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Review Article

Pediatric head injury: a pain for the emergency physician?

Shu-Ling Chong[1], Khai Pin Lee[1], Jan Hau Lee[2], Gene Yong-Kwang Ong[1], Marcus Eng Hock Ong[3]

[1]Department of Emergency Medicine, KK Women's and Children's Hospital, Singapore
[2]Children's Intensive Care Unit, KK Women's and Children's Hospital, Singapore
[3]Department of Emergency Medicine, Singapore General Hospital, Singapore

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The prompt diagnosis and initial management of pediatric traumatic brain injury poses many challenges to the emergency department (ED) physician. In this review, we aim to appraise the literature on specific management issues faced in the ED, specifically: indications for neuroimaging, choice of sedatives, applicability of hyperventilation, utility of hyperosmolar agents, prophylactic anti-epileptics, and effect of hypothermia in traumatic brain injury. A comprehensive literature search of PubMed and Embase was performed in each specific area of focus corresponding to the relevant questions. The majority of the head injured patients presenting to the ED are mild and can be observed. Clinical prediction rules assist the ED physician in deciding if neuroimaging is warranted. In cases of major head injury, prompt airway control and careful use of sedation are necessary to minimize the chance of hypoxia, while avoiding hyperventilation. Hyperosmolar agents should be started in these cases and normothermia maintained. The majority of the evidence is derived from adult studies, and most treatment modalities are still controversial. Recent multicenter trials have highlighted the need to establish common platforms for further collaboration.

Keywords Pediatrics; Child; Craniocerebral trauma; Brain injuries

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Correspondence to: Shu-Ling Chong
Department of Emergency Medicine, KK Women's and Children's Hospital, 100, Bukit Timah Road, Singapore 229899
E-mail: Chong.Shu-Ling@kkh.com.sg

Capsule Summary

What is already known

Children with head injuries present with varied complaints and a wide spectrum of severity. The ED physician is frequently challenged to make prompt yet important decisions in the early hours after the injury.

What is new in the current study

In this clinical review, the authors appraise current literature in the diagnosis and management of pediatric head injury, from the ED physician's perspective.

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INTRODUCTION

Children with traumatic brain injury (TBI) are at risk of death and permanent neurological disability. Children are especially vulnerable to TBI due to the softer pliable skull[1] and susceptibility to accelerating and decelerating forces. Infants present mainly after falls, while older children suffer from transportation accidents and sports-related injuries.[2] In the absence of a clear mechanism of injury, the physician must also consider inflicted TBI.

When faced with a head-injured child, rapid and accurate diagnosis may be hindered by the variable presentation of the pediatric patient. Early decisions on the need for neuroimaging, immediate resuscitation, and prompt treatment of raised intracranial pressure (ICP) are pivotal for good patient outcomes.

In this review, we aim to critically appraise the current literature on diagnosis and initial management of pediatric head injury. Specifically, this narrative review is meant to be emergency department (ED)-centric, and focuses on the dilemmas faced in the management of paediatric TBI. The following areas are the focus of this review: indications for neuroimaging, choice of sedatives, applicability of hyperventilation, utility of hyperosmolar agents, prophylactic anti-epileptics, and effect of hypothermia in pediatric TBI.

MATERIALS AND METHODS

A comprehensive literature search was performed in each specific area of focus corresponding to the relevant questions: PubMed was searched using the MeSH search terms: brain injuries; child; neuroimaging; hypnotics and sedation; hypocapnia; hypertonic solution, saline; anticonvulsants and hypothermia. Embase was also searched using the terms: traumatic brain injury; child; neuroimaging; hyperventilation; hyperosmolar; anticonvulsive agent and hypothermia. Original and review articles were identified and selected based on the relevance to this review, and references were hand searched. The search was not limited by year of publication. Articles that were not written in English, and case reports were excluded. Relevant references from the adult TBI literature are included in this paper, due to the paucity of pediatric—specific literature regarding certain treatment modalities (Fig. 1).

RESULTS AND DISCUSSION

Which head-injured child requires a computed tomography for brain? Indications for neuroimaging

Children with head injuries present with varied complaints. It has always been a challenge for the ED physician to decide which head injured child requires urgent neuroimaging. While the fast-

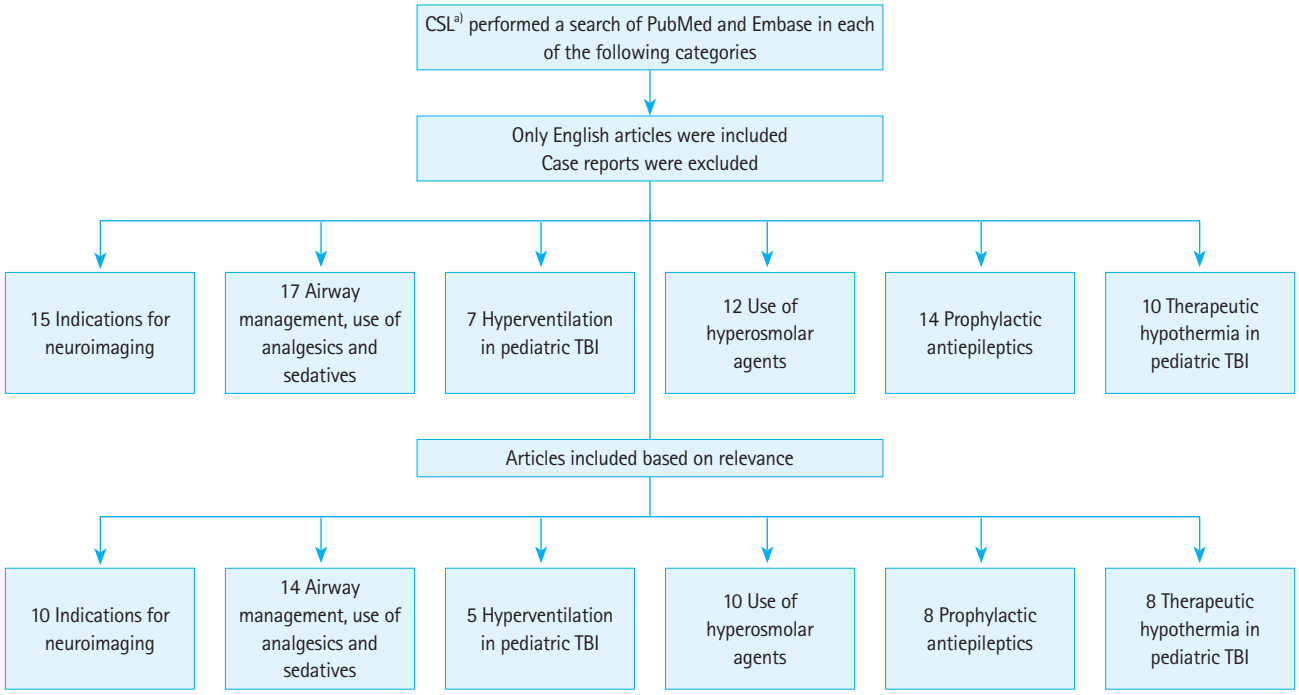

Fig. 1. Flow diagram of literature selection process. TBI, traumatic brain injury. [a]CSL (Chong Shu-Ling), first author, performed the literature search. The other authors reviewed the relevance of the literature included and the concurrence of recommendations in each area.

est way to exclude an intracranial bleed is to perform a computed tomography (CT) scan of the brain, but the resultant radiation is significant in children. A large data linkage study recently published showed that, after accounting for age, sex and the year of birth, the cancer incidence is 24% greater for children and adolescents exposed to CT scans compared to unexposed individuals.[3] Interestingly, for brain cancer and all cancers combined, the incidence rate ratio was greater at younger ages. The region being exposed to radiation is also relevant, with brain CTs being significantly associated with brain tumors.[4]

Clinical prediction tools (CHALICE, PECARN, and CATCH) have been derived to guide the ED physician on which child should be imaged.[5-7] These clinical prediction rules assist the ED physician in risk stratifying patients at risk for TBI. The PECARN rule was adequately powered by a large study population (n = 42, 412) in which the rule was not only derived but also validated.[6] Importantly, the study population comprised a significant number of preverbal children (< 2 years), among whom complaints are usually vague and to whom the risk of radiation is of particular concern. A recent prospective cohort study demonstrated that of the 3 rules, PECARN performed with the best sensitivity.[8] Still, others have proposed that a period of monitoring should be instituted in most cases, as that was shown to lead to more discretionary neuroimaging.[9] After adjusting for patient age, time from injury and physician type, it was demonstrated that every hour of ED observation time was associated with a decrease in CT rate for children across all risk groups.[10] In this study, there was no delay to the diagnosis of significant TBI. In a survey among parents of children 2 years or older presenting to the ED with the presenting complaint of head injury, the parents were divided in opinion, with a majority (57%) preferring observation over immediate CT.[11] The performance of the above 3 rules are currently being compared and validated in an ongoing prospective study by a large research network.[12] In the meantime, ED physicians need to weigh the advantage of prompt diagnosis against the disadvantage of radiation exposure.

Airway management and the use of analgesics and sedatives

A patient with a presenting Glasgow Coma Scale ≤ 8 (or one that is fluctuating), is at risk of losing airway protection. At the ED, timely endotracheal intubation and effective ventilation prevents one of the most important causes of secondary injury to the brain: hypoxemia.[13] This also allows for the management of raised ICP.

The use of sedatives facilitates the ability to maintain a definitive airway and perform invasive interventions. They mitigate the effect of stress and pain, and also have anti-seizure and anti-emetic properties,[14] and attenuate the rise in ICP during interventions. Hypotension must be avoided during induction because of the resultant reduction in cerebral perfusion pressure (CPP) and consequently secondary injury to the brain.[13,15]

Because of the paucity of data in this area, we utilized pertinent adult data to discuss some of the commonly used sedative drugs available for use in the ED setting for a child with TBI. A systematic review of 13 randomized controlled trials among adults with severe TBI (Glasgow Coma Scale ≤ 8) did not demonstrate the superiority of any sedative agent on mortality or neurologic outcomes, nor on ICP and CPP.[16]

Etomidate, favored in the setting of hemodynamic instability, has been associated with reduced ICP and improvement in CPP among pediatric patients with severe TBI.[17] When using etomidate, the physician must however bear in mind the possibility of adrenal suppression. A single bolus dose for induction has been demonstrated to reduce the synthesis of cortisol, and increase the risk for relative adrenocortical insufficiency.[18]

The use of propofol in adults has shown favorable effects on the cerebral blood flow and ICP.[19,20] However, propofol can cause a drop in the mean arterial pressure and CPP especially in unstable hypovolemic patients. Concerns have arisen due to the propofol infusion syndrome, particularly in children—as defined by acute bradycardia, enlarged or fatty liver, metabolic acidosis, rhabdomyolysis or myoglobinuria.[21] Brugada-like electrocardiogram changes with potential malignant arrhythmias have also been reported.[22]

Benzodiazepines, easily available and frequently used in many EDs, can provide amnesia, anxiolysis and anti-convulsant effects.[15] However, besides the risk of hypotension, benzodiazepines also cause significant respiratory depression, and the accumulation of metabolites may prolong the sedation, affecting subsequent neurological assessment.[15]

Ketamine was previously believed to worsen raised ICP. However, key studies have shown otherwise. When compared to other sedative agents, ketamine does not decrease mean arterial pressure and therefore maintains CPP.[23,24] In a small prospective series, Bar-Joseph et al.[25] showed that among 30 children with raised ICP, a single dose of ketamine (1 to 1.5 mg/kg) was able to prevent further increases in ICP during stressful procedures, as well as reduce ICP among those with refractory intracranial hypertension. This study, however, did not have any control for confounders. A more recent systematic review of 10 adult randomized and non-randomized prospective studies reported no significant differences in CPP, or patient-centered outcomes (mortality, intensive care unit length of stay, or neurologic outcomes) with the use of ketamine in the setting of TBI.[26]

We recommend that among TBI patients with stable hemodynamic status and the absence of known adrenal insufficiency, etomidate may be used. If benzodiazepines are used, strict blood pressure monitoring must be performed. For TBI patients who have hypotension or unstable hemodynamic status, ketamine can be used.

Hyperventilation in pediatric traumatic brain injury

Hyperventilation produces hypocapnia-induced cerebral vasoconstriction, thereby reducing cerebral blood flow and blood volume. It decreases cerebral oxygenation and may induce brain ischemia.[27] Ischemic thresholds are exceeded in a dose-dependent relationship with increasingly aggressive hyperventilation.[28] Curry et al.[29] showed in a large retrospective cohort pediatric study that with increasing episodes of severe hypocarbia (P_aCO_2 < 30 mmHg), the mortality-adjusted odds ratio (OR) increased. It has since been recommended that prophylactic severe hyperventilation to P_aCO_2 < 30 mmHg should be avoided in the initial 48 hours after injury.[30]

Another retrospective study performed among children with severe TBI showed that patients with admission P_aCO_2 between 36 to 45 mmHg had better discharge survival rate (adjusted OR 5.47 for discharge survival) compared to those with admission hypocarbia (P_aCO_2 ≤ 35 mmHg) and hypercarbia (P_aCO_2 ≥ 46 mmHg).[31]

In cases of refractory intracranial hypertension, if hyperventilation is to be considered, then advanced neuromonitoring for evaluation of cerebral ischemia should be instituted.[30] In the ED, hyperventilation should not be performed routinely for head injured patients (level III evidence).

The use of hyperosmolar agents

Mannitol previously dominated in the use of hyperosmolar therapy. While useful to reduce ICP,[32] the effect on mortality and functional outcomes has been equivocal when compared to placebo.[33] Concerns have surrounded the adverse effects of mannitol causing hypovolemia due to diuresis and the association with renal failure.[34]

Hypertonic saline has gained increasing favor recently.[35] It treats hyponatremia (which can result from cerebral salt wasting, syndrome of inappropriate anti-diuretic hormone and sodium losses from cerebral spinal fluid drainage).[30] Hypertonic saline increases the mean arterial pressure, therefore avoiding the secondary insult of hypotension on the injured brain.[36] By raising the serum osmolality, it reduces the influx of water into the extracellular spaces, and reduces the resultant cerebral edema. It was shown in a small prospective observational study done among children[37] to reduce the ICP spikes and increase the CPP. Possible side effects include a rebound in the ICP, central pontine myelinolysis, renal impairment and natriuresis.[38]

In two randomized controlled trials, the use of hypertonic saline was associated with reduced need for additional interventions to treat the raised ICP.[39,40] Simma et al.[40] reported fewer interventions, and shorter duration of mechanical ventilation among children who received hypertonic saline compared to those who received lactated Ringer's solution, but there was no difference in the survival rates between the groups. Among 68 children studied retrospectively, Peterson et al.[41] found that the use of hypertonic saline resulted in a survival rate that was higher than expected based on trauma and Injury Severity Score. Moreover, none of the patients in that cohort developed central pontine myelinolysis or rebound increase in ICP. Based on current medical literature, hypertonic saline is one of the few therapies with level II evidence and the recommended dose of 3% hypertonic saline ranges from 6.5 to 10 mL/kg.[30] A continuous infusion between 0.1 to 1.0 mL/kg/hr may be considered subsequently.[30]

Prophylactic anti-epileptics in children with head injury

Post traumatic seizures (PTS) are classified as early PTS if they occur within 7 days of injury.[2] The risk factors for PTS include: young age, severe injury, presence of intraparenchymal hemorrhage[42] and non-accidental trauma.[43] Seizures among critically ill children may be subtle and challenging to diagnose.[44] In a randomized double-blinded study of 404 adults, Temkin et al.[45] reported that there was a statistically significant risk reduction in the incidence of early PTS in head-injured patients, with the use of phenytoin (risk ratio, 0.27; 95% confidence interval [CI], 0.12 to 0.62).

Specific to the pediatric population, Young et al.[46] recruited 102 children less than 16 years old in a randomized, double-blinded and placebo-controlled study which showed no reduction in rate of PTS within 48 hours of injury despite the use of phenytoin. However, this study had very low seizure rate (6%) and a marked decrease in enrolment without waiver of consent. There was also a significant number that was lost to follow up. In contrast, a more recent retrospective observational study of children (n = 275) with moderate to severe TBI found the use of anti-epileptic drugs (fosphenytoin or phenytoin, or phenobarbital) to be protective against the development of early post-traumatic seizures (OR, 0.2; 95% CI, 0.07 to 0.5).[47] In this study, the rate of early post-traumatic seizures was 12%.

Besides phenytoin, the use of levetiracetam has been reported in a phase 2 study for the prevention of posttraumatic epilepsy.[48] A small cohort was followed up for 2 years,[49] and the authors report that it is safe and feasible for further prospective studies.

Until further evidence is available, the utility of anti-epileptic prophylaxis in children remains controversial. We feel that the fi-

Table 1. Summary recommendation table

Area of study	Recommendations	Comments
Indications for neuroimaging	Physicians can use current clinical prediction tools: PECARN,[6] CHALICE,[5] or CATCH[7] to aid in their decision-making	PECARN[6] has been shown to perform with highest sensitivity. A period of observation is recommended in most patients with Glasgow Coma Scale 14–15[10]
Choice of sedatives	Unstable hemodynamics: consider ketamine Stable hemodynamics: consider ketamine or benzodiazepines. Etomidate can be considered in the absence of known adrenal insufficiency.	Hypotension should be avoided during induction
Applicability of hyperventilation	Severe hyperventilation to P_aCO_2 < 30 mmHg should be avoided	Increasingly aggressive hyperventilation may induce ischemia in a dose-dependent relationship[28]
Utility of hyperosmolar agents	Use of 3% hypertonic saline is recommended	Use of 3% hypertonic saline is likely to reduce the need for other interventions to treat raised intracranial pressure[39,40]
Prophylactic anti-epileptics	There is no conclusive evidence to recommend the routine use of prophylactic anti-epileptics	Phenytoin should be started in the event of clinical suspicion of seizure activity
Hypothermia in traumatic brain injury	Normothermia is recommended	Hypothermia is associated with hypotension and unfavourable outcomes[53,55,56] Hypothermia also affects drug elimination[57]

nal decision depends on the physician's discretion, but would recommend starting the anti-epileptic if there is a clinical suspicion of possible seizure activity.

Therapeutic hypothermia in pediatric traumatic brain injury

Several small studies had demonstrated a positive effect of cooling on intracranial hypertension in TBI patients.[50,51] However, in a meta-analysis that included randomized controlled trials in pediatric TBI comparing hypothermia groups versus normothermia, the authors found a tendency towards increased risk of cardiac arrhythmias (relative risk, 2.57; 95% CI, 1.01 to 6.54) and death (relative risk, 1.73; 95% CI, 1.06 to 2.84].[52] A significant contribution to this pooled effect came from the Hutchison study[53] in which 225 children were randomized to either cooling to 32°C to 33°C within 8 hours of injury or normothermia. They found an unfavorable outcome at 6 months with more deaths, more hypotension and more use of vasoactive agents in the hypothermia group, especially during the rewarming period. Concerns were raised regarding the use of marked hyperventilation (P_aCO_2 < 30 mmHg) as part of the standard protocol, as well as the speed of rewarming.

In the closely followed Cool Kids Trial, the phase II study[54] showed that the ICP was significantly reduced in the initial 24 hours after TBI. In the follow up phase III trial, patients were enrolled within 6 hours of injury and randomly allocated to either hypothermia 32°C to 33°C for 48 to 72 hours or normothermia.[55] No difference was detected for mortality (15% in hypothermia group versus 5% in normothermia group, P = 0.15) nor functional outcomes and the study was terminated early for futility after an interim data analysis.[55] A later meta-analysis suggested an increased risk of death with hypothermia therapy compared to the normothermia group, although not statistically significant.[56]

Another important consideration in utilizing therapeutic hypothermia is the effect of cooling on drug metabolism. Phenytoin elimination in children with TBI has been shown to decrease with therapeutic hypothermia,[57] posing an extended risk for drug toxicity. Based on the current evidence, maintaining normothermia is recommended in the setting of pediatric TBI (level II evidence).

DIRECTIONS FOR FUTURE RESEARCH

The evidence available to guide first line physicians when approaching a head-injured child is still found lacking in many crucial areas (Table 1).[5-7,10,28,39,40,53,55-57] Understanding of age-specific variations and developing individualized strategies[58] would enable the physician to apply these treatment principles in a more selective way. We eagerly await the results from ongoing trials that are studying the physiologic mechanisms in pediatric TBI[59] and exploring the impact of shared decision making with parents in deciding on head CT.[60] As already done in adult TBI research, panels of experts in pediatric TBI have determined data elements that are essential in the various areas of TBI.[61-64] These common platforms will allow for further collaborations and conduct of larger studies.[65] There is a pressing need for more collaborative research in this area to inform important decisions that the ED physicians must make when managing a child with TBI.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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