Management of Pediatric Severe Traumatic Brain Injury 2019 Consensus and Guidelines

Jiří Žurek
Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition: Update of the Brain Trauma Foundation Guidelines

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Management of Pediatric Severe Traumatic Brain Injury: 2019 Consensus and Guidelines-Based Algorithm for First and Second Tier Therapies

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• update the Second Edition of the guidelines that was published in 2012

• essential to optimizing critical care and improving outcomes

• 48 new studies were included in this Third Edition

• over 90 articles, 68 protocols

• high-quality randomized studies that could support level I recommendations remain absent; only three level II recommendations, most recommendations are level III, supported by lower quality evidence.

• Approaches and Decisions in Acute Pediatric TBI (ADAPT)
Approaches and Decisions in Acute Pediatric TBI Trial (ADAPT)

The ADAPT investigators will enroll 1,000 children with a severe traumatic brain injury who require the placement of an ICP monitor an observational cohort study to test the address the following aims:

Specific Aim 1: Compare the effectiveness of first-line intracranial hypertension strategies

Specific Aim 2: Compare the effectiveness of strategies that mitigate iatrogenic ischemia and hypoxia

Specific Aim 3: Compare the effectiveness of strategies that provide metabolic support on outcome
Topics of the guideline

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Part I : Monitoring

Intracranial pressure monitoring

Neuroimaging

Advanced neuromonitoring
Strength of Recommendations: Weak

Levels I and II
There was insufficient evidence to support a level I or II recommendation for this topic.

Level III
To Improve Overall Outcomes. III.1. Use of ICP monitoring is suggested.

• asociace mezi intrakraniální hypertenzí a nepříznivým outcome a mortalitou
Advanced Neuromonitoring

Strength of Recommendation: Weak

Levels I and II
There was insufficient evidence to support a level I or II recommendation for this topic.

Level III
To Improve Overall Outcomes. III.1. If brain tissue oxygenation (Pbro2) monitoring is used, maintaining a level greater than 10 mm Hg is suggested.

- nejsou dostatečné důkazy pro doporučení Pbro2 pro zlepšení outcome
- pouze u pacientů bez kontraindikace, jako je koagulopatie, diagnostika smrti mozku
Strength of Recommendation: Weak

Levels I and II
There was insufficient evidence to support a level I or II recommendation for this topic.

Level III

To Improve Overall Outcomes. III.1. Excluding the possibility of elevated ICP on the basis of a normal initial (0–6 hr after injury) CT examination of the brain is not suggested in comatose pediatric patients.

III.2. Routinely obtaining a repeat CT scan greater than 24 hours after the admission and initial follow-up is not suggested for decisions about neurosurgical intervention, unless there is either evidence of neurologic deterioration or increasing ICP.
Opakování CT vyšetření u dětí se závažným TBI:

- nezlepšující se neurologický stav
- přetrvává, nebo se zvyšuje ICP
- neschopnost posoudit neurologický stav – sedace, relaxace,…
Part II : Thresholds

Intracranial pressure (ICP)

Cerebral perfusion pressure (CPP)
Thresholds for Treatment of Intracranial Hypertension

Strength of Recommendation: Weak

Levels I and II
There was insufficient evidence to support a level I or II recommendation for this topic.

Level III

To Improve Overall Outcomes

III.1. Treatment of ICP targeting a threshold of less than 20 mm Hg is suggested.
Thresholds for CPP

Strength of Recommendations: Weak

Levels I and II
There was insufficient evidence to support a level I or II recommendation for this topic.

Level III
To Improve Overall Outcomes. III.1. Treatment to maintain a CPP at a minimum of 40 mm Hg is suggested.

III.2. A CPP target between 40 and 50 mm Hg is suggested to ensure that the minimum value of 40 mm Hg is not breached. There may be age-specific thresholds with infants at the lower end and adolescents at or above the upper end of this range.

1. problém s měřením CPP rozdílu 5–10 mmHg
2. variace CPP-ICP terapie
3. statistické zpracování
Thresholds for Treatment of Intracranial Hypertension

- normální hodnoty MAP a CPP jsou nižší zejména u kojenců a malých dětí, ale optimální ICP v období po poranění není definováno

- spodní limit CPP autoregulace mozkového průtoku krve (CBF) je podobný u mladších i starších dětí a neklesá níže ~ 60 mm Hg

- rozdíl v CPP mezi normálním a dolním limitem autoregulace je menší u kojenců a malých dětí → možná potřeba stanovit nižší terapeutický cíl ICP → udržovat adekvátní perfuzi pro kojence a malé děti

- s ohledem na různorodost patologie a patofyziologie u dětských TBI může být v některých případech nutné individualizovat hodnoty ICP.
Part III : Treatments

HYPEROSMOLAR THERAPY
ANESTHETICS, ANALGESICS, AND SEDATIVES
CEREBROSPINAL FLUID DRAINAGE
SEIZURE PROPHYLAXIS
VENTILATION THERAPIES
TEMPERATURE CONTROL
BARBITURATES
DECOMPRESSIVE CRANIECTOMY
NUTRITION
CORTICOSTEROIDS
Hyperosmolar Therapy

Level III

*For ICP Control.* III.1. Continuous infusion HTS is suggested in patients with intracranial hypertension. Suggested effective doses as a continuous infusion of 3% saline range between 0.1 and 1.0 mL/kg of body weight per hour, administered on a sliding scale. The minimum dose needed to maintain ICP less than 20 mm Hg is suggested.

III.2. Bolus of 23.4% HTS is suggested for refractory ICP. The suggested dose is 0.5 mL/kg with a maximum of 30 mL.

Safety Recommendation (applies to all recommendations for this topic). In the context of multiple ICP-related therapies, avoiding sustained (> 72 hr) serum sodium greater than 170 mEq/L is suggested to avoid complications of thrombocytopenia and anemia, whereas avoiding a sustained serum sodium greater than 160 mEq/L is suggested to avoid the complication of deep vein thrombosis (DVT).
Hyperosmolar Therapy

• přestože se mannitol v managementu TBI běžně používá - žádné studie, žádná evidence

• cílem je euvolémie, nikoliv dehydratace !!!
Analgesics, Sedatives, and NMB

Recommendations

Strength of Recommendations: Weak

Levels I and II
There was insufficient evidence to support a level I or II recommendation for this topic.

Level III

*For ICP Control.* III.1. With use of multiple ICP-related therapies, as well as appropriate use of analgesia and sedation in routine ICU care, avoiding bolus administration of midazolam and/or fentanyl during ICP crises is suggested due to risks of cerebral hypoperfusion.
## Analgesics, Sedatives, and NMB

<table>
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<tr>
<th>Study</th>
<th>Design</th>
<th>Outcome</th>
<th>Selection Bias</th>
<th>Indirect Evidence</th>
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<tbody>
<tr>
<td>Bar-Joseph et al (119)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Prospective</td>
<td>Pre/post</td>
<td>Post ketamine administration</td>
<td>ICP decreased by 30% (from 25.8±8.4 to 18.0±8.5 mm Hg) (p &lt; 0.001)</td>
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<tr>
<td>Meyer Children’s Hospital, Rambam Medical Center, Israel</td>
<td></td>
<td>n = 30</td>
<td>Overall in both groups</td>
<td>After 65 ketamine administrations 61 ICP decreased 3 increase &lt; 2 mm Hg 1 increase &gt; 2 mm Hg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 (17%) not TBI</td>
<td>CPP increased from 54.4±11.7 to 58.3±13.4 mm Hg (p &lt; 0.005)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Age: mean, NR; range, 6 mo to 18 yr ICP; CPP</td>
<td>Group 1</td>
<td>Mean ICP decreased from 25.2±5.4 to 17.9±5.5 mm Hg within the first 2 min of ketamine administration (p &lt; 0.001) and during distressing activity increased slightly up to 19.6±6.7 at minute 7 and then decreased again.</td>
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<td>All elevated ICP (&gt; 18 mm Hg) resistant to first-tier therapies received a single ketamine dose (1–1.5 mg/kg)</td>
<td>Group 2</td>
<td>ICP decreased by 33% (from 26.0±9.1 to 17.5±9.1 mm Hg) (p &lt; 0.0001) within 2 min following ketamine administration.</td>
</tr>
<tr>
<td></td>
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<td>Group 1: to prevent further ICP increase during a potentially distressing intervention</td>
<td></td>
<td>Result contradicts prior concerns that ketamine increases ICP.</td>
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<td>Group 2: additional measure to lower ICP</td>
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</table>

NMB – dyssynchrony during UPV, prevention of třes

- Ketamine - no recommendation
CSF Drainage

Strength of Recommendation: Weak

Levels I and II
There was insufficient evidence to support a level I or II recommendation for this topic.

Level III
For ICP Control. III.1. CSF drainage through an EVD is suggested to manage increased ICP.

Changes From Prior Edition. The recommendation from the Second Edition about use of lumbar drain (LD) was eliminated. One new class 3 treatment series was added to the evidence base for this topic (127).
Seizure Prophylaxis

Strength of Recommendation: Weak

Levels I and II
There was insufficient evidence to support a level I or II recommendation for this topic.

Level III
For Seizure Prevention (Clinical and Subclinical). III.1. Prophylactic treatment is suggested to reduce the occurrence of early (within 7 d) PTSSs.
Seizure Prophylaxis

- PTS časné - do 7 dnů od zranění
  pozdní - od 8 dnů

- není dostatek důkazů k doporučení levetiracetamu nad fenytoin

- rizikové faktory – lokalizace léze, kontuze, fragmenty, porucha vědomí, hematom, věk – kojenci a děti nižší prahová hodnota

- ve srovnání s dospělými u dětí vyšší výskyt PTS o 70%
Strength of Recommendations: Weak

Levels I and II
There was insufficient evidence to support a level I or II recommendation for this topic.

Level III
To Improve Overall Outcomes. III.1. Prophylactic severe hyperventilation to a $\text{Paco}_2$ less than 30 mm Hg in the initial 48 hours after injury is not suggested.

III.2. If hyperventilation is used in the management of refractory intracranial hypertension, advanced neuromonitoring for evaluation of cerebral ischemia is suggested.
### Ventilation Therapies

- **hypokapnie** – mozková vasokonstrikce – redukce CBF a CBV → ↓ ICP

- **target arteriální pCO₂** 35–45mm Hg tj. 4,6–6 kPa

- použití hyperventilace je popsáno v článku o algoritmu terapie TBI – refrakterní hypertenze
Temperature Control/Hypothermia

*Strength of Recommendation: Moderate*

**Level I**
There was insufficient evidence to support a level I recommendation for this topic.

**Level II**

*To Improve Overall Outcomes.* II.1. Prophylactic moderate (32–33°C) hypothermia is not recommended over normothermia to improve overall outcomes.

**Level III**

*For ICP Control.* III.1. Moderate (32–33°C) hypothermia is suggested for ICP control.
Temperature Control/Hypothermia

- hypertermie koreluje se špatným outcome → u dětí s TBI prevence hypertermie
- hypotermie prokazatelně → ↓ metabolismus mozku, zánět, peroxidace lipidů, excitotoxicita, buněčná smrt, křeče
- hypotermie vs refrakterní nitrolební hypertenze – STUDIE ???

Safety Recommendation:

- po ukončení hypotermie a zahájení ohřívání rychlost 0,5–1,0 °C každých 12–24 hodin nebo pomaleji, aby se předešlo komplikacím
- při podávání fenytoinu během hypotermie důraz na monitoraci hladin a úprava dávkování – minimalizace toxicity
Barbiturates

Strength of Recommendations: Weak

Levels I and II

There was insufficient evidence to support a level I or II recommendation for this topic.

Level III

For ICP Control. III.1. High-dose barbiturate therapy is suggested in hemodynamically stable patients with refractory intracranial hypertension despite maximal medical and surgical management.
Barbiturates

- vysoké dávky barbiturátů snižují ICP potlačením metabolismu, ↓ CBF; naopak v poškozené oblasti mozku zlepšují regionální průtok krve → ↑ oxygenaci mozku
- hypotenze, ↓ CO → ↓ CPP, hypoxie
- terapie barbituráty vyhrazena pro refrakterní nitrolební hypertenzi

Safety Recommendation:

- kontinuální monitorace arteriálního tlaku, podpora hemodynamiky s cílem udržení adekvátního CPP
Decompressive Craniectomy

**Recommendations**

*Strength of Recommendation: Weak*

**Levels I and II**
There was insufficient evidence to support a level I or II recommendation for this topic.

**Level III**

*For ICP Control.* III.1. Decompressive craniectomy (DC) is suggested to treat neurologic deterioration, herniation, or intracranial hypertension refractory to MM.

Timing, komplikace, mortalita, *funkční* outcome ???
Nutrition

Strength of Recommendations: Weak

Level I
There was insufficient evidence to support a level I recommendation for this topic.

Level II
To Improve Overall Outcomes. II. 1. Use of an immune-modulating diet is not recommended.

Level III
To Improve Overall Outcomes. III. 1. Initiation of early enteral nutritional support (within 72 hr from injury) is suggested to decrease mortality and improve outcomes.
Nutrition

• během TBI zvýšení metabolismu →↑ kalorická podpora během kritické fáze
• preference EV
• hyperglykemie →↓ outcome
• insulin tight glucose control ↓ riziko infekce, doba hospitalizace, mortalita….↑ hypoglykemie
• v současné době nejsou u TBI k dispozici dostatečné údaje pro/proti tight glucose control
Corticosteroids

**Strength of the Recommendation: Weak**

Levels I and II
There was insufficient evidence to support a level I or II recommendation for this topic.

Level III
*To Improve Overall Outcomes*
III.1. The use of corticosteroids is not suggested to improve outcome or reduce ICP.

- vyjímka u pacientů s chron. substitucí kortikoidů, suprese nadledvin, poškození osy hypotalamus-hypofýza
ICP
Refractory to first tier therapies

Repeat CT scan (if surgical option is being considered)

New or expanding surgical lesion

YES
Surgery as indicated

NO

Surgical intervention: Remove mass lesion and/or decompressive craniectomy

Barbiturate infusion

Moderate hypothermia 32-34°C

Hyperventilation 28-34 mmHg

Higher levels of osmolar therapy

Consider additional advanced neuro-monitoring
- EEG
- TCD
- PRx
- CBF
Děkuji za pozornost