Journal of Clinical Neuroscience 26 (2016) 8–13

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Review

Multimodal neuromonitoring for traumatic brain injury: A shift towards individualized therapy

Serge Makarenko [a], Donald E. Griesdale [b,c,d], Peter Gooderham [a], Mypinder S. Sekhon [d,*]

[a] Division of Neurosurgery, Department of Surgery, Vancouver General Hospital, University of British Columbia, Vancouver, BC, Canada
[b] Department of Anaesthesiology, Pharmacology and Therapeutics, Vancouver General Hospital, University of British Columbia, Vancouver, BC, Canada
[c] Centre for Clinical Epidemiology and Evaluation, Vancouver Coastal Health Research Institute, University of British Columbia, Vancouver, BC, Canada
[d] Division of Critical Care Medicine, Department of Medicine, Vancouver General Hospital, Room 2438, Jim Pattison Pavilion, 2nd Floor, 899 West 12th Avenue, University of British Columbia, Vancouver, BC V5Z 1M9, Canada

ARTICLE INFO

Article history:
Received 6 April 2015
Accepted 30 May 2015

Keywords:
Brain tissue oxygenation
Intracranial pressure
Multimodal monitoring
Pressure reactivity index

ABSTRACT

Multimodal neuromonitoring in the management of traumatic brain injury (TBI) enables clinicians to make individualized management decisions to prevent secondary ischemic brain injury. Traditionally, neuromonitoring in TBI patients has consisted of a combination of clinical examination, neuroimaging and intracranial pressure monitoring. Unfortunately, each of these modalities has its limitations and although pragmatic, this simplistic approach has failed to demonstrate improved outcomes, likely owing to an inability to consider the underlying heterogeneity of various injury patterns. As neurocritical care has evolved, so has our understanding of underlying disease pathophysiology and patient specific considerations. Recent additions to the multimodal neuromonitoring platform include measures of cerebrovascular autoregulation, brain tissue oxygenation, microdialysis and continuous electroencephalography. The implementation of neurocritical care teams to manage patients with advanced brain injury has led to improved outcomes. Herein, we present a narrative review of the recent advances in multimodal neuromonitoring and highlight the utility of dedicated neurocritical care.

1. Introduction

Traumatic brain injury (TBI), is a major cause of death and disability worldwide with a significant proportion of survivors experiencing long term disabilities [1,2]. Outcomes are determined by both the primary insult and a complex cascade of pathophysiological sequelae culminating in secondary brain injury [3]. These sequelae include cerebral hypoxia, metabolic crisis, vasospasm, dysfunctional autoregulation and seizures, all of which ultimately lead to an imbalance of cerebral oxygen delivery and utilization, resulting in cell death and cerebral edema [3–7]. Cerebral edema reduces intracranial compliance and may cause a dangerous rise in intracranial pressure (ICP) which itself leads to reduced cerebral oxygen delivery and cerebral blood flow (CBF) [3].

ICP transduction, clinical neurological examination and CT scanning, have been the primary methods of monitoring patients with TBI. The clinical examination is an essential aspect of multimodal neuromonitoring; however, its accuracy is often confounded by intravenous sedation or concomitant metabolic derangements. In isolation, the clinical examination may be non-specific and deterioration occurs as a late manifestations of secondary brain injury have already taken place [8,9]. As such, ICP monitoring has traditionally been used to help detect changes in intracranial compliance and to optimize cerebral oxygen delivery by allowing cerebral perfusion pressure targeted therapy [10]. Unfortunately, observational evidence concerning ICP monitoring in TBI is disappointing without clear clinical benefit being demonstrated [11–14]. As such, some clinicians remain sceptical as to the clinical value of ICP monitoring in isolation [15].

With addition of brain tissue oxygenation ($PbtO_2$), assessment of cerebral autoregulation using the pressure reactivity index (PRx) and continuous electroencephalography (cEEG), to invasive ICP monitoring, multimodal neuromonitoring helps to promptly detect and treat early signs of cerebral ischemia and identify acute deterioration in neurologic function [9]. Cerebral microdialysis can further assist to identify inadequate cerebral oxygen delivery, neuroglycopenia and cellular metabolic crisis.

The Brain Trauma Foundation (BTF) guidelines recommend a universal (that is, one-size fits all) approach to the neurophysiologic management of TBI: maintain ICP < 20 mmHg and cerebral perfusion pressure (CPP) between 50 and 70 mmHg [10]. Although

* Corresponding author. Tel.: +1 604 875 5949; fax: +1 604 875 5957.
E-mail address: mypinder.sekhon2@vch.ca (M.S. Sekhon).

http://dx.doi.org/10.1016/j.jocn.2015.05.065
0967-5868/

clinical practice guidelines are important to educate providers and reduce the variability of clinical care, the current BTF guidelines do not consider the individual pathophysiological variations in patients or their injuries. A multimodal neuromonitoring strategy allows clinicians to employ individualized management within the context of protocolized care. The purpose of this narrative review is to discuss multimodal neuromonitoring, including continuous ICP transduction, assessment of autoregulation using PRx, $PbtO_2$, cEEG and cerebral microdialysis with a particular focus on individualizing patient care decisions. Finally, we will review the evidence pertaining to specialized neurocritical care.

2. ICP monitoring

Elevated ICP after TBI has consistently been associated with increased mortality and poor neurological outcome [16,17]. Therefore, invasive ICP monitoring has remained a cornerstone of critical care management of patients with severe TBI. The BTF recommends ICP monitoring in all patients with a severe TBI (Glasgow Coma Scale [GCS] score $\leqslant 8$) who have an abnormality on CT scan. The guidelines also recommend ICP monitoring in the setting of a severe TBI and normal head CT scan if at least one of the following is present: age greater than 40 years, posturing on clinical examination, or a systolic blood pressure < 90 mmHg [10].

Despite sound biological rationale, studies evaluating invasive ICP monitoring in TBI patients have yielded disappointing results [14,18]. Observational evidence is conflicting when examining ICP monitoring based management and outcomes in TBI patients [11,12,18–20]. The BEST-TRIP study, a randomized control trial of an ICP monitoring based management algorithm compared to a clinical examination plus CT scan based strategy in patients with TBI attempted to answer questions surrounding routine ICP monitoring in TBI [13]. BEST-TRIP included 324 patients with severe TBI (admission GCS $\leqslant 8$) admitted to one of six intensive care units in either Bolivia or Ecuador. Patients were randomized to receiving either ICP-monitoring (target ICP < 20 mmHg) or imaging and clinical examination. There was no difference in the two arms of the trial on the primary outcome, a novel composite score of 21 measures. Furthermore, there was no difference in either 6 month mortality or on the extended Glasgow Outcome Scale [13]. Of note, the image-clinical examination group had more aggressive ICP lowering interventions [13]. Despite no benefit to ICP monitoring in this trial, there are several important considerations when interpreting these results. First, pressure-monitoring had never previously been used in the study centers. Second, the generalizability of studies from the developing world, with minimal access to post-critical care rehabilitation services, is limited. This is evident as patients in the BEST-TRIP trial had much higher mortality (38%) compared to other randomized trials in patients with TBI [13]. To compare, patients in the DECRA trial, with similar admission GCS motor scores of 5, had a mortality of 19% [21]. Additionally, it is imperative to note that BEST-TRIP did not evaluate the effectiveness of ICP lowering therapy, as both groups underwent intensive ICP lowering therapies [22].

Although BEST-TRIP had limitations, the results of this trial have raised many important questions which have undoubtedly led to a deeper understanding of the complex pathophysiology at play in TBI. In particular, questions surrounding the current approaches to the management of TBI with a "one size fits all" approach targeting an ICP < 20 mmHg or whether an ICP < 20 mmHg is the correct treatment trigger for all patients have been raised. Ultimately, BEST-TRIP suggested that perhaps the approach to TBI management should move away from a "one size fits all" paradigm and instead individualize patient care decisions depending on the underlying injury and pathophysiology. This approach is best implemented with a multimodal monitoring platform. A fundamental weakness with the current classification of TBI is the failure to capture the underlying heterogeneous injury patterns that can occur after blunt trauma [9]. For example, diffuse axonal injury, contusions or subdural hematomas are entirely different pathophysiological entities, yet they are often treated in a similar fashion. It is not surprising that applying a universal approach with ICP monitoring to all severe TBI patients has not resulted in more consistent outcomes.

The recent recommendations from the International Consensus Conference on Neuromonitoring suggest ICP monitoring using intra-parenchymal catheter or external ventricular drains should be used in patients who are at risk of elevated ICP and should be used to guide medical and surgical interventions. The consensus statement supports an ICP treatment trigger of 20–25 mmHg in the context of data obtained from other monitor devices in a multimodal monitoring platform [9]. Furthermore, there is much more information to be gained from ICP monitoring beyond the single number. For example, intracranial compliance can be assessed by ICP waveform analysis [23,24] and correlation coefficient between the ICP waveform amplitude and the mean ICP (RAP index) [23,25]. Finally, the relationship between ICP and mean arterial pressure (MAP) fluctuations can provide vital information pertaining to the underlying cerebrovascular reactivity and autoregulation [26,27].

3. Assessment of cerebral autoregulation

In normal health, cerebral autoregulation ensures that CBF remains constant over a wide range of MAP [28] (Fig. 1a). Historically, the complete loss of cerebral autoregulation after brain injury was thought to result in a pure linear relationship between CBF and MAP. On the contrary, recent evidence has suggested that autoregulation is intact post-TBI but exists over a narrowed range [27,29] (Fig. 1b). Identification of this narrowed range and targeted individualized optimal CPP therapy has been made possible by real time measures of cerebral autoregulation [27,30].

PRx is a correlation coefficient between MAP and ICP [23]. It is a robust bedside measure of cerebral autoregulation and varies between values of −1 and +1 [27]. Within the narrowed zone of intact autoregulation post-TBI, cerebral vasculature will vasoconstrict or vasodilate in response to increasing or decreasing MAP, respectively. This is to ensure a stable CBF across a range of CPP. As an example, when MAP increases, cerebral vasoconstriction leads to a decreased cerebral vascular compartment volume with a resultant decreased in ICP [26,27] (Fig. 2). In this scenario, MAP and ICP are negatively correlated (negative PRx). A negative PRx indicates preserved autoregulation [27,29]. Outside the zone of cerebral autoregulation, pressure passive cerebral vascular vasodilation occurs with increasing systemic perfusing pressures [27]. The resultant increase in the cerebral vascular compartment volume gives rise to increased ICP. In this case, MAP and ICP both increase (positive PRx).

Continuous determination of PRx is made possible through bedside integration of MAP and ICP fluctuations with the ICM+ monitoring software (Cambridge Enterprise, Cambridge, UK) [27,29]. The ICM+ monitoring software generates a real time summation of continuous PRx values over a range of MAP. With PRx plotted on the y axis and a range of MAP or CPP plotted against the x axis, a "U shaped" curve is produced [27,29,31] (Fig. 3). The nadir of the U shaped curve corresponds to the particular range of CPP where the PRx is most negative, indicating the precise systemic perfusion pressure at which the injured brain maintains intact autoregulation [31] (Fig. 3). This "optimal CPP" (CPP_{OPT}) provides an opportunity to tailor cerebral perfusion therapy for each individual patient