cerebral perfusion and intracranial hypertension,⁹ identifying when ischemia happens continues to be a challenge. Recently, Steiner *et al* described a novel approach to individualising CPP therapy in patients with neurotrauma using cerebrovascular reactivity.¹⁰ They were able to define an optimum CPP range for their patients which appeared to result in improved outcome. Whilst attractive in concept, it needs to be validated in prospective randomised studies.

Transcranial Doppler (TCD)

TCD allows the measurement of blood flow velocity in the basal cerebral arteries using three naturally occurring acoustic windows - transtemporal, transorbital and transforaminal.¹¹ The systolic, diastolic and the mean flow velocity are measured, while the pulsatility index is a derived variable, calculated as the difference between the systolic and the diastolic flow velocity divided by the mean flow velocity. Potentially useful information provided by TCD in neurotrauma includes (a) assessment of cerebrovascular reactivity by utilising the response of flow velocity to changes in PaCO_2 (b) distinction between spasm and hyperaemia based upon

the comparison between extracranial and intracranial flow velocity (c) assessment of CPP using the pulsatility index and (d) detection of brain death.

The limitations of TCD include a variable relationship between velocity and flow, problems of long term fixation of the ultrasound probe, inter and intra-observer variability in the measurement process and presence of significant beat to beat variability in velocities even in healthy volunteers.^{12,13}

Jugular venous oximetry¹⁴

Jugular venous oximetry provides a measurement of the venous oxygen saturation in the jugular bulb (SjO_2). The jugular venous saturation is directly proportional to CBF and arterial oxygen saturation (SaO_2) and inversely proportional to cerebral metabolic rate of oxygen ($CMRO_2$). If SaO_2 remains constant and $CMRO_2$ is assumed to be constant, then changes in SjO_2 are proportional to changes in cerebral blood flow. Normal values range from 55 - 75%. There is unequivocal evidence that jugular venous desaturation is associated with poorer neurological outcome.

Despite a number of studies demonstrating its usefulness in the management of neurotrauma, this technique has not found uniform acceptance among intensivists. This is because of the invasive nature of the technique, the difficulty in identifying the appropriate side for cannulation, erroneous readings resulting from catheter malposition, impaction and thrombus formation. The SjO_2 data reflect global cerebral oxygenation and may miss important regional changes. SjO_2 has been found to correlate strongly with tissue PO_2 in the normal brain, but a similar relationship has not been demonstrable in contused brain. It is an index of CBF only if $CMRO_2$ is assumed to be constant. This is however not the case in patients with neurotrauma as they often have fever or seizures which will influence the $CMRO_2$. Finally, there is no evidence to suggest that prevention and treatment of jugular venous desaturation improves outcome.

Brain tissue pH, PCO_2 and PO_2 measurements

In the last 10 years, measurement of brain tissue oxygen tension has become popular in neurointensive care.¹⁴⁻¹⁶ This is largely due to miniaturisation of the Clark electrode and fiberoptic systems (optodes) which has permitted the measurement of gas tensions and pH in tissues.¹⁷ These probes can be placed in the brain surgically either at the time of craniotomy or through a burr hole. The range for normal brain PO_2 has been reported to be 10 - 20 mmHg. These measurements have allowed us to quantify cerebrovascular reactivity (the change in tissue PO_2 and PCO_2 for a given change in arterial oxygenation or ventilation). This is used as a

measure of cerebral autoregulatory status and as a means to prognosticate outcome. Furthermore, critical PO_2 thresholds have been identified in neurotrauma. A brain tissue PO_2 of 5 mmHg has been shown to be associated with poor neurological outcome in head injured patients. However, therapeutic measures designed to improve brain tissue PO_2 such as arterial hyperoxia, whilst improving oxygenation have not been accompanied by an improved neurological outcome.

There are a number of unanswered questions with these devices with regard to tissue oxygenation monitoring. Firstly, their insertion may be associated with tissue trauma. It has been previously demonstrated that the presence of clot and devitalised tissue may interfere with sensor measurements. Secondly, in vivo calibration is not possible as the "true" tissue gas tension is not known. Thirdly, the scanning area for these sensors is variable, reported to be 20 mm² for the Licox, which may not be large enough to detect ischaemia in the entire ischaemic penumbra. It has been shown that on the cortical surface, brain PO_2 varies markedly over a distance of a few millimetres. The issues of infection risk and costs also need to be considered.

Cerebral microdialysis

This technique enables prolonged measurements of extracellular fluid metabolites.¹⁸ The microdialysis catheter is inserted through a burr hole. The method uses an internally perfused semipermeable membrane probe, which allows water soluble substances such as lactate, glucose, amino acids and electrolytes to be collected for analysis outside the brain. In combination with a measure of cerebral blood flow, the method provides a novel approach to studying the relationship between cerebral perfusion and metabolism. Fluctuations in concentrations of extracellular fluid metabolites may provide evidence of ischaemic damage (glucose, lactate, pyruvate, L/P ratios, and glycerol) or excitotoxicity (glutamate, aspartate). The limitations of the microdialysis technique are its invasiveness, its ability to sample a small volume of cortical tissue and the potential for introduction of infection. Whilst it is used in many centres to monitor brain chemistry in neurotrauma, studies suggesting that therapy titrated to microdialysis parameters result in an improved outcome are lacking.

Biochemical markers of brain injury

There has been renewed interest in defining biochemical markers of brain injury which can be identified by a simple blood test.¹⁹ Most research on this topic to date has focused on neuron-specific enolase and S-100 proteins but these have not proven to be

satisfactory for a variety of reasons. Other markers under consideration include aquaporins, calpains and caspase-3. There are also published data to suggest that serum procalcitonin might reflect severity of neurotrauma in the absence of an infection.²⁰ Until more data become available, these markers can only be considered research tool.

Monitoring cerebral oxygenation - a realistic or an elusive goal?

Current management of neurotrauma focuses on prevention of secondary insults. This approach has borne fruit as illustrated by a fall in mortality in recent decades. Whilst class I data are lacking, few would disagree that this is in some measure due to an ability to monitor cerebral oxygenation, either intermittently or continuously. Whilst some techniques, are commonly used in clinical practice, others are still primarily research tools. Various monitoring techniques such as transcranial doppler, jugular venous oxygen saturation and ICP waveform analysis attempt to set individual therapeutic endpoints and to target therapy appropriately. The complex and as yet incompletely understood physiology of the injured brain necessitates certain assumptions to be made when these devices are used. This results in a decrease in sensitivity and specificity of the generated data to detect disturbances in cerebral oxygenation. In order to overcome some of these limitations, there has been a shift towards multimodal monitoring to provide an increased power of interpretation. Clearly, some of the currently available techniques need further refinement and evaluation before justifying their routine use in clinical practice. The other requirements for the use of these systems are 1) safety and 2) management based on the information provided should lead to an improved patient outcome. For example, no single trial has been large enough to detect a 1 in 1000 risk of complications. The first step has certainly been made in that direction with the generation of more accurate data. With increasing experience, future precise management of brain injury will become a realistic possibility.

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