Pediatric Traumatic Brain Injury: Present and Future Considerations in Management

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Traumatic brain injury is the leading cause of death and disability in children. Published evidence-based guidelines for the management of acute pediatric traumatic brain injury provide a guide to patient care using a multidisciplinary team approach by clinicians and researchers through an easily incorporated algorithm. While review of these guidelines highlights the considerable lack of data from well-designed, controlled studies resulting in few treatment standards, they do provide a starting point in our understanding and many opportunities for increasing the fund of knowledge in the area. Since the pediatric guidelines also included “key areas for future investigation” in each chapter, there exist already a potential roadmap for questions to be answered for future management.

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**Introduction**

At the present time, data from well-designed, controlled studies on acute management of traumatic brain injury (TBI) in the pediatric population is sparse and lacking. In 2003, the “Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolescents” (Adelson et al. 2003) were published as a multidisciplinary team effort by a group of clinicians and researchers, to highlight the known scientific literature in this field. This provided evidence-based strategies for the management of children following TBI by analyzing the current knowledge base. Systematic review of the methodology used for treating pediatric TBI showed significant dependence on information derived from the adult population or low levels of classes of data in children that lack strength to definitively support existing management. The guidelines aim to bridge this gap and they will be an ongoing project with revisions and additions in the future.

Present guidelines use standard evidence-based methodology that evaluates the literature in support of a specific clinical question. Each individual study that is evaluated is categorized by the strength of the science and methodology. Studies included in Class I evidence are those that were performed as well-designed, randomized, controlled clinical trials. Class II evidence is the next level and consists of less rigorous clinical trials or other reliable, retrospective series including observational, cohort, or case-control studies. Finally, there is class III evidence that includes small or unreliable retrospective observational studies and case reports. The available evidence on each individual topic is then used to define whether an intervention meets the criteria for a “standard”, a “guideline”, or an “option”, and whether it has been more recently supplanted by any level I through III...
recommendations, respectively. A level I recommendation is an accepted principle of patient management derived from Class I or strong Class II data. A level II recommendation reflects moderate clinical certainty and is derived from Class II or ample Class III data. Level III recommendations have an unclear clinical certainty and are based on Class III data. The goal of classifying data and providing levels of recommendations help clinicians identify well-proven interventions. Currently, the pediatric TBI guidelines have only three standards or level I recommendations. These include avoiding propofol as a continuous infusion, avoiding hyperventilation, and the lack of benefit of using anti-epileptic drugs to prevent late (>7 days) seizures. The remainder mostly consists of level II or III recommendations. This paucity of management standards provided the motivation to insert further “expert” recommendations for research within each chapter under the subtopic “Key Areas for Future Investigation”.

**Present Day Management**

**Primary Management Goal**

**Prevention of Second Insults**

Like any other form of traumatic injury, the best treatment of severe pediatric TBI lies in prevention. Ideally, a standardized protocol is started at the earliest possible time of intervention, at the scene and is continued throughout the acute, sub-acute and chronic courses while avoiding second insults and minimizing secondary injury in order to optimize the outcome. It is important to differentiate between these two sequelae.

Second insults are potentially avoidable outcomes of injury and management, and may include hypotension or conversely, severe hypertension, hyper or hypocarbia, and hypoxia that can occur following the primary injury (the injury that occurs at the time of impact). These second insults, on top of the primary injury, can worsen the outcome by potentiating the secondary injury response and can be avoided by strict adherence to a meticulous treatment protocol. Secondary injuries, on the other hand, are secondary mechanisms resulting from the cascade of physiologic and pathophysiologic events following the primary injury and any additional second insults. Some of these secondary injury responses include compromise of cerebral autoregulation, breakdown of the blood–brain barrier, inflammation cascade, oxidative stress pathways, excitotoxicity and apoptosis or delayed cell death. The resultant tissue damage to the already injured brain causes both local and diffuse intracellular and extracellular edema, and further ischemic brain injury. With our current knowledge base, secondary injuries are difficult to prevent, and thus their study provides the greatest potential for advancements in TBI treatment in the future. While the ideal or optimal treatment paradigm remains undetermined, the present day approach to severe TBI management utilizes a multidisciplinary dedicated team with an optimal environment for cerebral recovery, minimizing second insults and preventing secondary injury responses.

**Overview of Guidelines, Key Findings & Results**

The pediatric TBI guidelines aimed to be a comprehensive document reviewing the literature on all aspects of pediatric head injury management. The breadth of the issues discussed ranged from public policy to acute pre-hospital care to the medical and surgical management of these patients. In review of the recommendations, organizing pediatric trauma systems is encouraged since this can facilitate delivery and lead to better care. Transferring children with TBI to a pediatric trauma center leads to decreased morbidity and mortality. If this is not possible, they should be transported to an adult trauma center capable of treating pediatric patients.

All aspects of care of the critically injured children should be optimized from the very initial phases starting from pre-hospital management. Attention to detail in delivery of care throughout transport and admission to the hospital setting is imperative. At the scene, the primary goal is initial resuscitation including establishing a stable airway and circulation to prevent second insults. As hypoxia leads to worse neurological outcome, it should be prevented at all times during pre-hospital and in-hospital care. Depending on the expertise, supplemental oxygen, bag-valve-mask ventilation, and endotracheal intubation can be used to improve oxygenation. Intubation is the only means of securing the airway, reduces the likelihood of aspiration and provides a route to deliver medications. Although detrimental if applied poorly, intubation should be utilized in children with a Glasgow Coma Score (GCS)
Fig. 1 First tier

GCS: Glasgow Coma Scale, ICP: intracranial pressure, CPP: cerebral perfusion pressure, HOB: head of bed, CSF: cerebrospinal fluid, CT: computed tomography, PRN: as needed. (Reprinted with permission from Lippincott Williams & Wilkins)

<9. As right mainstem and esophageal intubation are common in pediatric patients, specialized training and the use of end-tidal CO₂ monitors should be employed. Thus, the optimal method for providing adequate oxygenation and ventilation depends on the available level of expertise.

Sedation, analgesia, and neuromuscular blockade can be used to facilitate management. Although no specific drugs are recommended, the Food and Drug Administration recommends against using continuous infusions of
propofol in the pediatric population due to evidence of unexplained metabolic acidosis and increased mortality with its use. Appropriate sedation and analgesia with selective agents can prevent fluctuations in intracranial pressure (ICP) and blood pressure. Similarly, events like coughing, bucking, and straining can be avoided by the use of paralytic agents. Hypotension also adds to ischemic brain injury and adverse neurological outcomes and should be prevented. Resuscitation fluids should be administered early as children can rapidly develop hypotensive shock.

**ICP Directed Therapy**

As a sustained ICP > 20 mmHg has been shown to be associated with worse outcomes\(^2\), using ICP-guided therapy to maintain ICP below this level may prove advantageous in the pediatric population. An intraventricular pressure transducer is the most accurate and reliable method to monitor ICP. Although useful, parenchymal monitors are prone to measurement drift and lack the benefit of cerebrospinal fluid (CSF) drainage. Currently, the goal of therapy in children with severe TBI is to keep ICP < 20 mmHg and cerebral perfusion pressure (CPP) in the 40 to 65 mmHg range. A recent paper by Adelson et al.\(^3\) showed that regardless of treatment, ICP < 20 and CPP > 50 were associated with good outcomes. The critical ICP value for different ages at injury remains unclear.

**First Tier Therapy**

Initial measures to avoid and/or treat elevated ICP include elevating the head of bed to 30 degrees, preventing obstruction to venous outflow, avoiding hyperthermia, and minimizing stimulation. First tier therapy for persistent ICP elevations includes sedation, paralytics, mild to moderate hypocapnea (30–35 mmHg), and hyperosmolar therapy (Fig. 1). Another strategy that is an option or level III recommendation includes CSF drainage via an external ventricular drain. Although early literature supported the use of prophylactic hyperventilation to counter “hypere- mia” following severe TBI, current evidence shows a low incidence of hyperemia and thus the vasoconstriction from hyperventilation may be more harmful than beneficial. The use of mild to moderate hypocapnea (\(\text{PaCO}_2\) 30–35 mmHg) is an option to lower ICP but should be minimized. As aggressive hyperventilation (\(\text{PaCO}_2 < 30\) mmHg) has the potential of reducing cerebral blood flow to ischemic levels, it is reserved as a second tier option for the management of refractory intracranial hypertension. It should only be utilized as a temporary measure and is to be used in conjunction with brain tissue oxygen monitoring to ensure against ischemia. Various modalities for brain oxygenation or delivery including brain tissue oxygen probes, cerebral blood flow imaging, or jugular venous oxygen monitoring can be used.

Another effective first line option for controlling ICP is hyperosmolar therapy. Euvolemic hyperosmolarity is favored based on current principles of management. There is no data to prove if either hypertonic saline or mannitol is superior to the other. Mannitol has been used for more than half a century and has a two-fold effect. It lowers cerebral blood volume and ICP by reducing blood viscosity, while augmenting cerebral blood flow because of higher blood flow velocity. It also osmotically dehydrates the brain with a resulting decrease in intracranial volume and pressure. In addition, mannitol may potentiate metabolic autoregulation. Mannitol can be titrated to a serum osmolarity of 320 mOsm/L, with concern that higher osmolarity may be associated with renal failure. Although there is more evidence to support its use, hypertonic saline has only recently been taken up at many centers. Its mode of action is similar to mannitol, and it also has the potential advantages of restoring resting membrane potential at a cellular level, stimulating the release of atrial natriuretic peptide, inhibiting the inflammatory cascade, and augmenting cardiac output. There is also evidence that it can augment ICP reduction in patients refractory to mannitol infusion. Hypertonic saline may be used with a serum osmolarity up to 360 mOsm/L. The difference in endpoints for serum osmolarity was only based on the available literature for each modality and not by direct knowledge for the likelihood of renal failure. The mechanisms of action rely on an intact blood brain barrier (BBB) to maintain the osmolality gradient between brain and the hyperosmolar blood. Functioning cerebral autoregulation is also necessary to induce vasoconstriction when lower blood viscosity induces higher blood velocity. The potential benefits of hypertonic saline favor this therapy when the BBB has been disrupted.

Except for the proven instances of hypocortisol, the literature does not support the use of steroids in the
management of pediatric severe TBI. Use of steroids does not improve outcomes and suppresses endogenous corticosteroid production and increases the risk of infection. Thus, steroids are not recommended in the acute injury period.

**Second Tier Therapy**

After the first tier of therapeutic interventions has been exhausted, the second tier of treatment comes into play for managing persistently elevated ICP. These include the use of high dose barbiturates, decompessive surgical procedures, lumbar drain CSF diversion, hypothermia and aggressive hyperventilation (Fig. 2). These are high-risk interventions and require a careful assessment of the risk-benefit ratio before any of these are administered.

The most commonly used barbiturate is pentobarbital at a loading dose of 10 mg/kg over a 30-minute period, followed by a maintenance dose of 1 mg/kg/hr that can be titrated for burst suppression on continuous electroencephalographic monitoring. A decrease in blood pressure is common in children receiving high-dose barbiturates and pharmacological intervention is usually required to maintain CPP > 40 mmHg.

Surgical procedures including decompressive craniectomy, duraplasty and lobectomy are options to lower the ICP refractory to a medical management level. This can be especially useful in patients with expanding mass intracranial lesions or diffuse cerebral edema at initial evaluation, GCS > 3 subsequent to injury, or worsening within 48 hours of admission. While this author is reticent to use a lumbar drain for CSF drainage in patients with severe TBI, there is literature supporting it as a second tier option provided there is no radiological evidence of intracranial mass lesion or focal herniation, open basal cisterns and a functioning ventricular drain.
Hypothermia is another second tier option. Hypothermia leads to poor outcomes by potentiating the acute pathophysiological response to the injury. Hypothermia can reduce secondary injury responses as well as seizures. Currently, there is no definitive evidence for use of hypothermia in children. Based on adult data\(^3\), a reduction of core body temperature below 35°C is considered an option. A phase II trial\(^3\) showed potentially lower mortality and improved outcome, but too few patients enrolled and limitations in the study design do not allow anything more than a level III recommendation at this time. Phase III trials for the study of hypothermia in the pediatric population are ongoing at the present time (PD Adelson—personal communication).

The incidence of post-traumatic seizures in infants and children is high. Anti-epileptic medications decrease the incidence of seizures that occur within seven days of the initial event. However, they offer no protection against chronic post-traumatic seizures or epilepsy of late onset. The drugs with the most data to support their use are phenytoin and carbamazepine.

Nutrition also plays an important part in the care of children with severe TBI, as an elevated rate of metabolism is noted in these patients. With no one method of administering calories proven to be better than others, nutritional supplementation, in one form or another, should begin within 72 hours of the initial injury, with the goal of providing 130 to 160% of resting metabolism expenditure.

**Potential Future Management**

The guidelines outline several key areas of research and investigation. As the goal is to individualize patient care for patients at risk, preventing primary injury avoiding second insults (and secondary injury) and developing environments conducive for recovery of the injured brain provide the best opportunities for further research to develop novel therapeutic approaches. Some of these key areas include measures for primary prevention of TBI (like raising public awareness), development of protocols for early, accurate assessment of pediatric TBI, development of treatment algorithms guided by individualized monitoring of pathophysiological and biochemical processes, better anatomical and functional imaging, and development of comprehensive physical, cognitive, and behavioral assessment scales for evaluating children with severe TBI.

**Conclusions**

While the present care of pediatric TBI is outlined in the pediatric guidelines, which provide a detailed, evidence-based system for management of children with severe TBI, there are clear limitations due to the lack of Class I evidence or proven efficacy for much of our present understanding. Protocol based care though does improve outcome and is a starting point for the development of future studies to address the deficits in our present understanding. By focusing on the key areas provided in the guidelines, breakthrough discoveries in the understanding and treatment of pediatric TBI can be expected, along with the development of new therapeutic interventions. These may also guide the way for newer, scientifically sound principles of management, with the possibility of individualization of care in the pediatric population, as realistic goals for study are defined while maintaining direction.

**References**


