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COMMENTARIES

State of the Art in Cerebral Trauma: A Neurosurgeon's Perspective

Frank P. K. Hsu · Joseph R. Keen

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Commentary

Neurosurgery has always played an integral role in the management of cerebral trauma but, historically, treatments were limited and mortality and morbidity high. While cerebral trauma remains a leading cause of death worldwide, advancements in basic science injury models, pharmacology, and prevention strategies over the past several decades have resulted in a better understanding of injury mechanisms and have lead to improved outcomes in certain groups. The elucidation of the pathophysiology of secondary brain injury has lead to more targeted therapies; and the establishment of evidence-based guidelines has systematized the management of cerebral trauma, spawning the growth of neurocritical care, multimodal neuromonitoring, and the resurgence of surgical management.

Cerebral trauma consists of a heterogeneous group of primary injuries with different causes, presentations, severity, and outcomes, but the final common pathway that leads to the most deleterious effects is that of secondary injury, which involves complex biomechanical and biochemical-triggered cascades that lead to cerebral ischemia, metabolic derangements, inflammation, edema, and cell death. Once cerebral blood flow, and therefore oxygenation, is diminished, neurons depolarize and release excitatory neurotransmitters, such as glutamate, that act at NMDA and AMPA receptors to permit massive influxes of sodium and calcium. The influx of calcium, in particular, activates multiple self-digesting mechanisms that lead to membrane damage, DNA degradation, and ultimately cell death [1]. These processes will often propagate until diffuse ischemia, inflammation, and edema lead to brain herniation and death, unless there is prompt intervention.

The goal of neurocritical care is to anticipate the evolution of secondary injury and intervene early. Traditionally, this has been accomplished by measuring intracranial pressure (ICP) with external ventricular drains and parenchymal monitors to derive cerebral perfusion pressure (CPP) by subtracting ICP from mean arterial pressure. The goal has been to keep CPP above an acceptable threshold to ensure adequate cerebral perfusion and oxygenation. While consensus exists for treating ICP greater than 20 mmHg, CPP management has been less straightforward. Some studies have demonstrated improved outcomes with CPP >70 mmHg, whereas several others have not and revealed high rates of pulmonary complications [2]. Currently, the recommended threshold below which CPP should not fall is 50 mmHg, but artificially driving CPP higher than 70 mmHg has fallen out of favor [3]. The difficulty with an ICP and CPP management strategy is that some individuals may benefit from higher or lower CPP values depending upon the nature of their injury. Another complicating factor is that focal injury causing regional metabolic derangements may not be detected by more globally oriented monitoring techniques, such as intracranial pressure monitoring, whereas focal monitoring may not detect the presence of larger areas of injury if the devices reside in normal parenchyma. This underscores the need for multimodal monitoring to achieve the most accurate assessment of a patient's cerebral metabolic needs.

Although intracranial pressure monitoring has been a gold standard, it is an indirect method for evaluating cerebral perfusion and does not directly address other important

F. P. K. Hsu · J. R. Keen (✉)
Department of Neurosurgery,
Loma Linda University Medical Center,
11234 Anderson Street, Rm. 2562-B,
Loma Linda, CA 92354, USA
e-mail: jkeen34@gmail.com

pathophysiological aspects of secondary injury such as delivery of oxygen or metabolic substrate to the brain. For this purpose, adjunctive methods have been developed to measure brain oxygen levels and assess for metabolic stress. This can be achieved by monitoring either jugular venous saturation, which provides a global assessment of cerebral oxygenation, or brain tissue oxygenation, which provides more focal information at a site of injury. A third, less popular, method that can provide information regarding cellular stress is cerebral microdialysis. Regardless of the modality, proper neuromonitoring requires an understanding of cerebral blood flow and metabolism matching. For example, low flow in the setting of normal or high metabolic rate represents ischemia, whereas low flow and a low metabolic rate represent blood flow–metabolic matching and may not reflect a pathological state.

For jugular venous saturation monitoring, which continuously measures venous oxygen content via a fiberoptic catheter placed near the origin of the internal jugular vein, one or multiple desaturations (SjO_2 <50%), high SjO_2 values (>75%), and desaturation episodes within the first 48 h of injury were all associated with poor outcome [4]. Desaturations can be the result of hypotension, hypoxia, hypocarbia, anemia, elevated ICP, or vasospasm. As for brain tissue oxygen monitoring, which continuously measures oxygen content either at a site of injury or normal parenchyma via a fiberoptic probe, the likelihood of death increased with increased duration of time of PbO_2 less than 15 mmHg. A PbO_2 level of 10 mmHg represents the minimally acceptable value, whereas others advocate for thresholds between 15 and 20 mmHg [4]. PbO_2 levels can be addressed by elevating arterial blood pressure, increasing the fraction of inspired oxygen, transfusing packed red blood cells, and reducing ICP by administration of hyperosmotics or, when refractory, evacuating of mass lesions or decompressive craniectomy. In contrast to oxygen based modalities, cerebral microdialysis measures extracellular markers of metabolism. Increased lactate, excitatory amino acids, and glycerol with concomitant decreases in glucose and pyruvate are suggestive of metabolic stress [5]. The use of these monitoring methods must be approached with caution, as it remains unclear whether treatment directed at improving $PbrO_2$, jugular venous saturation, or metabolic substrates leads to better outcomes. Moreover, the treatment strategies that are most effective at avoiding thresholds remain inconclusive.

While many of the therapeutic interventions have remained the same over the past several decades, such as temperature regulation, CSF drainage, sedation, paralysis, and barbiturate coma, the use of hyperventilation and hyperosmotics has changed. Hyperventilation is now reserved as one of the latter options for managing refractory intracranial pressure after it was discovered that clinical outcomes were worse due to loss of the vasoconstrictive effect and rebound ICP [6]. Regarding hyperosmotics, a recent review demonstrated that hypertonic saline was superior to mannitol in decreasing intracranial pressure; however, it was inconclusive whether hypertonic saline (HTS) surpasses mannitol in clinical outcomes [7]. The physiologic advantage of HTS is not only its intravascular oncotic effect, but its ability to reduce blood viscosity, increase RBC rheology, and induce endothelial cell shrinkage, which all lead to improved circulation, cerebral blood flow, and decreased intracranial pressure without the diuretic effect of mannitol that can further exacerbate secondary injury mechanisms. The optimal concentration is unclear as concentrations ranging from 3% to 23.4% have been effective.

When intracranial pressure becomes refractory to medical management, the final option in the stepwise treatment of cerebral trauma is decompressive craniectomy. Decompressive craniectomy is performed in two different scenarios of cerebral trauma: (1) in conjunction with the evacuation of any type of intradural lesion to avoid post-surgical increases in ICP or (2) in patients without operative mass lesions who have ICP refractory to medical management. Little has change regarding the evacuation of mass lesions but controversy continues regarding decompressive craniectomy in the setting of diffuse edema as it is unclear if outcomes improve. Unfortunately, the recent publication of the DECRA trial in the *New England Journal of Medicine* [8] has done little to settle the issue. The trial was designed to evaluate the effect of bifrontotemporoparietal decompressive craniectomy versus standard medical treatment in adults less than 60 years old with severe TBI and whose ICP were refractory to first tier medical management. While there was clearly a greater reduction in ICP, fewer interventions to decrease ICP, and shorter duration of mechanical ventilation and ICU stay, these patients had lower median Extended Glasgow Come Outcome Scale scores and a higher risk of unfavorable outcome than those receiving standard care (70% versus 51%). The major criticism of this study was that a greater number of patients in the craniectomy group had unreactive pupils at hospital admission, and when adjusted for this variable, the harmful effect of the craniectomy was no longer significant. This trial contradicted the large body of retrospective data demonstrating that good outcomes (48.3%) had outweighed bad outcomes (29.4%) in a total of 323 patients who underwent decompressive craniectomy by 2006. While the DECRA trial was the first prospective, randomized study, many aspects of decompressive craniectomy are unresolved and require additional prospective, randomized studies, of which the forthcoming RESCUEicp trial is one.

Once the decision has been made to perform a decompressive craniectomy, Polin et al. suggest doing so within 48 h of injury onset and report an advantage among pediatric patients when compared to matched controls taken

from the Trauma Coma Data Bank [9]. Additionally, Aarabi et al. found that patients with an admission GCS greater than 6 make them good candidates for decompressive craniectomy [10].

The two main techniques include bifrontal craniectomy and unilateral hemicraniectomy, depending upon the presence, location, and extent of mass lesions, penetrating injuries, and midline shift. When mass lesions are not present or there is no midline shift, nondominant unilateral hemicraniectomy or bifrontal craniectomy may be used, otherwise the side with the greatest lesion volume or edema is selected for unilateral hemicraniectomy. Regardless of approach, the decompression should be large enough to adequately decompress the inferior and posterior portions of the cranial vault (approximately 15 cm anterior–posterior diameter), making sure to decompress to the floor of the temporal fossa and subsequently the basal cisterns. The practice of decompressive craniectomy remains controversial and is not without its complications, which include leaving patients in a state of severe disability, hygromas, hydrocephalus, wound breakdown, seizures, and the syndrome of the trephine.

Cerebral trauma is a heterogeneous group of primary injuries that share a common final pathway of secondary brain injury, which involves a complex interplay of biomechanical and biochemical cascades that, when left unchecked, can lead to brain herniation and death. Through evidence-based guidelines and the development of multimodal neuromonitoring, the goal of neurocritical care is to anticipate the evolution of secondary injury and intervene early when cerebral blood flow, perfusion, and oxygenation are compromised. The neurosurgeon plays an integral role by placing various neuromonitoring devices into the brain and performing a decompressive craniectomy when intracranial pressure and cerebral perfusion is refractory to medical management. While many of the current strategies remain inconclusive, the current state of the art of cerebral trauma is evolving as more sophisticated neuromonitoring protocols, neuroimaging, and more targeted therapies are developed.

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