GUIDELINES FOR THE MANAGEMENT OF SEVERE TRAUMATIC BRAIN INJURY

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This is based upon the 2019 Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, 3rd edition.[1] The reader is encouraged to review the published guidelines by visiting the Brain Trauma Foundation website.

Injury is the leading cause of death for children in developed countries, of these 40 percent are due to traumatic brain injury.[2]

The only RCT of ICP guided vs. clinical/CT scan guided therapy for TBI was published in 2012.[3]

INTRODUCTION

Traumatic brain injury (TBI), is classified by severity according to the initial Glasgow Coma Scale (GCS):

Mild: GCS 13-15
Moderate: GCS 9-12
Severe: GCS <9

Glasgow Coma Scale (GCS) - level of consciousness

≥ 4 years		< 4 years	
Response	Score	Response	Score
Eye opening		Eye opening	
Spontaneously	4	Spontaneously	4
To verbal stimuli	3	To verbal stimuli	3
To painful stimuli	2	To painful stimuli	2
No response to pain	1	No response to pain	1
Best verbal response		Best verbal response	
Orientated and converses	5	Appropriate words or social smile, fixes, follows	5
Confused and converses	4	Cries but consolable; less than usual words	4
Inappropriate words	3	Persistently irritable	3
Incomprehensible sounds	2	Moans to pain	2
No response to pain	1	No response to pain	1
Best motor response		Best motor response	
Obeys verbal commands	6	Spontaneous or obeys verbal commands	6
Localises to stimuli	5	Localises to stimuli	5
Withdraws to stimuli	4	Withdraws to stimuli	4
Abnormal flexion to pain (decorticate)	3	Abnormal flexion to pain (decorticate)	3
Abnormal extension to pain (decerebrate)	2	Abnormal extension to pain (decerebrate)	2
No response to pain	1	No response to pain	1

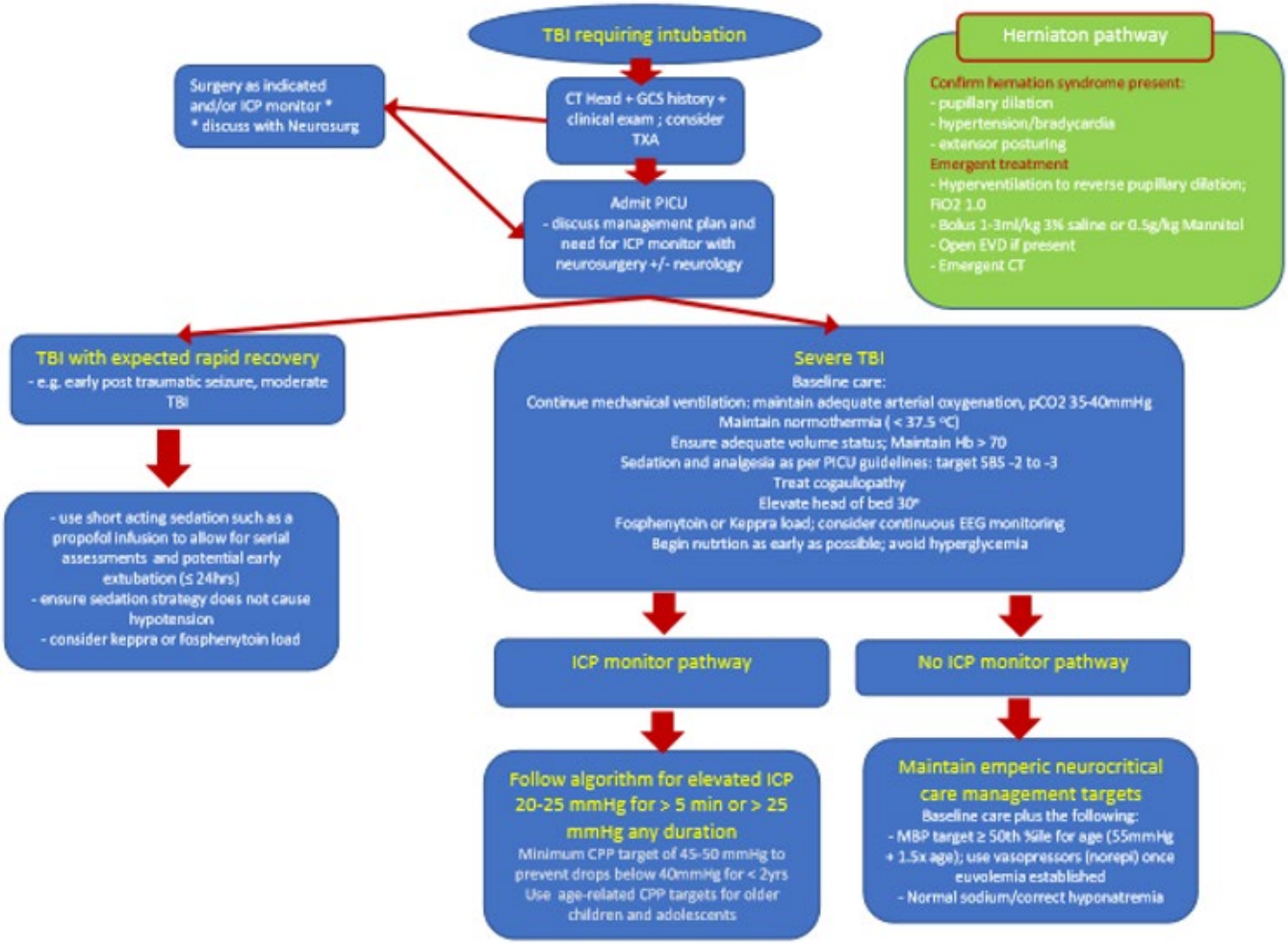
The initial reported GCS from the field or sending hospitals is occasionally inaccurate.

Therefore, it is recommended to obtain an accurate description from first responders and/or initial healthcare providers of the initial neurologic exam prior to intubation or introduction of sedating agents and use this information to re-score the Glasgow Coma scale independently.

The natural history of severe TBI involves two insults, the initial injury which can result in either diffuse or focal injury and secondary injury which is mediated by biochemical, cellular, metabolic and vascular mechanisms in response to the injury. It is the secondary injury which is the target of interventions in the management of TBI in effort to reduce and modify morbidity and mortality in these patients.

Low GCS may not be directly related to a brain injury and may have other causes such as post-traumatic seizure or are anticipated to recover quickly after surgery such as in the case of an epidural hematoma. Thus, decisions on placement of an ICP monitor or anticipation of the need for prolonged intubation should be based on the history, initial GCS and initial CT findings after review with neurosurgery. TBI patients suspected to not have a severe brain injury necessitating full application of the TBI guideline should be considered for a short-acting sedative approach over the first 12-24hrs that allows for serial examination and potential early extubation.

Please refer to the following algorithm to guide management for any TBI patient requiring intubation.



INITIAL MANAGEMENT

Initial management of the child with severe TBI should be directed at prevention of hypotension and hypoxia. Approximately one third of pediatric TBI patients lose cerebral autoregulation[4] which has been shown to be an independent predictor of poor prognosis.[5] This loss of autoregulation reduces the ability to prevent cerebral ischemia induced by hypotension; thus if autoregulation status is uncertain or cannot be measured then one should err on the side of maintaining a higher MAP and CPP.

Airway: With a GCS <9, or a declining GCS, steps should be taken to obtain a definitive airway. Intubation attempts should be minimized as laryngoscopy can contribute to increased intracranial pressure (ICP). Spinal cord injuries are common in severe TBI and spinal precautions should be maintained during intubation.

There is limited evidence comparing induction agents in pediatric TBI. Intravenous lidocaine is no longer routinely recommended to blunt ICP elevations during laryngoscopy as the evidence for benefit is mixed.[6] If it is used, doses ≤ 1.5mg /kg IV should be used to reduce the potential for hypotension.[7] Induction agents that either lower or do not adversely affect ICP and do not aggravate hypotension should be generally be chosen but must be customized to the individual patient circumstances. Succinylcholine is associated with increased ICP in brain tumor patients, but this relationship is not clear in TBI patients. The rapid offset of succinylcholine may outweigh risks of increased ICP depending on the clinical scenario. Ketamine probably does not increase ICP and can be used in the head injured multi-trauma patient to preserve hemodynamics.[8] A prospective study of 30 children in with a mix of closed head injury (80%) and penetrating head injury (20%), the use of ketamine was found to lower the ICP in both scenarios.[9]

Breathing: Hypoxia should be avoided through the administration of supplemental oxygen (paO2 >60 mmHg). Unless there is evidence of herniation, ventilation with a goal of normocarbia (pCO2 35-40 mmHg) should be maintained in order to prevent cerebral ischemia.

In the event herniation is suspected, aggressive hyperventilation (pCO2 <35 mmHg) can be used as a temporary measure to reduce ICP. But hyperventilation comes at the cost of decreased cerebral perfusion. The target of hyperventilation in a herniaton scenario is normalization or improvement in pupillary or Cushing responses as a bridge to other ICP-reducing therapies.

Circulation: Hypotension should be aggressively managed as it contributes to secondary brain injury, worsening outcome. Isotonic crystalloids are first line therapy, with early administration of blood and fresh plasma, especially in the case of multi-system trauma. Albumin should not be used.[10] If ICP and CPP cannot be measured then blood pressure goals targeting at least the 50th percentile for age should be used. A useful equation to identify age-based 50th percentile MBP goals is: 55mm Hg + (1.5 x age).[11]

Imaging: Once stabilized the patient with severe TBI requires urgent imaging with a CT scan to identify any focal injuries requiring urgent neurosurgical intervention. Extending the scan to include the cervical spine should be considered (See ACH Trauma Imaging Guidelines).

Tranexamic Acid: For patients with a GCS < 12 and suspected intracranial hemorrhage or with CT diagnosed-intracranial hemorrhage, TXA should be administered, ideally < 3 hrs from injury. The initial dose is followed by an infusion over the subsequent 8 hrs.[12] Recommended pediatric dosing is 15 mg/kg (max 1 gram) then 2mg/kg/hr over 8 hrs (max 1 gram over 8hrs or 125 mg/hr). Tranexamic Acid in Pediatric Trauma

Consultants: Neurosurgery should be consulted in the ED for all children with severe TBI for urgent management of significant intracranial hematomas and placement of an ICP monitor if indicated. In addition, consideration should be given to early decompressive craniectomy, although its role in improving outcome is

unclear.[13] [14] Decompression may be more successful in cases of unilateral swelling, based on stroke studies.[15] The presence of open fontanelles does not preclude the ability to develop intracranial hypertension, thus ICP monitoring should be considered in all age groups.

PICU should be consulted for ongoing care and management.

Neurocritical Care (NCC) or Neurology should be consulted when appropriate for on-going management.

ONGOING MANAGEMENT

The ongoing management of severe TBI is centered on preventing and minimizing secondary injury. The peak of post-traumatic edema occurs within 24-72 hrs following the initial insult.

Goals of therapy:
While there are no consensus guidelines for the management of intracranial hypertension in children, based upon current literature the following targets are viewed as appropriate initial goals:

MAP according to age (assuming no ICP monitor and ICP ~ 20 mmHg, lower number acceptable if ICP clinically unlikely to be elevated):

Infants and toddlers	60 mmHg
Children	70 mmHg
Adolescents	80 mmHg

The 50th percentile for age MAP equation should be used. (= 55 mmHg + (1.5 x age)[11]

ICP < 20-25 mmHg, consider a goal of < 15 mmHg for infants and toddlers

CPP (cerebral perfusion pressure = MAP - ICP)

Infants and toddlers	> 40 mmHg (set bedside goal at > 45 - 50 mmHg)
Children	> 50 mmHg (set bedside goal at > 55-60 mmHg)
Adolescents	> 60 mmHg (set bedside goal at > 65-70 mmHg)

These CPP levels should be viewed as critical thresholds below which existing evidence shows a significant increase in mortality.[16] A recent single center retrospective study suggests an association with improved mortality and higher CPP thresholds: 47 mmHg < 2yrs, 58 mmHg 2-8 yrs and 73 mmHg 8 > yrs of age. **Therefore, clinical targets at the bedside should be set 5-10 mmHg higher to prevent dips in CPP below the thresholds listed above**.[17] Be advised that targeting too high a CPP may be also associated with harm as seen in some of adult literature where sustained CPP targets > 70mmHg was associated with a higher incidence of ARDS.[18] This risk is reduced by judicious use of fluid and earlier use of vasoactive agents to achieve CPP goals.

At times vasopressors (norepinephrine) may be indicated in order to maintain CPP, even in the absence of hypotension. Alpha agonists such as norepinephrine or phenylephrine are preferred to dopamine and epinephrine as they provide a more predictable and efficient increase in MAP and CPP with less impact on the cerebral metabolic rate of oxygen.[19]

Algorithm for elevated ICP 20-25 mmHg for > 5 min or > 25 mmHg any duration

1st line

Evaluate and treat for the following potential causes of elevated ICP

- Hypotension (use age related targets for MAP and CPP‡)
- Hypercarbia
- Hypoxia / Need for suctioning
- Hyperthermia
- Inadequate sedation/analgesia
- Shivering
- Seizures
- Jugular vein obstruction (I.e. from head position or C-collar compression)

2nd line

1st Tier therapy for ICP > 20-25 mmHg for > 5 min or rapidly rising ICP

*Always consider expanding intracranial lesion and need for urgent CT

Step 1: Drain CSF for maximum of 10 minutes or until ICP improves if ventriculostomy present. Ensure no contraindications to rapid drainage

Step 2: Hypertonic saline 2-5 mL/kg IV or continuous infusion of 0.1-1.0 mL/kg/hr if serial doses required. Avoid serum Na+ > 160 or osmolarity >360 mOsm/L. Ensure no risks of rapid sodium correction of hyponatremic

Step 3: Additonal analgesia/sedation

Step 4: Neuromuscular blockade. Ensure EEG monitoring

Step 5: Additonal hyperosmolar therapy. Consider mannitol 0.25-1 g/kg IV q6h if serum osmolarity <320 mOsm/L

3rd line

2nd tier therapy for ICP refractory to 1st tier therapy

** A customized approach will be required based on unique patient characteristics

1) Reassess if surgical intervention and/or decompressive craniectomy is indicated with neurosurgery

2) Hyperventilate to a target pCO2 ≥ 30-34 mmHg

3) Optimize hyperosmolar therapy using a hypertonic saline infusion at 0.1 to 1ml/kg/hr titrated to a sliding scale and/or mannitol (avoid Na >160 mEq/L or osmolarity > 360 mOSm/L)

4) Targeted temperature therapy first to 34-35 degrees and then drop to 32-34 if required provided no contraindications such as coagulopathy

5) Barbiturate trial using pentobarbital infusion if hemodynamically stable. Target is ICP control and monitored with EEG so as not to exceed a burst suppression pattern; consider a 6 -24 hr trial and if no ICP control despite a burst suppression pattern on EEG, consider palliation. Start with 10mg/kg IV over 30 min and then 2-5mg/kg/hr infusion using 5mg/kg boluses q30-60 min as indicated.

Notes on selected 2nd tier therapies refractory to 1st tier therapies (see above algorithm)[1]

- Reassess surgical intervention that may include **decompressive craniectomy** (DC).
  - The quality of evidence that DC impacts functional outcome is mixed but should be considered to treat acute neurologic deterioration, herniation or elevated ICP refractory to medical management.
  - Patient selection is incredibly important. Patients with abusive head trauma, those with a significant component of hypoxic-ischemic secondary injury, or who have progressive severe refractory cerebral edema over a prolonged period of time with abnormal brainstem reflexes (i.e. late (>24-48hrs) vs early DC) are likely not good candidates.
- **Hyperventilation**
  - Target a pCO2 30-34mmHg
  - pCO2 < 30mmHg has been associated with ischemic injury and should be avoided unless advanced neurologic monitoring is used (i.e. brain tissue oxygenation, cerebral microdialysis, etc.)
- **Targeted temperature management**[20 21 22 23 24]
  - Prophylactic moderate hypothermia (32-33°C) is not recommended over normothermia but may be used to treat elevated ICP
  - Use a staged approach: if ICP control is achieved in the range of 34-35°C then maintain temperature in this range thereby mitigating known complications of hypothermia, such as infection, coagulopathy and rewarming.
  - Rewarming should occur at a rate of 0.5-1°C every 12-24 hours
  - If Phenytoin is being used, monitoring and dose adjustment is required both during hypothermia and rewarming.
- **Barbiturate therapy**
  - Proposed mechanism is through the suppression of metabolism and alteration of vascular tone. Reserved for use in refractory cases due to concerns of cardiorespiratory side effects (often requires blood pressure support), long half-life, zero order kinetics and interference with clinical exam.
  - Ideally should be used in conjunction with continuous EEG monitoring and consultation with the NCC/Neurology Service. Therapy should first target ICP control but should not exceed a burst suppression pattern on EEG.
  - A barbiturate infusion of pentobarbital vs intermittent boluses of phenobarbital is preferred. If ICP control cannot be achieved by 24 hrs of an effective dose based on EEG monitoring then palliation should be considered. One study found that only 4% of children who did not achieve ICP control within 6 hours of initiation of high dose barbiturate therapy went on to achieve ICP control between hours 7 and 24.[25] This shorter duration of evaluation can be considered if concerns about a longer duration of barbiturate therapy such as patient stability or other clinical characteristics.
  - Initial dosing recommendation of pentobarbital is as follows: Start with a 10 mg/kg loading dose over 30 min followed by 2-5 mg/kg/hr infusion with 5 mg/kg boluses doses as needed.

OTHER CONSIDERATIONS

Seizure prophylaxis:
Seizure in TBI can result in increased ICP and metabolic demand contributing to secondary injury. Therefore, use of prophylactic anticonvulsant such as fosphenytoin or levetiracetam should be considered for the first 7 days and then reassessed.[26 27 28 29 30]

EEG monitoring:
Continuous EEG should be arranged for a duration of 24-48 hours,[27] in consultation with the NCC service, as TBI has been associated with an increased risk of clinical, subclinical, and electrographic seizures with an incidence of upwards to 30%.[27] Further clinical seizure semiology can have a varied presentation[28] that may require EEG for delineation from other movement paroxysms. Risk factors for post traumatic seizure include abusive head trauma, younger age (<2yrs), intracranial hemorrhage, severe TBI, prolonged LOC, prolonged post-traumatic amnesia and depressed or open skull fractures.[29]

Choice of sedation and analgesia:
There is good evidence to support the use of adequate analgesia, sedation and, at times, neuromuscular blockade in order to control elevated ICP. Consider use of continuous EEG monitoring if prolonged use of neuromuscular blockade is anticipated (see above). Patients undergoing noxious stimuli (such as suctioning) should be pretreated with IV fentanyl and /or lidocaine (endotracheal or IV). Agitation, fighting the ventilator, and posturing are all associated with increased ICP and should be promptly treated.

The choice of agent is at the discretion of the individual practitioner with the ideal agent reducing ICP, increasing or maintaining CPP, and hemodynamically stable. There is some evidence to support the use of single doses of etomidate in controlling increased ICP, though there is concern of adrenal suppression. The extended use of propofol beyond 24 hrs should be avoided due to propofol infusion syndrome.[30] The use of ketamine, while traditional contraindicated as was thought to increase ICP may now in fact be considered.[9] [10] Neuromuscular blockade should be introduced for ICP refractory to treatment of reversible causes, hyperosmolar therapy and sedation optimization (see algorithm for elevated ICP).

Nutrition:
Hypoglycemia should be avoided and treated. There is no strong evidence for tight regulation of glucose in critically ill children but is less clear in children with TBI. Initiation of early enteral nutrition with 72 hours is recommended.

Imaging:
In the absence of clinical deterioration or increases in ICP there is no role for repeat CT scan in the brain injured child. Pending stabilization and clinical course an MRI may be of use in identifying diffuse injury as well as secondary injury for ongoing management and prognostication. SSEPs may be the best predictors of outcome.[31]

Corticosteroids:
There is no role for the use of corticosteroids in the management of severe TBI.[32]

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