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Update on the 2012 guidelines for the management of pediatric traumatic brain injury – information for the anesthesiologist

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Summary

Traumatic brain injury (TBI) is a significant contributor to death and disability in children. Considering the prevalence of pediatric TBI, it is important for the clinician to be aware of evidence-based recommendations for the care of these patients. The first edition of the *Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolescents* was published in 2003. The *Guidelines* were updated in 2012, with significant changes in the recommendations for hyperosmolar therapy, temperature control, hyperventilation, corticosteroids, glucose therapy, and seizure prophylaxis. Many of these interventions have implications in the perioperative period, and it is the responsibility of the anesthesiologist to be familiar with these guidelines.

Keywords

pediatric traumatic brain injury; acute care guidelines; pediatric trauma; quality of care; best evidence; brain outcomes

Introduction

Traumatic brain injury (TBI) is a significant contributor to death and disability in the United States. The Center for Disease Control estimates there are 1.7 million TBI cases per year in the United States, with approximately 30% (511 000 injuries) occurring in children aged 0–14 years; (1) approximately 35 000 require hospitalization, and over 2000 die.

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The first edition of the *Guidelines for the Acute Medical Management of Severe Traumatic Brain Injury in Infants, Children, and Adolescents* was published in 2003 (2). Updates in 2012 included changes in the level of evidence and recommendations in the areas of hyperosmolar therapy, temperature control, hyperventilation, corticosteroids, glucose therapy, and seizure prophylaxis (Table 1) (3).

The 2012 updates provide an opportunity during the perioperative period for anesthesiologists to continue ongoing resuscitation and to mitigate secondary insults (4).

Pathophysiology and therapeutic targets

Contributors to TBI include focal damage due to direct tissue injury and diffuse injury due to acceleration/deceleration, resulting in cerebral edema and diffuse axonal injury (5). TBI occurs in two phases: (1) primary injury, which is the tissue or mechanical damage incurred at the time of trauma, and (2) secondary injury or delayed damage, caused by inflammatory and excitotoxic processes, leading to cerebral edema and elevated intracranial pressure (ICP) (5). Secondary injury is also caused by physiologic insults, most commonly due to hypoxemia and hypotension (6). Other contributors include hypo- or hypercarbia, and hypo- or hyperglycemia. When TBI patients arrive at the hospital, the primary injury is nontreatable. However, secondary injury is preventable, through avoiding hypoxemia, hypotension, and other factors, and is also treatable, with cerebral edema and ICP interventions being therapeutic targets.

Anesthetic management

Cervical spine injury precautions

Children with TBI may also have cervical spine injury. In young children, the cervical spine has maximal movement at C1–C3, and after 12 years of age, movement occurs at C5–C6; hence, younger children have injuries to the upper cervical spine, while older children have lower ones. Clearance requires plain radiographic assessment of the C-spine (antero-posterior and lateral views including the cervicothoracic junction and views of the odontoid process) and a neurologic examination as well (7).

In infants under 6 months of age, the head and cervical spine should be immobilized using a spine board with tape across the forehead and blankets of towels around the neck. In infants greater than 6 months of age, the head should be immobilized in either the manner described above or using a small rigid cervical collar. Rigid cervical collar use is essential as it prevents cervical distraction whereas soft collars can permit 5–7 mm distraction of cervical spine during laryngoscopy (8).

Airway management

A child with a waxing and waning mental status or a Glasgow Coma Scale (GCS) score of <9 should have a definitive airway established (9,10). The chin lift and jaw thrust maneuvers can be safely performed to open the airway in the pediatric trauma patient and when performed correctly, they should not hyperextend the neck or risk cervical cord injury. Oral

airways can also be placed safely to relieve airway obstruction in an unconscious patient with possible cervical spine injury. Nasal airways are contraindicated in facial trauma.

Cricoid pressure should not be applied to vigorously as it can lead to subluxation at the injury site or laryngeal and tracheal compression and inadequate oxygenation and ventilation. The anterior portion of a rigid collar can be removed to facilitate cricoid pressure and laryngoscopy. In-line stabilization should be performed by a trained medical assistant. Gentle support should be given to prevent cervical spine movement, and traction should be avoided (11,12). A child with a GCS score of <9 or decreasing consciousness needs tracheal intubation for airway protection and ICP management (9,10). There is no survival or functional advantage of prehospital tracheal intubation compared with bag-valve-mask ventilation in children with severe TBI (13,14). There are no reported significant differences in neurologic outcome in patients with stable and unstable cervical spine fractures who had orotracheal or nasotracheal intubation (15), but nasotracheal intubations are contraindicated in patients with basilar skull fractures and almost impossible in awake pediatric patients. The most common approach to establishing an airway is to administer preoxygenation, induce anesthesia, perform direct laryngoscopy, and perform orotracheal intubation with cricoid pressure using in-line cervical stabilization.

Anesthetic technique

Although there are limited pediatric data regarding anesthetic choice, the 2012 *Guidelines* highlight that choice and dosing of analgesics, sedatives, and neuromuscular-blocking agents are left to the discretion of the treating physician.

Intravenous agents

Analgesics, sedative, and neuromuscular blocker drugs play an important role in mitigating secondary brain injury and intracranial hypertension by reducing cerebral metabolic rate and attenuating undesired physiologic responses, such as the stress response and shivering. All intravenous sedative induction hypnotic agents, including barbiturates, etomidate, and propofol, are potent cerebral vasoconstrictors and lead to coupled reduction in cerebral blood flow and cerebral metabolic rate of oxygen consumption, which leads to decreased intracranial pressure (16,17). Additionally, many of these medications have beneficial anticonvulsant and antiemetic properties.

The 2012 *Guidelines* outline that the use of these anesthetic agents should be limited to hemodynamically stable patients with a secure airway, receiving mechanical ventilation with satisfactory arterial blood gas values, and stable intravascular volume status. While these medications can provide benefit, they may worsen patients who are hemodynamically unstable. Two studies, examining etomidate and thiopental, have sufficient quality of evidence to allow inclusion in the 2012 *Guidelines*. However, commonly used opioids and benzodiazepines have not been investigated in this setting.

Etomidate

The use of etomidate is associated with reduction in ICP and significant improvements in cerebral perfusion pressure (CPP), without reductions in mean arterial pressure (MAP) (18).

In the same study, ACTH stimulation studies carried out six hours postetomidate administration showed laboratory but not clinical suppression in 50% of patients.

Barbiturates

A small prospective study with sufficient quality of evidence examined the effect of thiopental on middle cerebral artery (MCA) flow velocity (19). When compared with controls, these patients demonstrated a 15–21% reduction in middle cerebral artery flow velocity and significant reductions in ICP without affecting CPP.

Propofol

In contrast to the most recent adult TBI Guidelines, the 2012 *Guidelines* recommend avoiding the use of propofol infusion. This recommendation is supported by the collection of case reports and case series highlighting the potential for morbidity with propofol infusion in children. (20–25), which is the foundation for the FDA's statement that 'propofol is not approved in the USA for sedation in pediatric ICU patients' (26).

Other medications

Due to concerns about raising ICP, ketamine has previously been avoided in patients with TBI (27). Recent pediatric evidence shows that it may actually mitigate increases in ICP during stressful procedures and can be used to treat refractory intracranial hypertension (28).

Inhalational agents

Although not addressed in the Guidelines, inhalational agents are of interest to the anesthesiologist. All inhalational agents (sevoflurane, isoflurane, desflurane, and halothane) decrease cerebral metabolic rate, but also cause direct cerebral vasodilatation, effectively decoupling cerebral blood flow from metabolic rate (29), with the degree of vasodilation correlating with minimum alveolar concentration (MAC). No study has directly compared intravenous and inhalational agents in TBI outcome.

Muscle relaxants

Resistance to using succinylcholine in pediatric TBI due to concerns of (1) undiagnosed myopathies leading to hyperkalemic cardiac arrest (30), and (2) fasciculations and increased ICP (31,32) exist, but these concerns must be weighed against the risks posed by a full stomach in trauma patients. Therefore, succinylcholine is not contraindicated and is probably safer than high-dose rocuronium when there is concern for a difficult airway. The anesthesiologist must weigh the potential risk of aspiration and need to rapidly secure the airway against the possibility of increased ICP.

Steroids and glucose control

Steroid administration in severe pediatric TBI is not associated with improved functional outcome, decreased mortality, or reduced ICP (3). Instead, steroids may cause suppression of endogenous cortisol levels and may increase the risk of pneumonia (33,34), and thus are not recommended in pediatric TBI. (3).

Predictors of hyperglycemia include age <4 years old, GCS ≥ 8, and the presence of multiple lesions including subdural hematoma (35). Despite pediatric studies suggesting that posttraumatic hyperglycemia is associated with poor outcome (36–38), there was insufficient quality of evidence to include glycemic control after severe pediatric TBI in the 2012 *Guidelines* (3).

Systemic and cerebral hemodynamics

Cerebral autoregulation may be disrupted in pediatric TBI patients (39). As CPP is determined by the difference between MAP and ICP, hemodynamic support to maintain MAP and CPP is critical in TBI in order to prevent secondary injury (3). In children, both impaired cerebral blood flow autoregulation and systolic blood pressure less than the 5th percentile were found to be independent risk factors for a poor 6-month Glasgow Outcome Scale (GOS) score (40). Hypotension occurring during the first 6 h after injury has the highest prediction for poor discharge GOS (41).

The exact optimal CPP in the pediatric patient is unknown, and there are numerous studies included in the 2012 *Guidelines* (3). In a report of 188 head-injured children with ICP monitoring, no patient with a CPP less than 40 mmHg survived (42). The exact relationship between age and optimal CPP is unknown. In the absence of ICP monitoring and suspected elevated ICP, systemic mean arterial blood pressure should not be allowed to decrease below values normal for age. Maintaining CPP > 50 mm Hg in 6- to 17-year-olds and >40 mmHg in 0- to 5-year-olds are appropriate targets (43). Maintaining age-appropriate systolic blood pressure great or equal to the 75th percentile may also be associated with better outcome. (44).

Monitoring

Invasive arterial blood pressure monitoring is recommended for continuous blood pressure monitoring and for blood sampling. Central venous pressure monitoring is useful in examining trends in intravascular volume status. ICP monitoring has never been subjected to a randomized controlled trial in children. However, elevated ICP should be treated when it exceeds 20–25 mmHg. The presence of coagulopathy would contraindicate the placement of an ICP monitor, in which situation the Cushing reflex and autonomic dysfunction might be the only indicators of increased ICP. Urine output must be monitored in the child with significant TBI; electrolyte abnormalities due to diabetes insipidus or syndrome of inappropriate antidiuretic hormone may be present.

Advanced neuromonitoring includes cerebral micro-dialysis, transcranial Doppler (TCD), thermal diffusion probes, near-infrared spectroscopy (NIRS), and jugular oximetry. The evidence of these monitors in TBI is limited with little evidence showing how these can guide therapy. The 2012 *Guidelines* recommend maintaining $PbtO_2 \geq 10$ mmHg, based on level III evidence of brain oxygenation monitoring (3).

Imaging modalities

Computed tomography imaging can rapidly detect intracranial hematoma, contusion, skull fracture, cerebral edema, and obliteration of the basal cisterns in a pediatric TBI patient. In

childhood, conventional magnetic resonance imaging (MRI) compared with CT scan has high sensitivity and specificity, better correlation with outcome, and lack of radiation (45,46). Early MRI has been shown to improve 3-month outcome prediction in mild traumatic brain injury (47). There are growing concerns about cumulative radiation exposure during CT scans. According to the 2012 *Guidelines*, obtaining follow-up CT scans only when there is neurologic decline has been shown to alter treatment five times more than just routine follow-up of CT scans of all patients (48).

Treatment for intracranial hypertension

Hyperosmolar therapy

Hyperosmolar therapy, with mannitol or hypertonic saline, is used for treatment of intracranial hypertension (ICH) in severe pediatric TBI. The use of hypertonic saline has increased (49), as well as in comparison with other interventions. (50–53). Possible concerns with its use include natriuresis, dehydration, central pontine myelinolysis, and rebound in ICP (50). The 2012 *Guidelines* recommend both bolus therapy 3% saline and continuous infusion 3% saline for treatment of ICH in pediatric patients (3). Effective doses for bolus therapy range from 6.5 to 10 ml kg^{-1} for pediatric patients with elevated ICP after TBI (52). When compared to a bolus of 0.9% saline, bolus 3% saline was associated with a lower ICP and reduced need for additional interventions to control ICP (52), and was without side effects. Evidence for hypertonic saline infusions comes from a number of studies (49,53). A comparison between lactated ringers and 1.7% saline infusions found that children who received hypertonic saline required fewer ICP interventions, had fewer complications and shorter ICU stays, and had significantly lower ICP values and better cerebral perfusion (53). Three percent saline infusion titrated between 0.1 and 1.0 $ml \cdot kg^{-1} \cdot h^{-1}$ to keep ICP < 20 mHg was also associated with better ICP control without adverse effects (49).

There is limited clinical evidence to support the use of mannitol for the treatment of ICP. Potential complications include natriuresis and dehydration, possible concern for acute renal failure, and a reverse osmotic effect in brain injured tissue, where the accumulation of mannitol in the tissue causes movement of water into the brain parenchyma, possibly increasing ICP (54,55). Mannitol has not been subjected to controlled pediatric clinical trials comparing it with placebo, other agents, or other ICH interventions. (3).

Therapeutic hypothermia

The 2012 *Guidelines* recommend that if hypothermia is employed, it should be continued for >24 h, and rewarming should carried out at a pace slower than 0.5°C per h (3). Moderate hypothermia (32–33°C) combined with rapid rewarming (0.5°C per h) in severe pediatric TBI, resulted in excellent ICP control during hypothermia, but rebound increases in ICP during rewarming (56). In addition, the hypothermia group also showed a trend toward increased morbidity and mortality, with many patients having hypotension requiring hemodynamic support, and overall showing no benefit for long-term functional outcome (56). Longer duration of hypothermia and slower rewarming produced safer and more favorable outcomes, with no increased arrhythmia, coagulopathy, or infection, and a trend toward decreased mortality and lower ICPs (57). Since the publication of the 2012

Guidelines, a trial of 48- to 72-h duration of moderate therapeutic hypothermia (32–33°C) combined with very slow rewarming (0.5–1.0°C every 12–24 h) was terminated early due to futility after an interim analysis.

Hyperventilation

Hyperventilation may reduce cerebral blood flow (CBF) to the point of impaired oxygen delivery, causing cerebral hypoxemia and brain ischemia (58,59), and may result in poorer long-term outcomes (60). Prophylactic hypocapnia has been shown to reduce the buffering capacity of Cerebrospinal Fluid (CSF) (60). Regional CBF and oxygen consumption have been measured at three levels of arterial CO_2 (>35 mmHg, 25–35 mmHg, and <25 mmHg), and in this study, regional ischemia occurred in 28.9% during normocapnia and increased to 59.4% with $PaCO_2$ 25–35 mmHg, and 73.1% for $PaCO_2$ less than 25 mmHg, indicating increasing risk of cerebral ischemia associated with hyperventilation (61). A recent retrospective cohort study demonstrated that the incidence of severe hypocapnia is high, with the youngest children having the highest degree of hypocapnia (60% vs 52%, $P = 0.2$) (62). In this study, severe hypocapnia independently predicted inpatient mortality.

The 2012 *Guidelines* recommend avoidance of prophylactic severe hyperventilation to a $PaCO_2$ less than 30 mmHg within the first 48 h after injury (3). If hyperventilation is used in the management of severe intracranial hypertension, evidence suggests that advanced neuromonitoring for evaluation of cerebral ischemia should be used concurrently (3). Despite these recommendations, prophylactic hyperventilation alarmingly remains the most common intervention in pediatric TBI management. A large databank in the United Kingdom and Ireland showed a greater than 90% utilization of hyperventilation in severe pediatric TBI (63). The impact of transient application of hyperventilation in the setting of ICP crisis or brain herniation has not been reported in pediatric patients (3).

Barbiturate coma

The 2012 *Guidelines* recommend barbiturate therapy in hemodynamically stable patients when maximal medical and surgical therapy has failed to control ICP (3). Concerns regarding barbiturates include reductions in blood pressure and cardiac output, as well as increased intra-pulmonary shunt (64), while a specific concern in children is the wide variability in drug clearance (65). When barbiturate therapy is used, continuous arterial blood pressure monitoring and cardiovascular support to maintain adequate CPP are suggested. Hemodynamic support is needed fairly commonly with barbiturates, with 91% of patients requiring dopamine and 82% developing hypotension (64). In another study, 52% of the patients with refractory high ICP showed ICP control with addition of barbiturate therapy. Despite this, 6-month follow-up of the nonresponders showed 77% prevalence of poor outcome (severe disability or death) (66).

Decompressive craniectomy

The 2012 *Guidelines* recommend consideration of craniectomy in pediatric patients who are showing early signs of neurologic deterioration or herniation, or are developing intracranial hypertension refractory to medical management (3). Craniectomy has been successfully employed very early and very late in therapy, as well as in isolation and in combination with

other therapies. One study showed that craniectomy within 70 min of injury results is effective as a sole method of controlling ICP in the majority of patients (67). Multiple small case series (68–72) also show that craniectomy is an effective rescue intervention in patients with sustained ICP greater than 20 mmHg, clearly demonstrating craniectomy has a role in ICH management. Certain questions are still unanswered, including the ideal timing and method of craniectomy, as well as its impact on long-term outcome.

CSF drainage

CSF drainage for the management of intracranial hypertension works simply through the reduction in intracranial fluid volume, leading to a reduction in ICP. External ventricular drains (EVD) are increasingly being used in the management of pediatric TBI, with potential options being continuous or intermittent techniques (73).

The 2012 *Guidelines* recommend consideration of EVD to manage ICP CSF drainage via EVD resulted in ICP control in 87% of pediatric patients (74). In two pediatric studies on combined ventricular and lumbar drainage (75,76), lumbar drain was placed in patients with concurrent ventricular drain complicated by persistent ICD. Sixty percent of patients (3/5 patients) in one study (75) and 87.5% of patients (14/16 patients) in the second study (76) had good ICP control with lumbar drain. These three studies also confirmed that refractory ICH is associated with poor outcome, with 100% mortality in all patients with refractory intracranial hypertension after CSF drainage. It follows that perhaps the most important aspect of TBI management is control of refractory ICP and not necessarily the combination of methods that achieve this goal (3).

Conclusions

The 2012 *Guidelines* bring about many new recommendations for evidence-based practice in the care of pediatric patients with TBI. Although much of this information has been gathered in the ICU setting, the concepts are easily translated into the OR environment, and the topics should be familiar to pediatric anesthesiologists in order to facilitate better care of these patients.

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Table 1

Summary of the recommendation from the 2012 *Guidelines for the Acute Medical Management of Severe TBI in Infants, Children, and Adolescents*

Physiologic parameters	Recommendations	Level of evidence
Intracranial pressure	Consider ICP monitoring in infants and children with severe TBI	III
	Treatment of ICP may be considered at a threshold of 20 mmHg	III
Cerebral perfusion pressure[a]	A minimum CPP of 40 mm Hg may be considered in children with TBI	III
	A CPP threshold of 40–50 mmHg may be considered; there may be age-specific thresholds with infants at the lower end and adolescents at the upper end of this range	III
Brain oxygenation	If brain oxygen monitoring is used, maintenance of oxygen tension ≥10 mm Hg may be considered	III
Hyperosmolar therapy[a]	3% hypertonic saline (0.1 and 1 ml·kg^{-1} of body weight per hr) should be considered for the treatment of intracranial hypertension	III
	Footnote: no studies of mannitol met the inclusion criteria as evidence for this topic	
Hyperventilation[a]	Avoidance of prophylactic severe hyperventilation to a PaCO2 < 30 mm Hg may be considered in the initial 48 h after injury	III
	If hyperventilation is used in the management of refractory intracranial hypertension, advanced neuromonitoring for evaluation of cerebral ischemia may be considered	III
Temperature control[a]	Moderate hypothermia (32–33°C) beginning early after severe TBI for only 24-h duration should be avoided	II
	Moderate hypothermia (32–33°C) beginning within 8 hrs after severe TBI for up to 48-h duration should be considered to reduce intracranial hypertension	II
	If hypothermia is induced for any reason, rewarming at a rate of 0.5°C per h should be avoided	II
Cerebrospinal fluid drainage	CSF drainage through an external ventricular drain may be considered in the management of increased ICP	III
	The addition of a lumbar drain may be considered in the case of refractory intracranial hypertension with a functioning external ventricular drain, open basal cisterns, and no evidence of a mass lesion or shift on imaging studies	III
Barbiturates	High-dose barbiturate therapy may be considered in hemodynamically stable patients with refractory intracranial hypertension despite maximal medical and surgical management	III
	When high-dose barbiturate therapy is used to treat refractory intracranial hypertension, continuous arterial blood pressure monitoring and cardiovascular support to maintain adequate cerebral perfusion pressure are required	III
Corticosteroids[a] Analgesics, sedatives, and neuromuscular blockade[a]	The use of corticosteroids is not recommended to improve outcome or reduce ICP for children with severe TBI	II
	Etomidate may be considered to control severe intracranial hypertension; however, the risks resulting from adrenal suppression must be considered	III
	Thiopental may be considered to control intracranial hypertension	III
	Footnote: the specific indications, choice and dosing of analgesics, sedatives, and neuromuscular-blocking agents used in the management of infants and children with TBI should be left to the treating physician	
	As stated by the FDA, a continuous infusion of propofol for either sedation or the management of refractory intracranial hypertension in infants and children with severe TBI is not recommended	
Antiseizure prophylaxis[a]	Prophylactic use of antiseizure therapy is not recommended for children with severe TBI for preventing late posttraumatic seizures	III
	Prophylactic antiseizure therapy may be considered as a treatment option to prevent early posttraumatic seizures in young pediatric patients and infants at high risk of seizures after head injury	III

Physiologic parameters	Recommendations	Level of evidence
Nutrition[a]	Evidence does not support the use of immune-modulating diet to improve outcome	II
Decompressive craniectomy	Decompressive craniectomy with duraplasty may be considered for patients who are showing early signs of neurologic deterioration or herniation or are developing intracranial hypertension refractory to medical management during the early stages of their treatment	

CPP, cerebral perfusion pressure.

[a]Starred items were changes in recommendations from the first edition to the second edition.