Approach and Management of Children with Raised Intracranial Pressure

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ABSTRACT

Raised intracranial pressure (ICP > 20 mm Hg) is often seen in children with acute brain injury of various etiologies and often complicates the clinical picture and management; it may progress into herniation syndrome and death. The volume of intracranial compartments is tightly regulated, and cerebral blood flow (CBF) is kept constant despite fluctuations in systemic blood pressure by 'cerebral autoregulation'. Symptoms and signs of raised ICP are neither sufficiently sensitive nor specific; hence identifying patients at risk of developing raised ICP is a crucial for preventing secondary brain injury. Persistent elevation of ICP above 20 mm Hg for greater than 5 minutes in a patient who is not being stimulated should be treated immediately. Immediate goal of management is to prevent/reverse herniation and to maintain good cerebral perfusion pressure. The therapeutic measures include stabilization of airway, breathing and circulation, along with neutral neck position, head end elevation by 30°, adequate sedation and analgesia, minimal stimulation, and hyperosmolar therapy (mannitol or 3% saline). Short-term hypocventilation, to achieve PCO2 30 mm Hg, using bag ventilation can be resorted to if impending herniation is suspected. CPP targeted therapy (targeting CPP ≥ 60 mm Hg) is associated with better clinical outcome. Decompressive craniotomy may improve the outcome in raised ICP unresponsive to medical treatment. However, indiscriminate use of this surgery is not advised as the procedure and subsequent cranioplasty are associated with a number of complications.

Key words: Non-traumatic coma; Encephalopathy; Intracranial pressure monitoring; Cerebral Perfusion Pressure; Modified Glasgow coma score.

Introduction

Raised intracranial pressure (ICP > 20 mm Hg) is often seen in children with acute brain injury of various neurologic and non-neurologic etiologies and often complicates the clinical picture and management1. The most common etiologies of raised ICP in the pediatric intensive care unit (PICU) of developing countries are due to infections (ie, meningitis, encephalitis), hydrocephalus, hypoxic/ischemic brain injury, intraparenchymal bleed of vitamin K deficiency, metabolic encephalopathy, brain tumors, cerebral infarction, and traumatic brain injury (TBI)2. It accounts for about 20% of all admissions to PICU of Indian setting2. Unless diagnosed early and treated promptly, raised ICP can lead to severe neuromorbidity and mortality either because of decreased cerebral perfusion and global hypoxic-ischemic injury or herniation of brain tissue secondary to mass effect of compartmentalized ICP gradients1-3. Almost 93% of comatose children with acute CNS infections have signs of raised ICP at admission or develop these within 48 h of admission1,3.

Aim of management in a child with raised ICP is to break the vicious cycle of cerebral edema and compromised cerebral blood flow (CBF) at the
earliest and to maintain adequate cerebral perfusion pressure (CPP, \( \geq 60 \) mm Hg). The creation of standardized management protocol has reduced the fluctuation in ICP, decreased duration of raised ICP, maintaining target CPP independently associated with improved clinical outcome particularly in children with acute CNS infections\(^1,4\).

**Intracranial Physiology**

According to Monro-Kellie doctrine, under normal conditions the total volume within the skull remains constant and is determined by the sum of the brain-tissue compartments (\( \approx 80\% \)), blood (\( \approx 10\% \)) and cerebrospinal fluid (\( \approx 10\% \))\(^5-7\). The volume of these intracranial compartments is tightly regulated, and cerebral blood flow (CBF) is kept constant by vasoconstriction and/or vasodilatation cascades of the cerebral vessels despite fluctuations in systemic blood pressure called as autoregulation\(^6,7\). When additional volume is added to the compartment, one or more of the other components must decrease to keep ICP constant (compensatory mechanism; e.g., displacement of CSF to the spinal subarachnoid space and compression of the cerebral venous bed which are the only compartments that can compensate)\(^6\).

**Relationship between Intracranial Volume (IV) and ICP and Cerebral Compliance**

The relationship between intracranial volume and ICP is exponential. The quotient of volume differential (dV) and intracranial pressure differential (dP), that is, the volume necessary to obtain a known change in pressure, is known as cerebral compliance i.e. the cranial vault’s adaptive capacity that lets it tolerate an increase in volume depending on compensation mechanisms\(^6\). The inverse operation, that is, dP/dV, is known as cerebral elastance (pressure resulting from a known change in volume). Hence, the cause of resistance that opposes intracranial volume expansion. These ICP buffer systems are limited, as can be deduced from the intracranial pressure-volume curve\(^6,8\). This curve displays the relationship between changes in ICP and intracranial volume. It is made up of 3 stages (Figure 1)\(^6\). The sigmoidal behavior of the ICP-IV curve shows that major pressure changes are elicited by increases in IV\(^6,8\). Because of cerebral distensibility and buffering capacity, a change in volume will give rise to a tenfold increase in the numeric value of ICP. This is known as intracranial pressure volume index (PVI)\(^6\). Second issue is the pressure-volume curve corresponds to the craniospinal axis when the 2 spaces communicate freely. If CSF flow is blocked between the 2 compartments, as in a case of transtentorial or transforaminal herniation, the curve shows left displacement (cranial curve) with accompanying lower compliance\(^6\).

**Cerebral Blood Flow (CBF) and Cerebral Autoregulation**

The brain receives between 15\% and 25\% of the cardiac output and is tightly matched to metabolic demands\(^6\). CBF varies with age; in adults CBF is 50-70 ml/100g/min, whereas it is 40 ml/100g/min in neonates and as high as 108 ml/100g/min in children\(^7\). The critical threshold for ischemia is 20 ml/100g/min in the adult and 5 – 10 ml/100g/min in the infant and children\(^7\).

Values of CBF are determined by the cerebral metabolic rate of oxygen consumption (CMRO\(_2\)), which is in turn determined by the cerebral
autoregulation by means of cerebral vascular resistance (CVR). CBF is also determined by CPP (= MAP – ICP or CVP, whichever is higher). Cerebral autoregulation is primarily determined by PaCO₂, MAP, and to a lesser extent, by PaO₂, adenosine, pH, etc. Figure 2. Under normotensive conditions, CBF is estimated to fluctuate by 4% for each mmHg change of CO₂. However, when the upper or lower limits of these autoregulatory mechanisms are exceeded, CBF becomes absolutely dependent on MAP.

Figure 2: Autoregulation of Cerebral Blood Flow / Cerebral Vascular Resistance regulation. Pressure autoregulation maintains CBF constant between a CPP of 40 to 160 mm Hg. CBF is linearly related to PaCO₂, with a 4% change in CBF per mm Hg change in PaCO₂ between 20 mm Hg to 80 mm Hg. Below 20 mm Hg, this curve dramatically flattens and above 80 – 100 mm Hg, also more gradually flattens. The relationship between CBF and PaO₂ is relatively flat until a PaO₂ of 50 mm Hg is reached, below which, a dramatic increase in CBF is observed.

Normal CSF and ICP Values
The actual intraventricular volumes are ≈ 40 to 60 ml in infants, 60 to 100 ml in young children, 80 to 120 ml in older children, and 100 to 160 ml in adults. The turnover time for CSF is ≈ 5 to 7 hours. The normal range for ICP varies with age. The normal values for ICP in children are not well established. The usual normal range is considered as 5 to 15 mm Hg.5,6 In newborn term infants it is 1.5–6 mmHg, in young children 3–7 mmHg and in older children 10–15 mmHg.

ICP Threshold for Intervention
Based on current pediatric outcome studies, treatment threshold have been established to minimize poor outcome and therapeutic complications while improving mortality and good outcome.3,4,9 A definition of the persistent elevation of ICP above 20 mm Hg for more than 5 minutes in a patient who is not being stimulated requiring treatment. There is some rationale for treating smaller elevations (> 15 mm Hg) to avoid larger elevations that can cause cerebral herniation and irreversible brainstem injury.2,10 Sustained ICP values of more than 40 mm Hg defined as severe, life-threatening raised ICP. A surge in ICP normally occurs with activities such as suctioning, painful stimuli, and coughing and does not warrant intervention unless it does not return to baseline within about 5 minutes. It is important to distinguish “normal” or expected increases in ICP vs. intracranial hypertension because the latter requires immediate intervention. For all practical purposes, if symptoms and signs of raised ICP are present, one should consider that ICP is more than 20 mmHg and treat accordingly.

Etiology
Because of associated potential side effects of therapy and intensive ICP monitoring, identifying patients at risk of developing raised ICP is a crucial step in preventing pathologic changes that may result in poor outcome.2 Common causes of raised ICP with respect to pathophysiology are shown in Table 2.

Table 2: Common causes of raised ICP

<table>
<thead>
<tr>
<th>A. Increase in Brain Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cerebral edema: Primary CNS illness: encephalitis, meningitis, Head injury, Reye’s syndrome.</td>
</tr>
<tr>
<td>• Cerebral edema: Secondary to systemic illness: Hypoxic ischemic injury (hypoventilation, shock), ischemic stroke/infarct, metabolic encephalopathy– hyperpyrexia, hepatic failure, lead intoxication.</td>
</tr>
<tr>
<td>• Space-occupying lesions: Hematomas, tumors, abscesses</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. Increase in Blood Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Venous obstruction- Cerebral venous sinus thrombosis</td>
</tr>
<tr>
<td>• Hemorrhage</td>
</tr>
<tr>
<td>• Vasodilatation: Due to hypoxia, drugs or hypercapnia</td>
</tr>
<tr>
<td>• Status epilepticus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. Increase in CSF Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Obstructive hydrocephalus, Communicating hydrocephalus</td>
</tr>
<tr>
<td>• Impaired reabsorption: Subarachnoid hemorrhage.</td>
</tr>
<tr>
<td>• Increased production: Tumors</td>
</tr>
</tbody>
</table>

| D. Idiopathic or Benign Intracranial Hypertension |


**Approach and Management**

All patients with an modified Glasgow Coma Score (m-GCS) ≤8 Table 3 are likely candidates for raised ICP. Urgent neuro-imaging may be needed, after stabilization of airway, breathing and circulation and reversing potential or clinically manifest herniation, to rule out surgically correctable causes of raised ICP.

**Table 3:** Glasgow coma scale modified (m-GCS) for infants and children

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>Infants</th>
<th>Child</th>
<th>Coded value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye opening</td>
<td>Spontaneous</td>
<td>Spontaneous</td>
<td>4</td>
</tr>
<tr>
<td>Response to speech</td>
<td>Response to speech</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Response to pain</td>
<td>Response to pain</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>No response</td>
<td>No response</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Verbal Response</td>
<td>Coos/babbles</td>
<td>Oriented, Appropriate</td>
<td>5</td>
</tr>
<tr>
<td>Irritable cries</td>
<td>Confused</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Cries</td>
<td>Inappropriate words</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Moans</td>
<td>Incomprehensible sounds</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>No response</td>
<td>No response</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Best motor response</td>
<td>Normal</td>
<td>Normal</td>
<td>6</td>
</tr>
<tr>
<td>Withdraws to touch</td>
<td>Localizes painful stimulus</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Withdraws from pain</td>
<td>Withdraws from pain</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Flexor response</td>
<td>Decorticate posturing</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Extensor response</td>
<td>Decerebrate posturing</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>No response</td>
<td>No response</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

**Clinical Signs and Symptoms**

Clinical signs and symptoms highly variable and depend on the nature of the primary brain injury (ischemic, traumatic, or hemorrhagic), the extent of compartmentalization, the presence and location of a mass lesion, and the rate of increase in ICP\(^4,6\).

*In conscious patients* irritability, headache, vomiting, confusion and decreased alertness, and neck retraction may be the presenting features. These are neither sufficiently sensitive nor specific for timely recognition of raised ICP. Tense fontanel on palpation and papilledema, are reliable signs of raised ICP, but the later is usually absent in acute conditions, even in patients with documented elevated ICP. The most common symptom is progressive decline in mental status, eventually leading to a comatose state\(^4,6\).

*In unconscious/comatose patients*, raised ICP should be suspected in all patients with head injury, meningitis, encephalitis, liver disease and diabetes mellitus. The clinical features highly specific of raised ICP are generally seen late, when brain herniation is imminent or has already set in. These are abnormal posturing (decerebration or decortication), abnormal pupillary dilatation, hypertension, bradycardia, irregular breathing, sixth nerve palsy and papilledema\(^6\).

Focal neurologic findings may occur, but are most commonly due to horizontal tissue shifts that may not be associated with increased ICP. Cushing reflex (hypertension, bradycardia, irregular breathing) becomes evident only later in the course of illness, and may not occur in young children. Abnormal pupillary dilatation and posturing can occur in the absence of raised ICP.

All patients at risk of raised ICP should have a neuroimaging (head CT) on admission and repeat imaging within the first 24 hours, or more emergently if new symptoms or signs appear. Emergent neuroimaging is critically important to evaluate the cause of the patient’s change in examination. When time permits, MRI may be useful to further define the brain pathology. CT scan signs (i.e. loss of sulci, slit-like ventricle, loss of gray-white distinction, and obliteration of suprasellar and quadrigeminal cistern) of brain swelling are predictive of increased ICP, but the CT scan may be normal even in the presence of documented raised ICP (> 20 mm Hg) in 25% of patients\(^3\).

**Overt Sign of Raised ICP- The Herniation Syndromes**

Pressure gradient between various intracranial compartments may lead to herniation of brain from one compartment to another Table 4. Early signs of herniation are mainly due to compression and ischemia rather than displacement of brain tissue. Prompt recognition of the clinical signs of herniation is critical to salvage life.
Table 4: Overt Sign of Raised ICP - The Herniation Syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Mechanism</th>
<th>Clinical Findings</th>
<th>Imaging Findings</th>
</tr>
</thead>
</table>
| Transtentorial—Descending Unilateral - Lateral (Uncal) | Medial temporal lobe pushes downward into the posterior fossa through the incisura | -Variable impairment in consciousness.  
- Earliest sign: Ipsilateral pupil dilatation.  
-External ophthalmoplegia.  
-Contralateral hemiparesis.  
-Decerebrate posturing. | -Widening of contralateral temporal horn, ipsilateral ambient cistern and ipsilateral prepontine cistern.  
-Uncus extending into the suprasellar cistern. |
| Transtentorial-Descending Bilateral (Central) | Downward displacement of the cerebral hemispheres and the basal nuclei compressing and displacing the diencephalon and the midbrain rostrocaudally through the tentorial notch. | -Early coma  
-Medium sized, fixed pupils  
-Decorticate posturing  
-Cheyne-Stokes respiration  
-Diabetes insipidus | -Effacement of sulci  
-Obliteration of the suprasellar cistern  
-Compression and posterior displacement of the quadrigeminal cistern |
| Transtentorial-Ascending | Infratentorial mass effect protruding upward compressing the midbrain. | -Nausea/vomiting  
-Progressive stupor | -Spinning top appearance of midbrain.  
-Narrowing of bilateral ambient cisterns.  
-Filling of quadrigeminal cisterns. |
| Tonsillar | Cerebellar tonsils protruding below the foramen magnum compressing the medulla and upper cervical cord. | -Hypertension-bradycardia-bradypnea (Cushing reflex).  
-Coma  
-Respiratory arrest  
-Bilateral arm dysesthesia | -Cerebellar tonsils at the level of the dens on axial images.  
-Cerebellar tonsils on sagittal images 7 mm below foramen magnum (5mm in adult). |
| Subfalcine-Cingulate | Brain tissue extending under the falx in the supratentorial cerebrum. | -Small reactive pupils  
-Headache  
-Contralateral leg paralysis | -Attenuation of ipsilateral aspect of frontal horn.  
-Asymmetric anterior falx.  
-Obliteration of ipsilateral atrium of lateral ventricle.  
-Septum pellucidum shift. |

Overview and Targets of Management

ICP Monitoring

ICP monitoring is advocated for patients at high risk of raised ICP Table 1, especially for those with a worsening examination due to the poor reliability of clinical signs and symptoms and the need for prompt recognition and timely intervention. ICP monitoring

Table 1: Patients at risk of developing raised ICP who may benefit from ICP monitoring

A. Non-traumatic
- Acute CNS infections (Meningitis, encephalitis with stupor)
- Acute hepatic encephalopathy, Hepatic encephalopathy Grade III or IV, or hepatic failure with arterial ammonia > 150 micromol/L
- Refractory hypertensive encephalopathy
- Diabetic Ketonacidosis Encephalopathy
- Metabolic/Toxic Encephalopathy with radiologic evidence of cerebral edema or hydrocephalus
- Ischemia: Hemispheric Infarction > 50% middle cerebral artery (MCA) territory
- Hemorrhage: Subarachnoid Hemorrhage with radiologic evidence of hydrocephalus Intraparenchymal hemorrhage with mass effect Subdural or Epidural hematoma with associated midline shift

B. Traumatic brain injury (TBI)
- Severe TBI (Glasgow Coma Scale < 9)
- Mild to moderate TBI with abnormal admission head CT scan
- Mild to moderate TBI with normal admission head CT scan with hypotension and motor posturing
makes raised ICP management straightforward with clear goals of therapy, enabling early identification of refractory cases for more aggressive interventions. The most common sites used for ICP monitoring are intraventricular and intra-parenchymal. With technological refinement, monitoring of ICP has become reliable and safe in patients with acute severe brain injury. Pediatric intensivists can perform bedside burr hole for intraparenchymal ICP monitoring, successfully and safely. This could potentially reduce the waiting period for initiating ICP monitoring in PICU, for which ordinarily one has to wait for a neurosurgeon and can potentially improve the clinical outcomes. The current intraparenchymal monitor systems have added capabilities to monitor brain tissue oxygenation, temperature, and compliance and may be preferred in selected cases.

**Multimodal Brain Monitoring**

Adjuncts to ICP or CPP monitoring include assessment of global (jugular venous O2 saturation, SjvO2) and regional (brain tissue O2 saturation, PbtO2) oxygenation, temperature monitoring, microdialysis and amplitude-EEG, enabling individualized CPP and ICP thresholds, although this has not yet been shown consistently to improve outcome in children.

**Goals and Principles of Therapy**

The management of raised ICP primarily revolves around reduction in volume of 1 of the 3 intracranial compartments: brain, blood, and CSF. Treatment response is highly dependent on multiple factors, including the nature of primary brain injury, the extent of tissue shift, cerebral edema, mass effect, obstruction of CSF flow, and the status of the cerebrovascular autoregulatory reserve. In an ICP-based management, the primary goal is reduction of ICP to <20 mm Hg. On the other hand, proponents of CPP-based therapy recommend withholding treatment for ICP >20 if CPP can be maintained ≥ 60 mm Hg. This is based on the fact that brain metabolism may be maintained in relatively normal state at CPP above 60 mm Hg and become abnormal below 60 mm Hg. Recent controlled study in children with acute CNS infections has shown advantage of CPP-based management over ICP-based management. The principles of management include maintaining normoxia and normocarbia; avoiding factors that aggravate or precipitate raised ICP namely fever, hypoxia, hypoglycemia, hypotension and any noxious stimulation; treatment of underlying cause—whether intracranial or extracranial including surgical intervention; maintain adequate MAP (more than 50th centile for given age and gender) with help of fluid and, if needed vasoactive therapy; and bringing down ICP.

Therapeutic measures to bring down ICP, after surgical management of mass lesions, are divided into first-tier and second-tier therapies. First-tier therapies include elevation and positioning of head, sedation and analgesia, hyperosmolar therapy, and mild hyperventilation and placement of an ICP monitor. Second and third tier therapies include lumbar drainage of CSF, deep sedation, high-dose barbiturates decompressive craniectomy, and hypothermia; these treatments reserved for increased ICP that does not respond to first-tier therapies. Much of these treatment principles and guidelines are extrapolated from studies on adult patients and patients with traumatic brain injury. Few studies have directly evaluated treatment of raised intracranial pressure in children.

**Initial Stabilization: Airway, Breathing and Circulation**

Once the patient is identified as high risk raised ICP, general measures as outlined below should be instituted as soon as possible. The patient should be monitored and evaluated serially for presence of signs and symptoms of raised ICP Table 4. This is ideally done in the pediatric intensive care unit. In patients who are at high risk of raised ICP but do not have overt signs of herniation, the basic tenets of acute resuscitation should be kept in mind. Based on availability and feasibility of ICP monitoring, management guidelines were outlined for “No ICP Monitoring in Place” and “ICP Monitoring in Place” in Table 5 and Table 6 respectively.
Airway

In unconscious patients, proper positioning of the head or by positioning the patient on the side and suctioning the oral secretion should ensure airway patency. Oro- or naso-pharyngeal airways can be used.

**Indications for endotracheal intubation**:

1. Modified Glasgow coma score (m-GCS) ≤ 8
2. Patients with signs of respiratory distress
   - Declining \( O_2 \) saturation
   - Increasing \( FiO_2 \) requirement

**Rapid sequence induction (RSI) accompanied by cricoid pressure (Sellick maneuver)** is preferred for emergency intubation to prevent aspiration and sudden surge in ICP. The medications that facilitate intubation without increasing the ICP should be used. Monitor heart rate, blood pressure, \( SpO_2 \); provide

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**Table 5: Management of Patients With Sign of Raised ICP: No ICP Monitoring in Place**

<table>
<thead>
<tr>
<th>I.</th>
<th>Perform ABC’s while preparing patient for emergent neuroimaging (head CT/MRI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A–Airway:</td>
<td>Secure airway, do rapid sequence intubation, maintain/induce sedation-analgesia with Midazolam and/or Morphine or Fentanyl</td>
</tr>
<tr>
<td>B–Breathing:</td>
<td>Perform hyperventilation using ambu-bag while waiting for intubation, maintain ( PaCO_2 ) ≈ 30 - 32 mm Hg</td>
</tr>
<tr>
<td>C–Circulation:</td>
<td>Assess for euvolemia, give NS bolus if evidence of hypoperfusion / hypotension present particularly prior to instituting osmotic therapy (20% mannitol)</td>
</tr>
</tbody>
</table>

II. Once airway is secured, euvolemia is established, patient is sedated, initiate the general measure (**Table 7**) like Head End Of Bed (HOB) elevated to 30 degrees. Plan to do neuroimaging.

III. Plan for blood biochemistry (Serum Na, K, BUN, Glucose, Osmolality stat, and Q4–6 h thereafter)

IV. Mannitol 0.5 g/kg IV bolus stat then 0.25 g/kg if required Q4–6 h.
   - Hold mannitol dose for if Osmolar Gap > 10 or Change in Osmolar Gap > 10.

V. 3% NaCl 10 mL/kg IV bolus over 15–30 min followed by 0.1 to 1 ml/kg/hr infusion if no significant ICP reduction within 1 hr of Mannitol administration, or if unable to give Mannitol due to high baseline serum Osmolality or osmolar Gap.

VI. Once neuroimaging results are available, call neurosurgery stat as indicated, while continuing above maneuvers.
   - Focal mass lesion with midline shift—considered for early emergent decompressive craniectomy.
   - Diffuse brain edema/swelling—refer for intraparenchymal catheter placement where facility is available.
   - Hydrocephalus—refer for emergent EVD insertion and CSF drainage where facility is available, insertion for Intraventricular catheter monitoring and CSF drainage.

**Table 6: Management of Patients With Sign of Raised ICP: ICP Monitoring in Place**

<table>
<thead>
<tr>
<th>General measures and First tier therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Head in neutral position, 30° elevation.</td>
</tr>
<tr>
<td>• Ensure oxygenation- Normoxia (( PaO_2 &gt;60 ) mmHg, ( SpO_2 &gt;92% ))</td>
</tr>
<tr>
<td>• Ensure adequate circulating volume- Normovolemia</td>
</tr>
<tr>
<td>• Maintain normal BP</td>
</tr>
<tr>
<td>• Ventilation to achieve ( PaCO_2 ) &lt;35 mmHg</td>
</tr>
<tr>
<td>• Osmotic diuretic- Mannitol 0.25–0.50 /kg i.v. over 20 min, repeat S.O.S or</td>
</tr>
<tr>
<td>( \text{Hyper} )tonic (3%) saline infusion: 10 ml/kg bolus, followed by 0.1 ml–1.0 ml/kg/h infusion</td>
</tr>
<tr>
<td>• Dexamethasone - 1–2 mg/kg i.v. Q 6 h—cytotoxic cerebral edema (brain abscess, granuloma, tumor)</td>
</tr>
<tr>
<td>• CSF drainage- Obstructive hydrocephalus</td>
</tr>
<tr>
<td>• Prevent all events that increase ICP</td>
</tr>
<tr>
<td>• Fever / hypothermia, pain- adequate sedation-analgesia, seizures- anticonvulsant, loud noise, invasive stimuli.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second tier therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hyperventilation (( PaCO_2 ) 30–35 mmHg)</td>
</tr>
<tr>
<td>• Barbiturates coma- Thiopental or pentobarbital</td>
</tr>
<tr>
<td>• Moderate hypothermia(32–34°C)</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Third tier therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Decompressive craniectomy or temporal lobectomy</td>
</tr>
<tr>
<td>• Profound hyperventilation to ( PaCO_2 &gt;25 &lt; 30 ) mm Hg (use transiently)</td>
</tr>
</tbody>
</table>

**Airway**

In unconscious patients, proper positioning of the head or by positioning the patient on the side and suctioning the oral secretion should ensure airway patency. Oro- or naso-pharyngeal airways can be used.

**Indications for endotracheal intubation**:  
1. Modified Glasgow coma score (m-GCS) ≤ 8  
2. Patients with signs of respiratory distress  
   - Declining \( O_2 \) saturation  
   - Increasing \( FiO_2 \) requirement

(3) Patients unable to protect airway

(4) Signs of inadequate ventilation and oxygenation, such as irregular respiratory efforts, inadequate chest movements, poor air entry, and central cyanosis. Rapid sequence induction (RSI) accompanied by cricoid pressure (Sellick maneuver) is preferred for emergency intubation to prevent aspiration and sudden surge in ICP. The medications that facilitate intubation without increasing the ICP should be used. Monitor heart rate, blood pressure, \( SpO_2 \); provide
100% oxygen and bag ventilation as tolerated by patient and if no airway contraindications, administer sedation and neuromuscular blocking agents: Midazolam (0.2–0.3 mg/kg IV), Morphine (0.1 mg/kg IV) / Fentanyl (5–10 μg/kg IV), and Lidocaine (1–1.5 mg/kg IV) and short acting non-depolarizing neuromuscular blocking agents (vecuronium 0.1 mg/kg IV/atracurium 0.5 mg/kg IV/ rocuronium 0.6–1.2 mg/kg IV). Ketamine and succinyl choline should be avoided.

Breathing
Maintain normoxia and normocarbia. 100% oxygen should be started with non-re-breathing mask and if needed, bag valve mask ventilation to ensure adequate oxygenation. Although not effective and harmful for prolonged use, hyperventilation for acutely symptomatic patients may be lifesaving. Mild short-term hyperventilation should be undertaken if danger of impending herniation is present (unequal pupils, posturing; see above). To achieve this with manual ventilation, administer double the normal breathing rate for given age for 10 min duration. Monitor reversal of unequal pupils, posturing and improvement in mentation. Target a PaCO2 ≈ 30–32 mmHg. There is no role for prophylactic, prolonged and overt (PaO2< 25 -28 mm Hg) hyperventilation.
The ventilator settings should be adjusted to the optimal setting required to maintain a SpO2 saturation > 92%< 99%, a PaO2 between 80 to 100 mm Hg and a PaCO2 within 35 to 40 mm Hg range. The mode of ventilation should be selected based on patient response and comfort.

Circulation
Maintenance of euvolemia and avoidance of hypotension is paramount in early management of acute brain injury and is important for hemodynamic stability. If there are signs of poor perfusion, give a bolus of normal saline 20 ml/kg. Maintain MAP to achieve desired CPP, if needed by using fluid and vasoactive agents (dopamine, nor-epinephrine). Colloids are not recommended in acute brain injury (except in acute ischemic stroke) due to their adverse effect on survival. Normal saline is the preferred solution for fluid bolus/maintenance in the neurocritical care unit. Prophylactic uses of osmotic agents are not advocated due to their volume-depleting effect and questionable benefit. Norepinephrine is the vasopressor of choice due to its favorable cerebral hemodynamic effects. It may cause reflex bradycardia. Combined inotropes or vasopressors such as dopamine or norepinephrine may be used especially in patients with marginal or poor cardiac status.

General Measures and First Tier Therapy
1. Head Position
Elevate head end of bed by 30° and keep head in neutral position to prevent kinking of the jugular venous system promote venous drainage via the external jugular veins. The study has been shown to reduce ICP while maintaining an adequate CPP in acute brain injury patients except in patients with large ischemic stroke when it may compromise flow through a stenosed proximal cerebral vessel. Ensure adequate intravascular volume to prevent orthostatic hypotension.

2. Sedation and Analgesia
One consideration in the choice of sedative should be to minimize effects on blood pressure because most available agents can decrease blood pressure. Hypovolemia predisposes to hypotensive side effects and should therefore be corrected before administering sedatives. Selection of a shorter acting agent (midazolam) may have the advantage of allowing brief interruption of sedation to examine neurologic status. Use midazolam 1–3 μg/kg/min, Morphine 0.1 mg/kg/dose Q6h. Sedative doses have to be individualized, and titrated to achieve Ramsay sedation scale score of 3–4. At score 3 the patient responds to commands only and at score of 4 the patient is asleep, but has brisk response to glabellar tap or loud auditory stimulus.

3. Osmotherapy-Mannitol, 3% hypertonic saline (HTS)
Mannitol (20%): It has been the preferred osmotic agent due to its availability and physician’s familiarity of use. It has several mechanisms of action. Early
effect includes reduction of blood viscosity, with improvement in microvascular CBF, cerebral oxygenation, and CPP with reduction in cerebral blood volume (CBV), and ultimately lowering of ICP. Late effect, that occurs within 15–30 min and lasts up to 6 h, results from direct osmotic effect on neural cells with reduction in total brain water. Additional effects include reduced CSF production. For optimal effect, serum osmolality should be maintained below 320 mOsm. The osmolar gap correlates better with the mannitol level and is the preferred monitoring parameter to prevent mannitol-induced renal failure. The osmolar gap >10 or change in osmolar gap from baseline >10 correlate with poor mannitol clearance and increased risk of renal toxicity. Standard dosage: 0.5 g/kg i.v bolus, if further dose is required uses 0.25 g/kg/dose. Do not repeat mannitol in less than 4 h. Monitor the urine output and take care of hypovolemia. Mannitol is contraindicated in shock, oliguria, anuria and heart failure.

Hypertonic Saline (3%-HTS): HTS use in neurocritical care is increasing due to its favorable effect on systemic hemodynamics, ease of use, and proven efficacy4. It creates an osmotic force to draw water from the interstitial space of the brain parenchyma into the intravascular space. It promotes rapid CSF absorption, increases cardiac output, and expands intravascular volume thereby augmenting the CPP with a positive inotropic effect, diminishing the inflammatory response, and inducing glutamate re-uptake. Standard dosage: For continuous infusion, 3% HTS is preferred via central line. Usual dose is 10 ml/kg as a loading followed by 0.1–1 ml/kg/h. In cerebral edema, the initial serum sodium goal is commonly set at 145–155 mEq/L and is intensified up to 160 mEq/L if clinically indicated. In general it is well tolerated and complications are rare. Monitor serum sodium and creatinine every 6 h. It is contraindicated if serum sodium is >150 mEq/l, and/or osmolality >320mOsmol/L. Prolonged increase in osmolality induces the cerebral homeostatic mechanism to produce idiogenic osmoles to reduce the osmotic gradient. Because of this phenomenon, osmotic therapy must be tapered after 24 hours of continued use to avoid rebound raised ICP. Other osmotically active agents that have been evaluated include glycerol, sorbitol, and urea were found inferior to mannitol and associated with more severe rebound edema4.

Mannitol vs. Hypertonic Saline: It is unclear which of these two therapies is superior for reduction of ICP. Hypertonic saline is effective in reducing raised ICP, but does not have clear survival or outcome benefit. A recent systematic review found that HTS appears to achieve a greater reduction in ICP than other osmotic agents in TBI and in one series of non-traumatic encephalopathies; there was less mortality with use of HTS as compared to mannitol11. Unpublished data from our recent randomized trial in children with raised ICP due to acute CNS infections found that HTS was associated significant reduction in mean ICP (14 vs. 22 mmHg) with a corresponding increase in CPP (67 vs. 53 mmHg) during 72-hrs. HTS successfully controlled raised ICP in 79% of patients, in contrast to 50% by mannitol (RR=0.63, 95% CI 0.42-0.95) and HTS-group had a lower poor outcome than Mannitol-group (34.5% vs. 68%) (RR=0.49, 95% CI 0.27 - 0.89) (Kumar R, Singhi S, Bansal A, Unpublished data 2013).

4. Temperature
Fever increases metabolic rate by 10% to 13% per degree Celsius and is a potent cerebral vasodilator. Keep the temperature below 38°C (36–37°C axillary). If child is febrile, use paracetamol 15 mg/kg/dose oral or IV Q4h and surface cooling.

5. Glucose Control
Strict glucose control is essential to the management of acutely injured brain, as hyperglycemia has been correlated with poor outcome. Currently, a less aggressive glucose target of random blood sugar (RBS) around 150 mg/dl (80 – 140 mg/dl) recommended for patients with acute brain injury. Hypoglycemia (<60 mg/dl) and hyperglycemia (>180 mg/dl) should be avoided.

6. Seizure Prophylaxis
A significant number of patients with acute brain injury are at risk of seizures. Seizures acutely increase the ICP and amplify metabolic demand. Consider seizure prophylaxis in patients at high risk of seizures such as those with severe head injury, focal
symptoms and signs and CNS infections (meningitis and encephalitis). Use phenytoin—20 mg/kg IV loading, followed by 5 mg/kg/d for the first 7 d only. The duration of therapy remains controversial. Comatose children should also be considered for EEG monitoring and seizure prophylaxis, as non-convulsive seizures are not uncommon in them. These can cause sudden surge in ICP.

7. Use Lidocaine
1 mg/kg/dose 5 min before endotracheal suctioning and procedure (IV and ET). Do not repeat within 2 h.

8. GI bleed prophylaxis
Use Antacid 1 ml/kg/dose Q 8 h or pantoprazole 1 mg/kg/dose Q 12 h, (if G.I bleed is present use pantoprazole).

9. Anemia
Maintain Hb concentration around 10 g/dl, to help cerebral oxygen delivery. In cases with severe anemia, a marked increase in CBF occurs to maintain cerebral oxygen delivery. A large randomized trial of critically ill patients showed better outcome with a more restrictive transfusion threshold of 7 g/dL. The issue of optimal hemoglobin concentration in patients with raised ICP needs further study.

10. Hypertension
Increase in blood pressure is common in response to raised ICP. Characteristically rise in systolic-BP increase is greater than diastolic-BP. When autoregulation is impaired, hypertension may increase CBF and ICP, and may exacerbate cerebral edema and postoperative IC bleeds. Generally it is left untouched in acute raised ICP unless underlying cause is hypertensive encephalopathy. Treatment is also reasonable in patients with impending congestive cardiac failure, those with evidence of rapidly worsening brain edema on CT scan, and those with a persistent extreme surge in blood pressure. If it is decided to treat hypertension, vasodilating drugs, such as nitroprusside, nitroglycerin and nifedipine, should be avoided; these could increase ICP. Sympathomimetic-blocking drugs (esmolol, labetalol) or centrally acting α-receptor agonists (clonidine) are preferred because they reduce BP without affecting ICP.

11. Corticosteroids
Corticosteroids are commonly used for primary and secondary brain tumors, to decrease vasogenic edema. The most commonly used regimen is IV dexamethasone 0.15 mg/kg/dose every 6 h (max.16 mg/d). Routine use in TBI is not recommended.

12. Antibiotics/Antiviral/Antimalarial
In a febrile child give empiric first dose of ceftriaxone (50 mg/kg IV q 12 h) and acyclovir 30 mg/kg iv in 3 divided doses 8 h as infusion over 1–2 h for herpes encephalitis. If child is a resident of P. falciparum endemic area, and has hypoglycemia, anemia or absent meningeal signs then give empiric IV Artesunate/Quinine.

13. Glycerol
It is not used for acute reduction of raised ICP. However, oral glycerol (6 g/kg/d, 6 h for 2 d) has been shown to improve outcome in children with acute meningitis.

Second Tier Therapy
These options may be considered in hemodynamically stable patients with raised ICP refractory to other measures, if continuous cardiovascular and electroencephalogram monitoring and mechanical ventilation are available.

1. Heavy Sedation
Use morphine and midazolam and titrate the dose to achieve the Ramsay sedation score 5, which correspond to state where child is asleep, and has sluggish response to glabellar tap.

2. Barbiturates coma-Thiopental or pentobarbital
Barbiturates can reduce the cerebral metabolic rate and lower ICP. However, they can also cause significant fall in systemic blood pressure. Pentobarbital is given in a loading dose of 10 mg/kg followed by 5 mg/kg each h for 3 doses. The maintenance dose is 1 to 2 mg/kg/h, titrated to achieve a burst suppression pattern on electroencephalogram shows. Despite its efficacy, barbiturate therapy has a variable effect on outcome and no benefit has been shown with prophylactic administration. Systemic hypotension almost always occurs with barbiturate therapy,
often requiring vasopressor therapy and meticulous fluid management. Barbiturate infusion should be discontinued if significant hypotension occurs that compromises CPP despite vasopressor and fluid management. Other side effects of barbiturate therapy include sepsis, electrolyte abnormalities, and hepatic and renal dysfunction.

3. Induced Hypothermia

Induced hypothermia is effective in reducing ICP from multiple causes by suppressing all cerebral metabolic activities, thereby reducing CBF\(^1\). Surface cooling or endovascular cooling catheter may be used to induce mild (34°C–36°C) to moderate (32°C–34°C) hypothermia. Surface cooling with a body vest is the preferred method due to its noninvasive nature and relative efficacy in achieving the temperature goal. Induced hypothermia is controversial and the increased amount of resources associated with its use in addition to potential adverse effects make hypothermia a second tier therapy in refractory ICP. Neuromuscular blocking agents and sedation must be used during hypothermia to prevent shivering.

Third Tier Therapy

Decompressive Cranectomy (DC)

It may be a useful option for control of increased ICP unresponsive to medical treatment. Cranectomy performed within the first 24 h after severe head injury, and in refractory raised ICP due to CNS infections may improve outcomes. However, the exact indications for DC, optimal timing of treatment and effects of DC on long-term functional outcome remain unclear, and a need to increase our understanding of DC-associated complications and costs has been recognized\(^1\).

Key Points

- Identifying patients at risk of developing raised ICP is a crucial step in preventing pathologic changes in patients with acute brain injury.
- All patients at risk of raised ICP should have a neuroimaging (head CT) on admission and repeat imaging more emergently if new symptoms or signs appear.
- The CT scan may be normal even in the presence of documented raised ICP (> 20 mm Hg) in one fourth of the patients.
- ICP monitoring is advocated for patients at high risk of raised ICP especially for those with a worsening examination.
- Immediate goal is to prevent progression to herniation or to reverse herniation if present and to maintain CPP > 60 mmHg and ICP < 20 mmHg.
- CPP-based management (target CPP > 60 mm Hg) is advantageous over ICP-based management in children with acute brain injury due to CNS infections.
- Identify the signs of impending brain herniation and treat immediately.
- Although not effective and harmful for prolonged use, short-term hyperventilation for acutely symptomatic patients may be lifesaving.
- Hyperosmolar therapy (mannitol or 3% saline) is useful in achieving rapid fall in ICP. In general, 3% saline is well tolerated and complications are rare.
- Avoid factors that aggravate or precipitate elevated ICP and identify and treat reversible and acute causes.

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References


