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Management of Adult Traumatic Brain Injury: A Review

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Abstract

Traumatic brain injury (TBI) is a significant source of morbidity and mortality in the adult population. The management of traumatic brain injury depends on its severity. It must be recognized that almost all forms of treatment for TBI are geared towards the minimization of secondary injury, as it is assumed that primary injury is irreversible. The discussion here represents much of what is known up-to-date concerning TBI management, but its treatment continues to evolve once new mechanisms of injury are discovered and those that we know of now are refined. The treating staffs are encouraged to keep up with the current state of the literature to stay informed.

Keywords: Traumatic brain injury; Glasgow coma scale; ICP monitor; Hypothermia; Adult population; Computed tomography

Introduction

Traumatic brain injury (TBI) is a significant source of morbidity and mortality in the adult population. It is estimated that 2.5 million adults are affected every year [1]. Management of TBI has been the subject of significant research, which has escalated in volume to a large extent with recognition of chronic traumatic encephalopathy as a common entity among athletes and the degree to which TBI has characterized battlefield injuries in conflicts such as Operation Iraqi Freedom.

In general, TBI can range from mild to severe, with the following classification (Table 1). Often, the classification of TBI will show different severity for each metric. In these cases, the most severe classification is accepted. For example, a patient with GCS of 13 with loss of consciousness (LOC) of 48 hours with post-traumatic amnesia (PTA) of 3 days would be classified as "severe" TBI.

The injury sustained in the setting of TBI can be broken down into primary and secondary injury. Primary injury is what is sustained at the time of trauma. This includes direct injury to the parenchyma of the brain, such as axonal shear and rupture. Generally, primary injury is considered irreversible, but may be minimized with preventative measures, such as the use of a helmet.

Secondary injury, on the other hand, is that sustained in the ensuing biochemical cascade after TBI is experienced. This can range from local inflammation causing damage to global ischemia due to increased intracranial pressure (ICP). Most medical management after an injury is designed to minimize this secondary injury with the aim of optimizing the patient's recovery from the primary insult.

Classification	GCS	Loss of Consciousness	Post-Traumatic Amnesia
Mild	13-15	0-30 minutes	< 1 day
Moderate	09-Dec	30 min - 24 hours	1-7 days
Severe	03-Aug	>24 hours	> 7 days

Table 1: Classification of TBI, classifying the patient based on the highest severity in any column [2].

Management of Concussion

Clinical Characteristics

Concussion is characterized by the following:

Observed or documented disorientation or confusion immediately after an event

- Impaired balance within 1 day after injury
- Slower reaction time within 2 days from the injury
- Impaired verbal learning and memory within 2 days from the injury

Concussions are generally considered mild in isolation, but can be somewhat problematic if repeated injury occurs or if an injury is worse than initially recognized [2]. There have been many tests developed to determine whether a concussion has occurred in someone with a head injury. Many of these tests are designed to be administered by non-physician personnel during an athletic contest, and in this capacity are not designed to "rule out" concussion or determine fitness for continued play [3]. Examples of these assessments include the standardized assessment of concussion (SAC), post-concussion symptom scale (PCSS) and graded symptom checklist (GSC). The SAC was developed to assess football players at the sidelines, and showed a sensitivity of 80-94% and specificity of 76%-91% for clinician-diagnosed concussion [4,5]. The PCSS and GSC are also designed for

non-physician use at the sidelines, and reach a sensitivity of 64%-89% and specificity of 91%-100% [5]. These assessments can be found at the following URLs:

- SAC: http://knowconcussion.org/wp-content/uploads/2011/06/SAC.pdf
- PCSS: http://www.hawaiiconcussion.com/PDF/Post-Concussion-Symptom-Scale.aspx
- GSC: http://knowconcussion.org/wpcontent/uploads/2011/06/graded_symptom_checklist.pdf

Imaging

If a head injury is suspected, imaging is often appropriate. Usually computed tomography (CT) is the imaging of choice given its high sensitivity for blood. However, in mild TBI, there are cases in which imaging is not necessary. The classically used "Canadian CT Head Rule" (Table 2) has provided a means to determine the need for a CT of the head in the setting of mild TBI [6]. If any sign or symptom is present from the list, a CT of the head is warranted. If a hemorrhage is found on CT, repeat imaging is warranted generally within 6 hours of the initial scan or with a decline in mental status to determine whether worsening of the lesion has occurred.

MRI is also commonly used to evaluate TBI in the later stages, but is best to evaluate for prognostication and has higher sensitivity for microbleed-type pathologies like diffuse axonal injury [7,8]. It should be noted that head-to-head comparison of MR and CT demonstrated that more lesions are detected via MR, but findings did not necessarily change management or explain otherwise unexplained neurologic deficits [8]. In the acute setting, due to factors such as screening processes, potential for implants, delay in obtaining staffing, and the length of time required to get a scan, MR tends not to be favored as much as CT as an initial test.

High Risk	GCS <15 after 2 hours from the time of injury
	Suspected open or depressed skull fracture
	Sign of basal skull fracture
	2 or more episodes of vomiting
	Patient is 65 years old or older
Medium risk	Amnesia of more than 30 minutes prior to impact
	Dangerous mechanism (Pedestrian struck by motor vehicle, Ejection from motor vehicle, fall from >3 feet or five stairs)

Table 2: Canadian CT Head Rules-If any of the following characteristics are present, a CT of the head is warranted.

Management

Management of mild TBI in the acute setting involves supportive care. Symptoms such as headache and nausea may be treated directly with appropriate medications. Some symptoms such as dizziness require specialty rehabilitation consults to ensure they are addressed appropriately, especially if such symptoms are prolonged in duration [9].

Management of moderate TBI

Unfortunately, Moderate TBI is an area in which there is a paucity of evidence. This middle ground is often lumped together with mild or severe TBI with regards to interventions and outcomes given the heterogeneity of this population and of definitions of "moderate TBI" in the literature. It is estimated that around 20% (8%-28%) of TBI patients can be classified as "moderate" [10]. The definition noted above, which included GCS 9-12, LOC for up to 24 hours, and PTA for 1-7 days is a common one, though some authors include GCS of 13 in this definition due to the increased prevalence of intracranial lesions on CT [11].

In these cases, management should be directed by the appropriate guideline. In the setting of no mass lesion, such as contusions, subdural hematoma (SDH), or epidural hematoma (EDH), supportive care is warranted along with frequent repeat clinical exams, preferably by the same person. Decline in status warrants repeat evaluation with imaging along with repeating labs for electrolytes or cultures depending on the context.

In the setting of a hematoma, repeat imaging within the appropriate time interval is warranted, generally 6 hours from the initial CT of head to monitor for expansion. Repeat imaging is also warranted if the patient has a decline in his or her neurologic status, which at our institution is monitored hourly with repeat Glasgow Coma Scales.

A coagulation profile (Complete blood count or CBC, Prothrombin time/International Normalized Ratio or PT/INR, and activated Partial Thromboplastin Time or aPTT) is recommended on admission. The most-studied factor in this case has been the INR in patients on anticoagulation, and it has been shown that fast correction of a patient's INR to 1.3 or lower decreases hematoma growth and improves outcomes [12]. Platelet transfusion is recommended for thrombocytopenia (platelet count less than 100,000) in the setting of intracranial hemorrhage, but its use to correct for platelet dysfunction due to antiplatelet agents, such as aspirin or clopidogrel, is considered uncertain given conflicting outcomes that have been reported [13]. There is currently no widely-accepted practice regarding reversal of newer anticoagulants, such as direct thrombin inhibitors or Factor Xa inhibitors; however, new reversal agents are on the horizon, such as idarucizumab for dabigatran reversal or andexanet alfa for reversal of anti-Factor Xa agents [14,15].

Hemorrhage on CT, especially subarachnoid hemorrhage (SAH) warrants up to 1 week of antiepileptic drug (AED) therapy, which is often levetiracetam or phenytoin [16,17]. If a person with TBI experiences a seizure, a prolonged course of AEDs is necessary.

The above recommendations on management for mild TBI also apply to moderate TBI, where symptomatic treatment is recommended

for common post-TBI symptoms, including headache, nausea, and dizziness. Early consultation of psychiatry, physical and occupational therapy, and speech and language pathology is recommended to assess for a long-term rehabilitation plan.

Severe TBI

Severe TBI has been extensively studied and focus revolves around external support for oxygenation and cerebral perfusion pressure, either through optimizing hemodynamics or by keeping intracranial pressure (ICP) within an acceptable range. The above recommendations with regard to moderate and mild TBI also apply.

Hemodynamic support

Just as in any other medical context, the ABCs (Airway, breathing, circulation) must be prioritized above all other aspects of a patient's care. Intubation of the patient with a GCS <8 is a commonly-accepted practice to ensure an adequate airway, good ventilation, and adequate oxygenation. Avoiding hypotension and hypoxia are of paramount importance beyond this. An arterial pressure of oxygen (PaO_2) >60 mmHg and systolic blood pressure (SBP) >90 mmHg are the commonly-accepted thresholds to maintain in the severe TBI patient [18]. To ensure these parameters are met, frequent arterial blood gases must be drawn and invasive blood pressure monitoring via an arterial catheter must be implemented. The patient must be assessed for other injuries that be preclude the ability to ventilate effectively or that will allow significant blood loss, such as thoracic, abdominal, pelvic, or extremity injuries. A severe TBI patient that is hypotensive indicates another significant injury is likely present and sources of significant blood loss must be ruled out. The hypotensive patient must be resuscitated adequately with crystalloid fluids and blood transfusion.

In the setting of a severe TBI patient without apparent blood loss or that has been adequately resuscitated that cannot maintain SBP >90 mmHg must be examined for other sources of shock. Frequently, vasoactive medications such as norepinephrine, phenylephrine, or dopamine must be used, and a central access must be achieved for these medications.

ICP monitoring

ICP monitoring is recommended for all salvageable patients with a traumatic brain injury whose exam cannot be followed clinically or whose GCS <8 with an abnormal CT scan of the head [19,20]. The most common devices used to monitor ICP include the external ventricular drain (EVD) and the fiber optic intra-parenchymal probe. Subdural catheter and epidural monitoring of ICP are less reliable, and no noninvasive method of measuring ICP has been found to be acceptable to date. External ventricular drainage tends to be the preferred method given the potential for cerebrospinal fluid (CSF) drainage as a means to control ICP; however, placement carries a greater risk for further brain trauma, tract hemorrhage, and infection when compared to the fiberoptic pressure monitor. Of note, lumbar drainage has been proposed as an alternative to the EVD and has shown effectiveness in some series [21].

ICP must be managed if it approaches or exceeds 20 mmHg, due to the loss of cerebral blood flow auto-regulation at this pressure and subsequent decrease of cerebral perfusion pressure [22]. Multiple methods have been found to decrease the intracranial pressure, some with questionable effects on outcome.

Hyperventilation

Hyperventilation as a means to decrease ICP is controversial, especially given the chance of ischemia at low levels of $PaCO_2$ due to cerebral auto-regulation. Generally, it is accepted that hyperventilation will decrease ICP, but the risk of ischemia becomes unacceptable at $PaCO_2$ <30 mmHg [23]. It is most commonly accepted as a temporizing measure only.

Hyperosmolar therapy

Hyperosmolar therapy relies on the use of an agent to decrease intracellular fluid volume and shift it into the vascular compartment. Two drugs are primarily used in this situation: mannitol and hypertonic saline. Mannitol has been shown to shift fluid effectively across the blood brain barrier as well as improve regional cerebral blood flow [24-26]. Hyperosmolar saline has the same effect, but may be associated with a larger and longer-standing ICP reduction when given in equiosmolar amounts as mannitol [27]. However, hopes of hypertonic saline as an initial resuscitation fluid in those with severe TBI have been dashed [28,29]. There are no trials demonstrating improvement in outcome of hypertonic saline compared to mannitol. It is recommended in the current Brain Trauma Foundation Guidelines that mannitol be used to control ICP after monitoring has been initiated, while hypertonic saline has no specific recommendations [30].

Sedation

Current guidelines recommend sedation with propofol to control ICP as a measure to be taken if hypertonic treatment fails to maintain ICP <20 mmHg; however, there is no benefit with regard to morbidity after 6 months or mortality [31]. Other sedatives have been used, such as dexmedetomidine; however, their benefit is yet to be proven, and some series have demonstrated poor effects, such as hypotension [32].

Barbiturate use is still recommended; however, most evidence concerning them was obtained prior to widespread use of hyperosmolar therapy and other sedatives to control ICP [31]. More recent reviews of barbiturate use have demonstrated that there is no mortality benefit and concomitant hypotension is likely to offset any benefit from ICP management in barbiturate responders [33].

Neuromuscular blockade

Neuromuscular blocking agents (NMBAs) have been studied as another adjunct to decrease intracranial pressure. They have demonstrated success primarily in decreasing ICP increases during stimulatory events, such as endotracheal suctioning and physiotherapy [34,35]. In this respect, there appears to be a benefit, but overall outcome and overall control of ICP is an issue. Retrospective studies that examined overall outcome demonstrated that there was no improvement. In some cases, with the use of a depolarizing NMBA, there have been issues with increased time with ICP >20 mmHg when the paralytic was used as a routine measure in the ICU [36]. These are supported by prospective studies that demonstrate succinylcholine specifically appears to cause increased ICP [37,38]. There has been one study to show a decrease in ICP with a non-depolarizing NMBA, but it was associated with a concomittent decrease in mean arterial pressure [39]. Finally, with regard to overall outcome, there was also noted to be an increased complication rate with the use of NMBAs, such as an increased rate of pneumonia that may explain the paucity of findings demonstrating decreased morbidity and mortality from their use [40].

Craniotomy and craniectomy

Craniotomy and craniectomy are commonly used in the setting of intracranial hematoma after trauma. Table 3 gives commonly-accepted guidelines for at what point intracranial hematomas warrant decompressive surgery [41-44]. It must be understood, though, that these are guidelines, and that individual patients may require surgery for smaller hematomas or may not be surgical candidates despite meeting the below requirements. In fact, given the variability of patient presentation, it is unsurprising that significant variability exists between neurosurgeons with regard to treatment [45].

Type of hematoma	Without respect to decline	With respect to Decline
Subdural	Thickness of 10 mm or more, MLS of 5 mm or more	Thickness <10 mm and MLS <5 mm if GCS decreased by 2 points or more since presentation
Epidural	Volume is 30 cc or more	GCS 8 or less with anisocoria
IntraparEnchymal	Elevated ICP refractory to medical management, signs of mass effect on CT, Lesion volume is 50 cc or more	Signs of deteroriation referable to the lesion, GCS 6-8 and >20 cc of frontal or temporal contusions and MLS of 5 mm or more and/or cisternal compression
Posterior Fossa	Mass effect in posterior fossa (evidence of 4th ventricular distortion, effacement of basal cisterns, hydrocephalus)	Any deterioration that may be attributed to the hematoma

Table 3: Indications for surgical evacuation of intracranial hematomas with respect to decline in mental status (GCS). Thickness is in regard to the maximum thickness on CT of the head. MLS, midline shift

A decompressive craniectomy, either unilateral or bilateral, to treat medically refractory ICP without a mass lesion to evacuate is an area of controversy. This is especially evident after the randomized and controlled DECRA trial demonstrated better ICP control and shorter ICU length of stay with bilateral frontotemporoparietal craniectomy, but more unfavorable outcomes on the extended Glasgow outcome scale (GOS), which was thought to be secondary to the increased survival of vegetative patients [46]. Another randomized controlled trial with unilateral decompressive craniectomies on patients with unilateral diffuse swelling arrived at a different conclusion, demonstrating improved outcomes on the GOS but noted frequent complications, including delayed intracranial hematoma, half of which required surgical evacuation, and contralateral subdural effusion [47]. The largest randomized controlled trial to date, the RESCUEicp trial, has been underway and has completed its enrollment. However, results are forthcoming [48]. Smaller retrospective or nonrandomized studies have had mixed results, as well.

Hypothermia

Hypothermia is a common approach to control of intracranial pressure when many other proven methods have failed. It has been a major focus of many trials since the early 1990's, with positive results from small studies, but equivocal results from larger studies and randomized ones [49,50]. 32-33 degrees and 33.5-34.5 degrees Celsius was a common target point for hypothermia and patients were kept 24-48 hours at the target temperature before being rewarmed. Most recently, the Eurotherm3235 Trial demonstrated worsened outcomes on the GOS-E and worsened mortality, requiring early termination due to apparent harm being performed [51]. However, it must be noted that these studies often had a heterogenous population and careful patient selection may allow hypothermia to be used beneficially as had been demonstrated in smaller trials.

Steroids

The use of corticosteroids was a mainstay for TBI for 30 years. There had been findings that had demonstrated benefit, but there had been no large randomized controlled trials until the MRC CRASH trial [52]. Expectations were that there would be a treatment benefit; however, the trial was halted early by the project steering committee after it was determined the treatment group was significantly worse off than the control group (21% mortality *vs* 18% mortality) [53]. This astonishing result in the largest randomized-controlled trial for the drug single-handedly removed steroids from the armamentarium to treat TBI.

Conclusion

The management of traumatic brain injury depends on its severity. It must be recognized that almost all forms of treatment for TBI are geared towards the minimization of secondary injury, as it is assumed at this time that primary injury is irreversible. The above discussion represents much of what is known concerning TBI, but there almost certainly will be multiple changes in the future once new mechanisms of injury are discovered and those that we know of now are refined. The reader is encouraged to keep up with the current state of the literature to stay informed.

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