Management of Severe Traumatic Brain Injury

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Background

Traumatic brain injury is one of the leading causes of paediatric death and disability around the world. Falls and motor vehicle accidents account for the majority of cases of head trauma in children and adolescents. In infants less than one year of age, abusive head trauma can account for up to half of all cases receiving intensive care for traumatic brain injury. Some risk factors for poor outcome include a history of non-accidental injury, multiple trauma, presence of early coagulopathy, lower GCS and higher Injury Severity Scale at presentation.

The severity of TBI is typically defined based on the initial Glasgow Coma Scale (GCS). Severe traumatic brain injury is defined as a presenting GCS ≤8 with a preceding history of head trauma. The discussion in this chapter is focused on the management of children with severe traumatic brain injury. Additionally, patients with moderate TBI (GCS 9 – 13), particularly those presenting with lower GCS of 9-10, may also benefit from the treatment strategies discussed here and these may be instituted at the discretion of the treating intensivist.

Patients with severe TBI require multidisciplinary care in close conjunction with paediatric neurosurgeons as well as with paediatric general, trauma or orthopaedic surgeons when significant extra-cranial injuries are present. Input from neurologists may also be required if seizures are suspected or observed.

Pathophysiology

Brain injury associated with TBI falls into two categories, primary injury which results from mechanical impact of the trauma and secondary injury which results from biochemical, cellular and physiological events that occur during and following the primary injury and can last from hours to days. The inflammatory and neurotoxic cascade that follows the primary injury results in cerebral edema, hypoperfusion, hypoxia, temperature dysregulation and loss of cerebral autoregulation. The primary injury to the brain is irreversible. The goal of neurocritical care for these patients is to minimize secondary brain injury by controlling intracranial pressure, optimising cerebral perfusion and oxygenation and avoiding iatrogenic insults such as hypoxia and hypotension.

History and Examination

Important factors to note in the history include information about the mechanism of injury and impact, loss of consciousness, and presence of seizures.

Examination should include the assessment of GCS and hemodynamic parameters, presence of Cushing's reflex, extra-cranial hematomas, step deformities of the skull, examination of pupils, and an assessment for focal neurological deficits. Patients with severe TBI often have associated extra-cranial injuries. Clinical examination should also be directed to identify other associated injuries including fractures and injury to internal organs.

Initial stabilization

Initial management should include c-spine stabilization, intubation and airway protection, volume resuscitation with crystalloids or packed red blood cells to ensure adequate mean arterial blood pressure to maintain cerebral blood flow and oxygenation. Early stabilization is based on rapid assessment and management of life threatening injuries following Advanced Paediatric Life Support (APLS) and Advanced Trauma Life Support (ATLS) guidelines.

Patients should first be stabilized before imaging is considered. However full stability may not be possible and imaging may be important to identify life-threatening injuries such as an expanding intracranial hematoma that requires emergent surgical evacuation, for stabilization.

Imaging

Imaging that should be considered at presentation includes:

- Non contrast CT Brain
- CT spine
- Lateral c-spine x-ray (if CT Spine not possible)
- Chest x-ray
- Pelvis x-ray
- Long bone x-rays
- Abdominal/thorax CT if severe TBI
- MRI Brain should be considered where there is a discrepancy in clinical severity and CT findings or when MR imaging is required for better delineation of the lesion for surgical intervention

Repeat CT Brain should be performed in the event of clinical deterioration or new and persistent elevation in ICP. In the absence of any changes in the clinical status, a repeat CT scan in the first 24-36 hours is unlikely to result in changes in clinical therapy.

Management of Severe TBI

Patients with severe TBI should undergo a non-contrasted CT Brain as early as possible followed by neurosurgery as indicated. An intracranial pressure monitor should be inserted to allow ICP monitoring and ICP targeted therapies. This should be considered after initial assessment and stabilization in the Children's Emergency and prior to transfer to CICU.

Baseline care

All patients should receive the following baseline care (Table 1) to maintain intracranial pressure (ICP) < 20 mmHg and to minimize the evolution of secondary brain injury. At all times, manipulation of the hemodynamic parameters and treatment decisions should be made with the concomitant goals of maintaining ICP < 20 mmHg while at the same time maintaining adequate age appropriate cerebral perfusion pressure (CPP). Patients should also receive continuous cerebral regional venous oxygen saturation ($CrSO_2$) via near-infrared spectroscopy (NIRS). Neuroprotective measures should be continued for 72 hours.

Patients should be intubated and mechanically ventilated to maintain adequate arterial oxygenation, normocarbia and have intra-arterial blood pressure and central venous

pressure monitoring to achieve appropriate intravascular volume and mean arterial blood pressure. Patients should have adequate sedation and analgesia, strict temperature regulation to maintain normothermia with antipyretics and cooling blankets as necessary. The head of the bed should be elevated to 30° elevation and the patient's head should be placed in a neutral midline position to allow unobstructed cerebral venous drainage. C-spine should be immobilized until cleared by neurosurgeons. Coagulopathy should be treated when bleeding is present or if surgical interventions are planned. Haemoglobin should be maintained at 9-10g/dL.This target should be discussed with the neurosurgeon and higher values may be preferred depending on the clinical situation.

All seizures should be treated and seizure prophylaxis with intravenous levetiracetam should be considered for all patients after discussion with neurosurgeons to reduce the risk of early post traumatic seizures (within 7 days). If possible, continuous EEG monitoring should be considered.

Early enteral nutrition (<72h of injury) should be started to reduce mortality and improve outcomes. Both hypoglycemia and hyperglycemia should be avoided. Overhydration, and systemic hypertension should be avoided to avoid increasing the risk of cerebral hyperemia and intracranial hypertension. If the patient is hypertensive, care should be taken when reducing the blood pressure as this may be a compensatory physiological mechanism to maintain adequate cerebral perfusion.

Table 1: Baseline Care of Paediatric Patients with Severe Traumatic Brain Injury

Inclusion criteria	• Paediatric patients with GCS <=8 and history of traumatic brain injury • Paediatric patients with GCS 9-10 and history of traumatic brain injury may be included at the discretion of the intensivist and neurosurgeon Caution: Modified GCS scoring may be inaccurate in neonatal patients <28 days. Threshold for initiation of this protocol should be discussed with neurosurgeon.	
Exclusion criteria	• History not suggestive of traumatic brain injury	
Emergent considerations	• CT Brain • Neurosurgical intervention as indicated • Placement of ICP monitor, ideally EVD	
Baseline neuroprotective care	Intubate and ventilate	• pCO2 35-40mHg • paO2 90-100mmHg • optimize PEEP to reduce FiO2
	Optimize position to allow CSF drainage	• Elevate head of bed to 30° • Maintain head midline in neutral position • Immobilize c-spine*
	Lines and monitoring	• Insert intra-arterial line for continuous intra-arterial blood pressure monitoring • Consider central venous line for central venous pressure monitoring/central venous access • Intra-cranial pressure monitoring • Cerebral near-infrared spectroscopy monitoring

Baseline neuroprotective care (continued)	Hemodynamics	• MAP > 50th percentile for age and height, titrate to CPP • Fluid resuscitation if intravascularly depleted • Vasopressor infusion or bolus hypertonic saline as needed to ensure CPP and ICP within target
	Goals for neuromonitoring	• ICP < 20 mmHg • CPP above minimum target for age* • Neonates < 1 month ≥ 40mmHg • 1 -12 months ≥ 45 mmHg • 1-7 years ≥ 50 mmHg • > 7 years ≥ 55-60 mmHg • Cerebral NIRS CrSO2 60-80%
	Treatment and prophylaxis for seizures	• Prophylactic anti-epileptic therapy with IV levetiracetam) 40mg/kg dose followed by maintenance 10mg/kg/dose Q12Hly • Further titration of levetiracetam if seizures occur • Consider continuous EEG monitoring if paralysed or persistently elevated ICP
	Other therapeutic targets	• Appropriate sedation and analgesia - aim SBS score of -1 or lower depending on ICP concerns • Maintain low normothermia (35-36°C) for 72H - See Targeted Temperature Regulation Protocol • Na 140-150 mmol/L • Normoglycemia (4-12mmol/L) - Avoid hypo or hyperglycemia - Consider insulin infusion if glucose persistently >12mmol/L • Hemoglobin 9-10 g/dL* • Treat coagulopathy, if bleeding or if surgical procedures planned
*goals should be discussed with neurosurgeons		

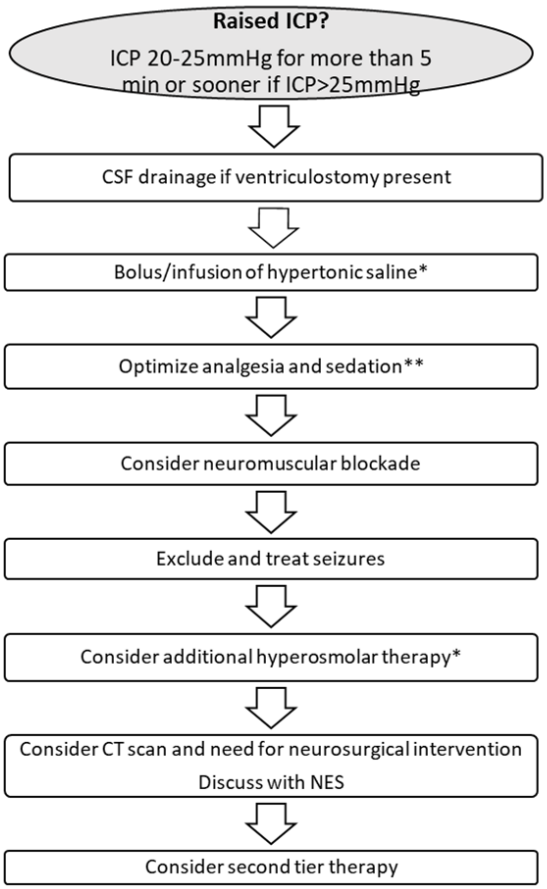
Management of raised ICP and herniation

Elevations in ICP despite baseline neuroprotective measures should be treated emergently. First tier interventions (Figure 1) should be instituted if ICP is 20-25mmHg for more than 5 min. Progression of intracranial pathology and acute herniation of brain tissue can occur at any time. As patients may be unconscious post trauma or heavily sedated for neuroprotection, repeated neurological examination is necessary to monitor for progression of intracranial pathology. The initiation of ICP directed therapies (Figure 1) may depend on many factors including the level of ICP elevation and tempo of disease progression. Interventions may need to be bypassed or repeated or given concurrently at the discretion of the treating intensivist. Persistent elevation of ICP despite first tier measures may indicate an expanding intracranial lesion and hence warrants repeat neuroimaging and discussion regarding the need for surgery. Second tier measures for the management of raised ICP (Figure 2) may be instituted at the discretion of the treating intensivist and neurosurgeon while balancing risks and benefits.

The onset of Cushing's reflex (hypertension with bradycardia), unequal or dilated pupils, new onset of focal neurological deficits, decerebrate or decorticate motor responses should raise concerns for acute herniation even in the absence of a spike in ICP and treatment should be instituted as per the herniation pathway (Figure 3).

Figure 1: First tier therapies for raised intracranial pressure

Treatments may be instituted concurrently and need not be in a stepwise manner



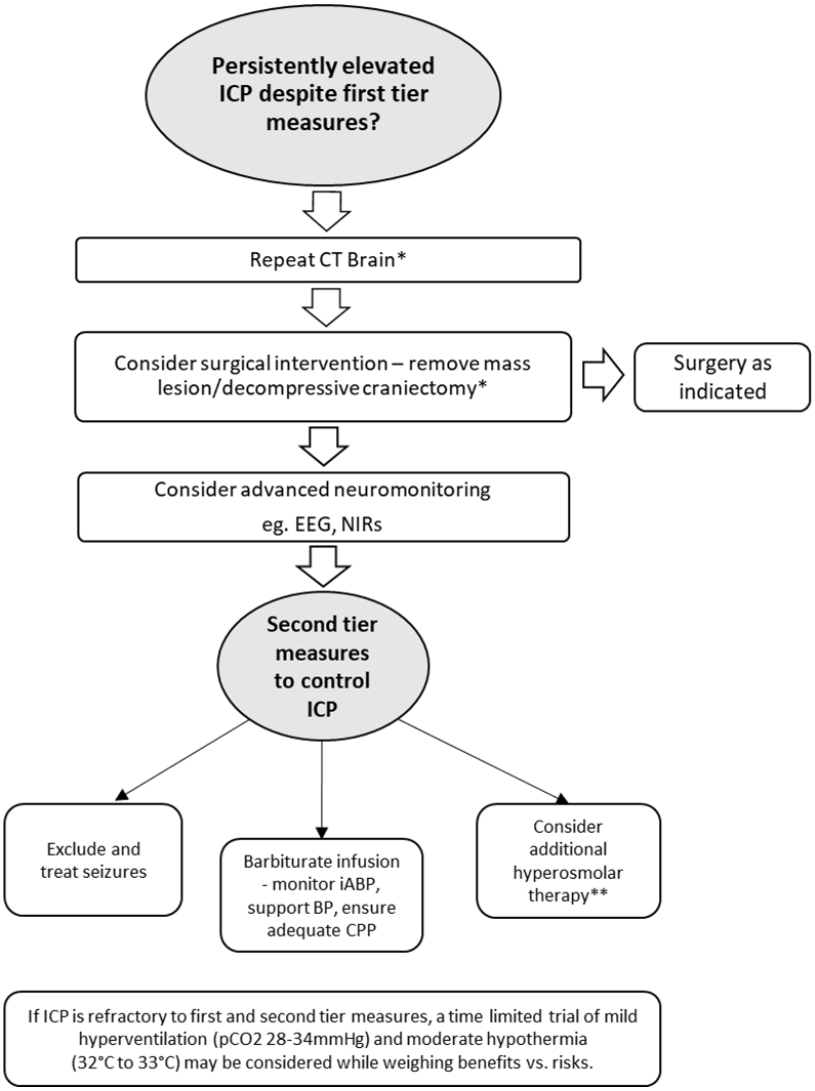
* Optimize Na, avoid >160 mmol/L. Monitor serum osmolality. Accept <360mOsm/L if using 3% hypertonic saline or <320mOsm/L for mannitol. Caution with use of hypertonic saline if platelet< 100, INR>1.4 or Cr 2X above baseline

**Avoid bolus administration of midazolam or fentanyl to reduce risk of cerebral hypoperfusion

Adapted from Kochanek, PM, Tasker RC, Bell M, Adelson D et al (2019). Management of Pediatric Severe Traumatic Brain Injury: 2019 Consensus Guidelines- Based Algorithm for First and Second Tier Therapies. Pediatric Critical Care Medicine: 20 (3) p 269-279

Figure 2: Management of persistently elevated ICP despite first tier measures

Treatments may be instituted concurrently and need not be in a stepwise manner



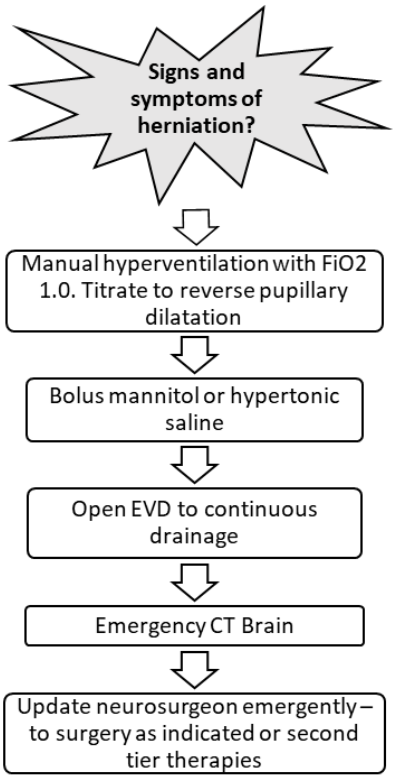
*Discuss with neurosurgeon re: role of neuroimaging and neurosurgical intervention including early decompressive cranienctomy (<24h of injury)

**Optimize Na, avoid >160 mmol/L. Monitor serum osmolality. Accept <360mOsm/L if using 3% hypertonic saline or <320mOsm/L for mannitol. Caution with use of hypertonic saline if platelet <100X10^9/L, INR>1.4 or Cr 2X above baseline

Adapted from Kochanek, PM, Tasker RC, BellM, Adelson D et al (2019). Management of Pediatric Severe Traumatic Brain Injury: 2019 Consensus Guidelines- Based Algorithm for First and Second Tier Therapies. Pediatric Critical Care Medicine: 20 (3) p 269-279

Figure 3: Herniation Pathway

Signs and symptoms of herniation include pupillary dilatation, hypertension/bradycardia/extensor posturing. If there are clinical concerns of brainstem herniation, the following emergent treatment should be given.



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EVD management

Keep EVD closed to drainage at 15cm above tragus (unless otherwise advised by neurosurgeons) with the goal to maintain ICP <20mmHg.

Choice of antiepileptic

For seizure prophylaxis, load with IV levetiracetam 40mg/kg dose followed by maintenance 10mg/kg/dose Q12Hly. If patient has seizures or status epilepticus, the same loading dose may be used, but a higher maintenance dose may be necessary and a referral to the Neurology service should be considered.

Hyperosmolar therapy

Hypertonic saline should be used as the first line hyperosmolar agent. If Na levels are not yet optimised, use 3% NaCL (2-5ml/kg over 10-20 min). Repeated dosing may be required. If necessary, a continuous infusion of hypertonic saline (0.1 to 1.0ml/kg/h) may be used. Infusion of 3% hypertonic saline may be titrated to ICP, using the minimum dose necessary to maintain ICP <20mmHg. Monitor serum sodium levels closely and avoid levels greater

than 160mmol/L, as this is associated with an increased risk of deep vein thrombosis. Serum sodium level above 170mmol/L is associated with thrombocytopenia and anemia. Hypertonic saline should be used with caution if platelet level is < 100 X 10^9/L, INR>1.4 or serum creatinine is two times above baseline or upper limit of normal. Mannitol (20%) may be used as second line hyperosmolar therapy (0.5g/kg/dose over 30 minutes). If using mannitol, close monitoring of hemodynamic parameters is important. It is advisable to monitor serum osmolality during hyperosmolar therapy. If using 3% hypertonic saline, accept <360mOsm/L and if using mannitol, accept serum osmolality <320mOsm/L.

Targeted temperature control

There is currently no evidence for routine use of hypothermia post TBI in children. However, fever and hyperthermia are associated with worse outcomes and should be aggressively avoided. Fever should be treated with anti-pyretics and cooling measures and a target temperature of 35-36°C, at the lower end of the normothermia range should be maintained. Initiate Targeted Temperature Regulation using Blanketrol (refer to CICU Targeted Temperature Management Protocol for “cooling” and “rewarming” protocols). If shivering occurs during temperature regulation it should be managed quickly by increasing sedation depth and if necessary with the use of muscle relaxants.

Prophylactic moderate hypothermia (32°C to 33°C) may be considered for ICP control in the setting of refractory intracranial hypertension (Figure 2). If hypothermia is used, this should be done with close monitoring for complications including coagulopathy, myocardial depression, arrhythmias, cold diuresis and electrolyte imbalances. Rewarming should be carried out slowly, at a rate of 0.5°C to 1.0° C every 12-24h to avoid complications including the risk of raised ICP.

Table 2. Reference List for Relevant Medications

Indication	Name	Dose	Notes/Precautions
Intracranial hypertension	Sodium chloride 3%	IV 2-5mL/kg over 10-20 minutes IV Infusion: 0.1 to 1.0ml/kg/h (titrate to ICP)	- Avoid Na >160 mmol/L. - Use only if serum osmolality <360mOsm/L. - May cause renal dysfunction in high doses. Aim <320mOsm/L to minimize adverse renal effects. - Caution in renal impairment, if platelet <100X10^9/L, INR>1.4 - Monitor for extravasation as drug is a vesicant
	Mannitol (20%)	IV 0.5-1g/kg/dose over 30 minutes	- Monitor for hypotension - Use only if serum osmolality <320mOsm/L - Monitor for extravasation as drug is a vesicant
	Thiopental	Acute increase in ICP: 1-2mg/kg/dose over 10mins, repeat PRN	- Loading dose may cause hypotension - For other cautions see below under “Barbiturate coma”
Seizure prophylaxis	Levetiracetam	Load: 40mg/kg over 5 minutes (max 3g/**dose**) Maintain: 20mg/kg/day Q12H (max 3g/**day**)	-If seizures occur despite prophylaxis, please refer to neurologist for titration of anti-epileptic treatment -Monitor for possible delayed hypersensitivity reactions (e.g. rash, SJS, DRESS, TENS)
Sedation/Analgesia	Midazolam	1-5 mcg/kg/min	- Monitor for hypotension - Titrate to SBS score
	Dexmedetomidine	Usual dosing range: 0.2 to 0.7mcg/kg/hr (can be increased up to 2mcg/kg/hr)	- Monitor for bradycardia, hypotension or hypertension - Titrate infusion to desired SBS score - Caution with doses >1mcg/kg/h; discuss with consultant
	Morphine	1-20 mcg/kg/h (up to 40mcg/kg/h)	Monitor for hypotension Titrate to SBS score

Table 2. Reference List for Relevant Medications (continued)			
Indication	**Name**	**Dose**	**Notes/Precautions**
Barbiturate coma	Thiopental	Medically induced coma: Load: 10-30mg/kg over 1hour followed by continuous infusion 1-2mg/kg/hr, up to 5mg/kg/hr	- Loading dose may cause hypotension. - Titrate rate of infusion to burst suppression with continuous EEG monitoring - Continuous ECG and iABP monitoring required - Watch for hypokalemia and supplement K with caution. May have rebound hyperkalemia when infusion is weaned - Drug is very alkaline (pH 10.6) and a vesicant - Central line is preferred as irritation, venospasm, extensive tissue necrosis, and/or sloughing have been reported with extravasation.

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