Severe traumatic brain injury and spinal cord injury in children

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Traumatic brain injury (TBI) is the single most common cause of permanent disability and death in infancy and childhood. The long-term survival and outcome is not only dependent on the nature of the primary injury but also on the effectiveness of measures to prevent and treat secondary injury.

In the UK, TBI accounts for 15% of deaths in 1–15-year-olds and 25% of deaths in 5–15-year-olds (Sharples et al, 1990b). Many of these deaths may be preventable. In a study of 255 children, potentially avoidable factors were identified in 22% who died before and in 42% who died after hospital admission (Sharples et al, 1990a).

Multiple physiological and treatment variables affect outcome in paediatric TBI. Age influences the quality of survival, with a poor outcome in 0–4-year-olds and even worse outcome in those <1 year (Adelson et al, 1997; Tilford et al, 2001). There are limited randomized controlled trials (RCTs) directed at neuroprotective strategies in children and practice varies between intensive care units (ICU) (Segal et al, 2001; Tilford et al, 2001). This article reviews the available paediatric neurocritical care literature focussing on severe TBI, with a view to suggesting a framework for management (*Table 1*). Selected papers have been tabulated for easy reference and are available on www.hospitalmedicine.co.uk.

INITIAL RESUSCITATION

The first few hours are crucial and a cascade of metabolic events begins almost immediately, marking a time of extreme vulnerability of the brain. Prehospital assessment and resuscitation is the first critical step in providing appropriate care to the head-injured child. The guiding principle is the prevention of secondary injury. Factors which potentiate secondary injury are hypotension, hypovolaemia, hypoxia, hypercarbia, hypoglycaemia, hyperglycaemia, seizures, coagulation abnormalities and electrolyte disturbances, all of which independently or in combination adversely affect intracranial pressure (ICP) and reduce cerebral perfusion.

Aggressive resuscitation and management of cranial as well as extracranial injury has shown improvement in morbidity and mortality. Early neuroimaging and paediatric neurosurgical consultation should be organized in any patient with Glasgow Coma Score (GCS) <13 at any point, fluctuating level of consciousness, observed loss of consciousness or amnesia, suspected open or depressed skull fracture, signs of basal skull fracture, clinical signs of raised ICP, focal neurological defect, post-traumatic seizures and dangerous mechanism of injury.

Cervical spine and traumatic brain injury

Paediatric spinal cord injury is relatively uncommon. The lower cervical spine is the most common site in children, and fractures are the most common type of injury (Proctor, 2002). Young children

TABLE 1.
Suggested protocol for management of severely head-injured child

All severely head-injured children need a CT scan of the head	
ICP monitoring	If severe traumatic brain injury (GCS ≤ 8) with abnormal admission CT scan
	If clinical signs suggest raised ICP or if there is presence of abnormal posturing or hypotension despite resuscitation even if initial scan is normal
	If no demonstrated improvement in GCS after adequate resuscitation
Maintain age-adjusted CPP	If low CPP because of low mean arterial pressure – fluid bolus while monitoring central venous pressure
If intracranial hypertension	Identify any precipitating factors and treat accordingly
	Examine pupils
	Ensure no hypotension, aim for normal arterial blood gas and electrolytes
	Consider possibility of seizure activity
	Maintain partial pressure of carbon dioxide between 4 and 5 kPa, serum sodium between 140 and 150 mmol/litre
	Maintain normothermia, strictly avoid pyrexia
	Pre-empt further rises with sedation (using fentanyl, remifentanyl or lidocaine) before nursing care or suctioning is undertaken
If sustained raised ICP >20–25 mmHg for >10 minutes with no response to above treatment	Discuss mannitol (0.25–1 g/kg intravenously) if patient euvolaemic
	Hypertonic (3%) saline (1–2 ml/kg) if low serum sodium <140 mmol/litre
	Repeat CT brain
	Consider use of paralysis
	Consider use of barbiturate therapy
	Discuss placement of external ventricular drain
Second tier therapies*	Large decompressive craniectomy
	Artificial elevation of systemic arterial pressure (perfusion pressure management)
	Limited period of induced mild hypothermia (temperature at 33–34°C)

*No direct evidence to support inclusion in protocol but individualized as per patient. CPP = cerebral perfusion pressure; CT = computed tomography; GCS = Glasgow Coma Score; ICP = intracranial pressure

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<2 years of age are more prone to high cervical injuries. Unique to children is spinal cord injury without radiographic abnormalities, which is difficult to diagnose and treat. Any child who has sustained TBI, who has an abnormal or fluctuating level of consciousness, neck pain, tenderness, paraesthesiae in the extremities or any other clinical suspicion of cervical spine injury, should have full cervical spine immobilization and cervical spine imaging.

In the National Emergency X-Radiography Utilization Study, a simple decision instrument based on five clinical criteria (midline cervical tenderness, altered level of alertness, evidence of intoxication, neurological abnormality and presence of painful distracting injury) was tested to help physicians to reliably identify patients who need radiography of the cervical spine after blunt trauma (Hoffman et al, 2000). If none of the above were present, the probability of cervical spine injury was considered to be low. The decision instrument had high sensitivity (99%; 95% confidence interval 98–99.6%) with a negative predictive value of 99.8% (95% confidence interval 99.6–100%) and application could potentially reduce unnecessary imaging.

A subsequent prospective, multicentre study in paediatric blunt trauma confirmed that this instrument performed well in children, and that its use could reduce paediatric cervical spine imaging by nearly 20% (Viccellio et al, 2001). However, it cautioned the applicability of criteria to infants and toddlers.

TRANSFER

The transport of severely head-injured children can be hazardous. Preservation of cerebral perfusion and oxygenation are important priorities. It is critical that the patient is safely transferred with the utmost urgency. The mortality for severe TBI is lower when referred directly from the accident scene (26.8%), increasing to 50% ($P = 0.021$) when referred indirectly (Johnson and Krishnamurthy, 1996). Sedation, analgesia and neuromuscular blockade are important considerations during transport to minimize changes in ICP and to ensure safety. The principles remain adequate oxygenation, prevention of hypotension, normocarbia and strict maintenance of cervical spine precautions. The Association of Anaesthetists of Great Britain and Ireland (Knowles et al, 1999) produced recommendations outlining the safe conduct of interhospital transfers for patients with acute head injuries. Transport should be undertaken by experienced staff and early consultation should be established with the neurosurgical team.

INTENSIVE CARE MANAGEMENT: NEUROPROTECTIVE STRATEGIES

Airway management

Airway obstruction, reduced respiratory drive and severe co-existing lung injury can contribute to hypoxia in the immediate post-injury phase. Assessment of airway reflexes should be done in all cases with evidence of reduced conscious level. Hypoxia (apnoea, cyanosis, partial pressure of oxygen in blood <60–65 mmHg or oxygen saturation <90%) and hypoventilation (ineffective respiratory rate for age, shallow or irregular respirations, frequent periods of apnoea and measured hypercarbia) are an indication for airway control and assisted ventilation with oxygen in the resuscitation phase.

Many studies have shown that hypoxia combined with hypotension worsens the outcome (Pigula et al, 1993; Kokoska et al, 1998; Chiaretti et al, 2002). Aggressive management of ventilation with elective intubation is crucial in any child with GCS < 9, or AVPU (alert (A), responds to voice (V), responds to pain (P), unresponsive (U)) score of P to avoid hypoxaemia, hypercarbia and aspiration. A consensus conference on the management of severe head injuries in children recommended a low threshold for intubation (Rekate, 2001; Society of Critical Care Medicine, 2003).

Arterial blood pressure management

Independent of injury severity or GCS, hypotension has been reported to be an early predictor of death in adults. Many paediatric studies have shown that early hypotension (blood pressure less than the fifth percentile for age) worsens neurological outcome. Prehospital hypotension was a statistically significant predictor of mortality with a positive predictive value of 61% in head-injured children (Pigula et al, 1993). Early hypotension (within 24 hours of injury) significantly increased morbidity and predicted poor functional outcome (Kokoska et al, 1998). When associated with hypoxia, hypotension resulted in a four-fold increase in the mortality of severely head-injured children (Sharples et al, 1990b).

Hypovolaemia associated with bleeding from intracranial and extracranial injury is an important correctable cause of hypotension. Traditional interventions aimed at reducing ICP such as mannitol infusion and administration of two-thirds maintenance fluids can be detrimental if the blood pressure is compromised. Hypotension should be assiduously prevented and treated aggressively using volume and vasopressors.

ICP-directed therapy, monitoring and treatment thresholds

The causes of raised ICP in paediatric TBI are multifactorial. A rapidly expanding intracranial haematoma – subdural or extradural – is an important treatable cause. ICP monitoring is indicated in patients with severe TBI (GCS ≤ 8) with an abnormal admission computed tomography (CT) scan (Brain Trauma Foundation et al, 2000; Society of Critical Care Medicine, 2003).

Although not subjected to a prospective RCT to establish efficacy in improving outcome, a large body of clinical experience indicates that ICP monitoring can help detect intracranial mass lesions, limit indiscriminate use of potentially harmful therapies, help determine prognosis and improve outcome. If clinical signs suggest raised ICP with presence of abnormal posturing or no improvement of GCS despite adequate resuscitation, then ICP monitoring needs to be considered even if the initial CT scan is normal.

The interpretation and treatment of ICP based on any threshold should be corroborated by frequent clinical examination and cerebral perfusion pressure (CPP) data. In practice, treatment is initiated at an upper threshold of 20–25 mmHg when persistent for at

least 10 minutes (Society of Critical Care Medicine, 2003). As blood pressure varies with age, CPP varies with age. In a long-term follow-up of 318 children with severe TBI, 11/17 (64.7%) with CPP <50 mmHg had severe disability compared to 9/33 (27%) with CPP >50 mmHg (Kieslich et al, 2001). Downard et al (2000) showed that no patient with a mean CPP of <40 mmHg survived and that, in those with CPP >40 mmHg, incremental CPP in deciles did not show any difference in outcome. Treatment of CPP without therapy aimed at decreasing ICP appears inappropriate and minimizing the variation of CPP around the clinically targeted level rather than elevating the level may be more beneficial.

Hyperventilation

Acute hyperventilation decreases ICP with the effect being rapid, predictable but short-lived. Data suggest that this therapy may be potentially harmful (Adelson et al, 1997; Skippen et al, 1997). A low partial pressure of carbon dioxide ($PaCO_2$) in the blood rapidly increases brain interstitial pH, and alkalosis produces arteriolar constriction and a global increase in cerebral vascular resistance. There is increasing evidence that hyperventilation can accentuate regional heterogeneity in cerebral blood flow (CBF) and lead to frank ischaemia in areas of marginally perfused brain (Skippen et al, 1997).

In the only prospective RCT of acute hyperventilation in TBI, 113 patients, primarily adults, were randomized to treatment with hyperventilation ($PaCO_2$ 25 mmHg), hyperventilation with supplemental buffer tromethamine infusion, or no hyperventilation (Muizelaar et al, 1991). Patients hyperventilated as part of their treatment had poorer outcomes at 3 and 6 months, although differences were no longer statistically significant at 1 year. Systematic review by the Cochrane group concluded that the data were inadequate to assess any potential benefit or harm from hyperventilation in severe TBI (Roberts et al, 1998; Schierhout and Roberts, 2000).

Prolonged hyperventilation should be avoided, particularly in the initial days after TBI. Brief hyperventilation to reverse malignant elevations in ICP or clinical signs of brain herniation until other measures take effect has not been studied. The potential catastrophic consequences of these conditions if left unchecked probably outweigh the theoretical risks of transient hyperventilation.

Hypothermia

There has been a resurgence of interest in the use of induced hypothermia in prevention of secondary injury. Hyperthermia raises cerebral oxygen consumption and increases ICP. A systematic review reported that hypothermia to a target temperature between 32 and 33°C, a duration of 24 hours, and rewarming within 24 hours were associated with reduced risks of poor neurological outcome compared with normothermia (McIntyre et al, 2003).

In an adult RCT, cooling to a target bladder temperature of 33°C within 8 hours of injury and maintaining hypothermia for 48 hours was shown to be not effective in improving the clinical outcome at 6 months (Clifton et al, 2001). The reasons why the earlier encouraging results are not repeated in larger trials are not clear. Timing of cooling might have been an important variable. Cooling the blood in the systemic circulation to the predetermined level of 33°C as measured by bladder temperature may have a limited effect in lowering temperature in areas of injured brain tissue, which has been shown to be consistently higher than systemic temperature by 0.41±0.26°C.

There is an ongoing multicentre, prospective RCT on the effects of hypothermia in paediatric TBI and patients are still being recruited. Until further evidence is obtained, hypothermia as an intervention outside of controlled trials appears inappropriate but hyperthermia should be avoided and the temperature should, at all times, be maintained below 37.5°C.

Hypertonic saline

Hyponatraemia causes brain swelling in the setting of TBI where syndrome of inappropriate secretion of antidiuretic hormone and salt wasting may occur. In a RCT (n=32), an inverse correlation was seen between serum sodium concentration and ICP (Simma et al, 1998). Although the hypertonic saline (HTS) treated group required fewer interventions, had fewer complications and had a shorter ICU stay, there was no difference in mortality. There have been few single centre reports that continuous infusion of HTS controls refractory ICP despite maximal therapy such as controlled hyperventilation and barbiturate coma (Khanna et al, 2000).

The mechanism of action and long-term effects of HTS on cerebral perfusion and metabolism in the traumatized brain are unclear. Unless there are large-scale trials, it cannot be recommended as standard practice. It is prudent to maintain the serum sodium between 140–150 mmol/litre and serum osmolarity at 300–320 mosm/litre in the presence of unstable raised ICP.

Anti-epileptic treatment

Early post-traumatic seizures can worsen secondary injury by increasing metabolic requirements, ICP and release of neurotransmitters, and by inducing a state of cerebral hypoxia. In a retrospective study, early post-traumatic seizures were present in 12% of ICU admissions with TBI, most (73%) developed seizures within 24 hours of trauma, and the severity of the injury (GCS<8), age (less than 3 years) and severe cerebral oedema were high risk factors (Chiaretti et al, 2000).

In 94 patients with moderate-to-severe brain injuries, continuous electroencephalogram monitoring in the ICU detected convulsive and non-convulsive seizures in 22% despite prophylactic phenytoin, with a high incidence of mortality in those with status epilepticus (Vespa et al, 1999). Routine use of anticonvulsants during the first 7 days after TBI is currently recommended, although further continuation does not prevent late posttraumatic seizures and is not recommended (Society of Critical Care Medicine, 2003).

Mannitol, barbiturates and steroids

A brief mention must be made of these traditional methods of controlling raised ICP. Mannitol is effective against raised ICP in patients who

show signs of cerebral herniation or acute neurological deterioration. Mannitol should be used with caution if any signs of hypovolaemia are present, and monitoring of electrolytes and osmolarity is needed. Repeated doses risk rebound increased ICP.

Barbiturate-induced coma may be considered if ICP is not controlled by conventional treatment (Society of Critical Care Medicine, 2003). Systematic Cochrane reviews of mannitol, barbiturates and steroids concluded that it was not possible to refute or support a real benefit from these interventions with the available randomized evidence (Roberts et al, 1998).

Neurosurgical interventions

External ventricular drain and decompressive craniectomy: CSF drainage may improve CBF, remove inflammatory mediators and reduce requirement of other therapies directed at raised ICP; however, there are no clinical trials proving its efficacy as an intermittent or continuous strategy in children. In intractable posttraumatic cerebral hypertension, decompressive craniectomy may be considered early as an alternative option (Society of Critical Care Medicine, 2003).

CONCLUSIONS

There is limited good evidence for paediatric TBI management strategies. However, this has not precluded use of neuroprotective strategies in the head-injured child in many paediatric ICUs in the UK. Early intubation, rapid transportation to an appropriate trauma care facility, prompt resuscitation with strict avoidance of hypotension and hypoxaemia, early neuroimaging and immediate evacuation of intracranial mass lesions followed by meticulous management in ICU remain core principles of management. More widespread adherence to these principles would significantly reduce paediatric head injury mortality and morbidity. HM

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KEY POINTS

- A well-defined treatment strategy from site of injury until admission to a neurointensive care facility is vital.
- Early liaison with neurosurgical services must take place, with rapid transportation to the appropriate centre.
- Initial adequate resuscitation is the single most critical factor for optimum survival.
- Hypoxia and hypotension are the two main secondary systemic insults that have the most impact on outcome.
- Meticulous attention must be paid to avoidance, recognition and treatment of hypoxia and hypotension at any stage.
- Early neuro-imaging and repeated re-evaluation of neurological status are essential.
- Immediate neurosurgical intervention should occur, with evacuation of intracranial mass lesions if present.
- Cervical spine precautions are needed until the child is awake, assessed and cleared.
- Early vigilance for identification and treatment of extracranial injury is important.

TABLE 1.
Studies in paediatric traumatic brain injury and the evidence classification

Study	Evidence class	Subjects	Description and conclusions
Chiaretti et al (2002)	Class II prospective	40 (<14 years)	Impact of management at scene on outcome after severe TBI (GCS ≤ 8) as correlated with GOS at 1 year after injury. Length of time before ICU admission influenced outcome among survivors. Severity of injury was significantly associated with hypoxia and hypotension
Tilford et al (2001)	Class II prospective	477 children	Severity of illness on admission to 3 ICUs over 18-month period, therapies used during ICU stay and patient outcomes at ICU discharge. Significant variation in therapy and outcome in different ICUs. Aggressive use of seizure medications resulted in significant reduction in mortality
Downard et al (2000)	Class III retrospective	118 (≤15 years)	Severe brain injury – 2 centres, no standardized treatment protocol, mean ICP, MAP, CPP over first 48 hours. No patient with mean CPP <40 mmHg survived; no significant difference in mortality/GOS distribution when mean CPP was stratified into deciles of 10. If mean ICP > than 20 mmHg, approximately 11 times more likely to die than children with lower values
Simma et al (1998)	Class I prospective, randomized controlled	35 (<16 years)	Patients with GCS ≤ 8 in the first 72 hours after injury randomly assigned (not blinded) to receive hypertonic saline or lactated Ringer's solution. Increasing serum sodium correlated with lower ICP and higher CPP. In the hypertonic saline group, fewer interventions needed to reduce ICP, fewer complications and shorter ICU stay but no difference in mortality
Kokoska et al (1998)	Class III retrospective	72 (3 months–14 years)	Single centre, GCS 6–8, morbidity from hypotension (<5th percentile for 5 minutes), F/U GOS at 3 months after injury. Early hypotension (within 24 hours of injury) significantly increased morbidity and predicted poor functional outcome. Maintaining adequate blood pressure in the early resuscitation phase improved outcome.
Skippen et al (1997)	Class II prospective	23 children (38 studies)	Single centre, cohort study, GCS ≤ 8, xenon CT CBF technique, and cerebral oxygen consumption studies with changes in CBF. Ischaemia increased three-fold with severe hypocarbia (<25 mmHg). Hyperventilation should be used with caution and monitored carefully
Adelson et al (1997)	Class II retrospective	30 children (≤8 years with GCS ≤ 8)	CBF and CO2 reactivity studies by xenon CT scans at variable times from admission to 9 days after TBI, outcome at 6 months by GOS scores. Young children represent particular high risk with early hypoperfusion after severe TBI. Low CBF in the early period after injury and low CO2 reactivity are associated with poor GOS scores
Johnson and Krishnamurthy (1996)	Class III retrospective registry based	1320 in total, 98 with severe TBI (GCS ≤ 8)	Comparison of outcome of children with severe TBI if transported directly to paediatric trauma centre vs if taken to the closest hospital and then transferred. In the former group, mortality was 26%, increasing to 50% if referred indirectly. Children brought directly from scene to paediatric trauma centre had better chance of survival
Pigula et al (1993)	Class II prospective	58 (<17 years)	Prospective, controlled, single centre, GCS ≤ 8, morbidity from hypotension (SBP <90 mmHg) and hypoxia. Hypotension, not hypoxia or hypercarbia, increased mortality. An episode of hypotension decreased survival fourfold. Initial adequate resuscitation single most critical factor for optimum survival
Sharples et al (1990a)	Class III retrospective	255 (<16 years)	Cause of death and potentially avoidable factors following TBI over an 8-year study period, multicentre, within a specific region in the UK. 50% died before admission. Potentially avoidable factors possibly or probably contributing to death in 32%. Preventable factors present in 22% who died before and in 42% who died after admission.

CBF = cerebral blood flow; CPP = cerebral perfusion pressure; GCS = Glasgow Coma Score; GOS =Glasgow Outcome Score; ICP = intracranial pressure; MAP = mean arterial pressure; SBP = systolic blood pressure; TBI = traumatic brain injury