Recent trends in the management of head injury

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Recommendations

Level I : Recommendations are based on the strongest evidence, represent principles of patient management that reflect a high degree of clinical certainty.

Level II : Recommendations reflect a moderate degree of clinical certainty.

Level III : Recommendations for which the degree of clinical certainty is not established.

Current concepts

- **Blood pressure and oxygenation**:

  - Single episode of hypotension (SBP < 90 mm Hg) increases the morbidity and doubles the mortality
    [**Traumatic Coma Data Bank**]

  - Reduction of even 10 mm Hg in MABP doubles the mortality
    [Luerssen and Klauber, 1995, Pediatric Neurosurgery]

  - Pre hospital hypoxia (SaO2 ≤90 %) strongly correlates with poor outcome after TBI.
    [Chi et al . Pre hospital Hypoxia affects outcome in patients with traumatic brain injury. Prospective multicentre study. 2006, J Trauma]

Current concepts

- **Blood pressure and oxygenation:**
- **Table 1. Summary of Brain Trauma Foundation**

Guidelines for Management of Systemic Oxygenation in severe TBI

Topic	Level of recommendation	Summary
Blood Pressure	II	Arterial hypotension (SBP < 90 mm Hg) should be avoided
Oxygenation	III	Hypoxia (PaO2 of < 60 mm Hg or oxygen saturation of <90 % should be avoided)

Current concepts

- **Intracranial pressure monitoring**
  - No RCTs confirming the benefits of ICP monitoring and treatment
  - BTF level II recommendation in severe head injury with abnormal CT findings
  - Level III recommendation in severe head injuries with normal CT scan and any of the 2 :
    - Age > 40 years
    - Decerebration
    - BP <90 mm Hg

Current concepts

- **Intracranial pressure monitoring**
- **Table: S**ummary of **Brain Trauma Foundation** guidelines for the management of intracranial pressure monitoring in severe traumatic brain injury

Topic	Level of recommendation	Summary
ICP monitoring	II	ICP should be monitored in all salvageable patients with sever TBI (GCS 3-8) and an abnormal CT scan
Mannitol	II	Mannitol is effective for control of raised ICP at doses of 0.5 g/kg to 1 g/kg body weight
Mannitol	III	Mannitol use should be restricted to patients with signs of herniation or neurological deterioration attributable to an intracranial cause

Current concepts

Cerebral perfusion pressure

- Indirect marker of cerebral blood flow and perfusion
- Low CPP = maximal cerebro-vascular dilatation
- High CPP = less CV dilatation but risk of cerebral edema and lung injury

[Nordstrom CH. CPP between 50 and 60 mm Hg is beneficial in TBI. Neurosurgery 2006]

Current concepts:

Table: Summary of BTF guidelines for the management of CPP

Topic	Level of recommendation	Summary
Upper threshold of CPP	II	Aggressive intervention to maintain CPP > 70 mmHg should be avoided
CPP target	III	Target CPP 50 – 70 mm Hg, however patients with intact auto regulation may tolerate higher CPP values.
Lower threshold of CPP	III	CPP below 50 mmHg should be avoided
Ancillary monitoring of cerebral parameters	III	Blood flow oxygenation or cerebral metabolism may facilitate CPP management

Current concepts:

- **Hyperventilation:**
  - **C**auses hypocapnia induced cerebral vasoconstriction
  - Lowers ICP by reducing CBF
  - The BTF guidelines discourage prophylactic hyperventilation ($PaCO_2$ <25 mm Hg)
  - As a level III recommendation HVT should be used only as a temporizing measure for reducing elevated ICP
  - If HVT is to be used for control of ICP then concomitant SpO_2 or brain tissue oxygen tension to be monitored.

Current concepts:

- **Hyperventilation :**
- Table 5: Summary of BTF guidelines for use of hyperventilation in severe TBI

Topic	Level of recommendation	Summary
Prophylactic hyperventilation	II	Prophylactic hyperventilation (PaCO2 of 25 mm Hg or less) is not recommended
Hyperventilation for ICP control	III	Hyperventilation is recommended as a temporizing measure for the reduction of elevated ICPs
Timing of use	III	Hyperventilation should be avoided during the first 24 h after injury
Measurement of oxygen delivery	III	Jugular venous oxygen saturation or brain tissue oxygen tension are recommended to monitor oxygen delivery

Current concepts

- **Body temperature and hypothermia:**
  - Target temperature for cooling is not clear.
  - Temperature < 30 º should be avoided
    - Increased risk of cardiac arrhythmias
    - Coagulation abnormalities
    - Infection

Current concepts: Hypothermia:

- **Table : Summary of BTF guidelines for the management of hypothermia in severe TBI**

Topic	Level of recommendation	Summary
Prophylactic hypothermia vs. normothermia: mortality	III	Prophylactic hypothermia is not significantly associated with decreased mortality compared with normothermic controls. Maintenance of target temparature for > 48 h may be associated with a greater decrease in risk
Prophylactic hypothermia versus normothrrmia : GOS	III	Prophylactic hypothermia is associated with higher GOS scores than normothermia

Current concepts:

- Sedation

- Agents used :
  - Propofol
  - Midazolam
  - Dexmedetomidine
  - Barbiturates

Current concepts:

- Propofol:
  - Rapid acting sedative-hypnotic
  - Double blind RCT comparing morphine and propofol
  - There was no difference in GOS but ICP was lower in propofol group on day 3.
    [Kelly et al, J Neurosurgery, 1999]
  - S/E: Propofol infusion syndrome: prolonged high dosage
    - Lactic acidosis
    - Rhabdomyolysis
    - Cardio-vascular collapse

Current concepts

- Midazolam:
  - Favored because of short half life (45 min.)
  - Minimal cardiovascular effects
- Dexemedetomidine:
  - New α-2 agonist
  - Sedation without respiratory depression facilitating neurological examinations

[Aryan HE et al, brain injury . 2006]
[Tang JF et al, Neurocritic. Care. 2010]

Current concepts

- **Sedation**:
- **Barbiturates**
  - MOA not known exactly.
  - ? Decrease both CBF and CMRO2
  - Considered as a second tier therapy for refractory ICP
  - A/W significant risk of severe hypotension, pneumonia and DVT.
  - BTF guidelines discourage prophylactic administration of barbiturates to induce burst suppression on EEG.

Current concepts

- Table 6: Summary of BTF guidelines on use of anesthesia and sedatives in severe TBI

Topic	Level of recommendation	Summary
Prophylactic administration of barbiturates	II	Not recommended for burst suppression prophylactically
Administration of high dose barbiturates	II	High dose is recommended to control elevated ICP s refractory to medical and surgical treatment
Administration of propofol	II	Propofol is recommended for the control of ICP. High dose can be a/w significant morbidity and is not recommended for improvement in mortality of 6 m outcome.

Hyperosmolar therapy

- **Mannitol**
  - Osmotic agent
  - Effects ICP, CBF, CPP and brain metabolism
  - Free radical scavenger
  - Reduces ICP within 30 minutes, last 6-8 hours
  - Volume expansion, reduces hypotension
  - BTF level II recommendation for short-term reduction of ICP
  - Dose:0.25 g/kg to 1 g/kg

Hyperosmolar therapy

- Hypertonic Saline
  - Improves CPP and brain tissue O_2 levels
  - Decreased ICP by 35% (8-10 mm HG)
  - CPP increased by 14%
  - MAP remained stable
  - Greatest benefit in those with higher ICP and lower CPP
  - Repeated doses were not associated with rebound, hypovolemia or HTN
  - 30 ml of 23.4% over 15 minutes

Hyperosmolar therapy

- Hypertonic saline
  - Increases intra vascular volume and shifts fluid away from uninjured brain
  - Increases volume of contused brain
  - Decreases volume of non contused brain
  - Effects are regional and blood brain barrier dependent

- Hyperosmolar therapy
  - Hypertonic saline
    - recent studies:
    - use of 23.4% hypertonic saline in 22 patients of severe TBI was associated with greater reduction in ICP than mannitol and no adverse events were identified

[Kerwin AJ et al. a pilot study. J. trauma. 2009]

Hyperosmolar therapy

- Hypertonic saline
  - Recent studies
  - Pre hospital administration of 250 ml of 7.5% saline : no benefits over administration of RL w.r.t GOS and survival rates at 6 months

    [cooper DJ et al. JAMA. 2004]
  - Administration of hypertonic saline alone (7.5 %) or in combination with dextran : no benefit over administration of normal saline (0.9%)

    [vanbelle G, et al. NCT00316004]

Hyperosmolar therapy

- Hypertonic saline
  - Hypertonic saline as a second tier therapy in patients refractory to mannitol was associated with increase in brain tissue O2 tension, higher CPPs and lower ICPs.

[Oddo M et al, J Neurol Neurosurgery psychiatry.2009]

Adjuncts to ICP Monitoring

- Brain tissue oxygen monitoring
  - Hypoxia is associated with worse outcome in TBI
  - Brain tissue oxygen monitoring is more accurate than jugular bulb oximetry in measuring regional and local brain tissue oxygenation.

[Zhi DS et al . Surg neurol.1999
Gupta AK et at. Anesth analg. 1999]

Adjuncts to ICP Monitoring

- Brain tissue oxygen monitoring
  - Monitored with LICOX probe placed on least injured side
  - Increased mortality:
    - longer duration PbtO2 <15 mm Hg
    - > 30 min of PbtO2 < 10 mmHg
    - even 1 episode of PbtO2 <6 mm Hg
  - Goal in TBI: maintain PbtO2 > 25 mm Hg.
  - No randomized studies.

Adjuncts to ICP Monitoring

- Jugular venous saturation or brain tissue oxygen monitoring measures cerebral oxygenation.
- Jugular venous oxygen monitoring.
- Is global in nature and insensitive to focal pathology.
- Normal SjVO2 :≥ 60%.
- Desaturations to < 50% suggests ischemia.

Adjuncts to ICP Monitoring

- BTF guidelines :

  Level III recommendation for threshold of jugular venous saturation (< 50 %) and brain tissue oxygen tension (< 15 mmHg)

Cerebral Microdialysis

- Measuring the partial pressure of oxygen of brain parenchyma and metabolites using microdialysis
- Electrode in vulnerable brain region measures O2 concentration
- Measures also local brain metabolism
- Compounds assayed include:
  - Lactate
  - Pyruvate
  - Lactate/pyruvate ratio
  - Glucose, glutamate, urea and electrolytes
- Lactate levels increase during SjVO2 desaturation
- Decreased extracellular glucose associated with higher mortality

Transfusion

- Traditionally Hct > 30 % should be maintained in TBI.

Why ?

- Reduced oxygen supply may lead to secondary injury.

But

- Transfusion is associated with poor outcomes

Transfusion:

- Blood transfusions are associated with significantly higher mortality and more complications.

- Patients with TBI should not have different threshold than other intensive care patients.(TRICC TRIAL)

- Hébert PC et al, a Multicentre, randomized, controlled clinical trial of transfusion requirements in critical care (TRICC trial). Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med. 1999
- Warner MA Transfusions and long-term functional outcomes in traumatic brain injury. J Neurosurg. 2010 Sep

Transfusion:

- Conclusion:
- Anemia in TBI is associated with worse outcomes but the correction of anaemia with transfusion is of uncertain benefit and potentially harmful

[Salim et al, J Am Coll Surg. 2008.][Jeremitsky E, J Trauma. 2003]

Glycemic control

- Hyperglycemia is associated with poor outcomes:
  - Secondary ischemia
  - Blood brain barrier injury
  - Brain tissue acidosis
- Intensive insulin therapy (BS between 80 and 100 mg/dl).
  - Low rates of ARF
  - Low blood stream infections
  - Lower critical illness polyneuropathy [van den Berghe G , 2001]
  - Protects endothelium [langouche L,2005]
  - Decreases cortisol response [vanhorebeek I, 2006]
  - Exerts anti inflammatory effects [Hansen TK,2003]

Glycemic control:

- Meier et al , critical care. 2008:
  - Higher incidence of
    - raised ICP
    - Hypoglycemic episodes
    - UTI
    - Bacteremia
    - Impaired cerebral metabolism
- Bilotta F et al , Neurocritc Care. 2008: RCT
- Coester A et al, J Trauma . 2010: RCT
  - Intensive insulin therapy (80-120 mg/dl) Vs conventional therapy (<220 mg//dl).
  - Hypoglycemic episodes were significantly higher BUT duration of ICU stay was shorter.
  - No difference in GOS scores or mortality at 6 months

Glycemic control:

Conclusion:

Follow the middle way “ less strict insulin”

- Providing benefits of hyperglycemic control while avoiding the risks of hypoglycemic episodes.

Decompressive craniectomy History

- Decompressive craniectomy first described by Annandale in 1894.

- Cushing reported subtemporal and sub occipital decompression to alleviate high ICP in 1905

CUSHING, H. (1905). The establishment of cerebral hernia as a decompressive measure for inaccessible brain tumor ; with the description of intramuscular methods of making the bone defect in temporal and occipital regions. Surg. Gynecol. Obstet. **1, 297–314.**

Decompressive craniectomy

Recently used for

- High ICP or
- As a primary procedure in the evacuation of acute subdural hematoma when the surgeon felt that the brain was tight and oedematous
- These procedures allow the brain to expand and consequently facilitate the control of high ICP

Types of surgical decompression

- Two types:

1. Prophylactic decompression or ‘primary decompressive craniectomy

2. Therapeutic decompression or ‘secondary decompressive craniectomy’

Potential adverse effects

- Increased brain oedema
  - Brain herniates rapidly through the defect resulting in a tense flap despite lower ICP
- Subdural collections
- Hydrocephalus
- brain infarctions
- Meningitis
- Cerebral abscess

Evidence

- Only one RCT performed
  - Taylor et al
- Small study, paediatric population
- Interim analysis showed clear efficacy in reducing death and disability from DC
- Two (14%) of the 14 children in the control group were normal or had a mild disability after 6 months, compared with 7 (54%) of the 13 children in the decompression group

Taylor A, ButtW, Rosenfeld J, Shann F, DitchfieldM, Lewis E, et al. A randomized trial of very early decompressive craniectomy in children with traumatic brain injury and sustained intracranial hypertension. *Child's Nervous System* 2001;**17(3):154–162.**

Conclusions

A Cochrane review concluded that there is no evidence to support the routine use of DC in TBI for the treatment of medically refractory elevated ICP

Conclusions

- Decompressive Craniectomy appears to produce a significant decrease in ICP
- It remains a high risk procedure
- Still used mainly as a salvage procedure when other options have failed
- Further evidence is awaited

Clinical trials

- Citicoline
- Progesterone
- Cyclosporine
- Decompressive craniectomy

Clinical trials

- Trials failed to show any benefits:
  - Glutamate antagonists (cerestat, selfotel)
  - Free radical scavengers (tirilizad, PEG – orgatine)
  - Decompressive craniectomy

Clinical trials

- Citicoline
  - Intermediary in the biosynthesis of phosphatidylcholine.
  - MOA: improved phosphatidylcholine synthesis, membrane stabilization and repair.
  - Studies in dementia, stroke and TBI show early promise.
  - Cochrane meta-analysis (2005)reported improvement in memory and behavior.

Clinical trials

- Citicoline
- Evidence of improvement in post concussive symptoms [Levin, J neurol Sci, 1991]

- RCTs in French literature suggest faster recovery from focal motor deficits
- Ongoing Trial.
  - COBRIT: citicoline brain injury trial , 2009, J Neurotrauma

Clinical trials

- Progesterone
  - Progesterone receptor widely distributed in the
    - Forebrain,
    - Limbic sysytem, and
    - Hypothalamus
  - Found to provide neuroprotective effects by :
    - Decreasing edema
    - Increasing blood brain barrier protection, and
    - Limiting cellular necrosis and apoptosis
  - RCTs : 5 days of progesterone decreased mortality rates and significantly improved 30- day functional outcome.

Clinical trials

- Progesterone

- Ongoing Trial:

  Phase III trial launched in the U.S in May 2010, **Synapse** [study of the neuroprotective activity of progesterone in severe traumatic brain injuries]

Clinical trials

- Cyclosporine
- Widely used immunosuppressive drug
- Stabilizes the mitochondrial membrane and attenuates axonal disruption.[Signoretti S et al, J neurotrauma. 2004]
- 2 phase II trials showed improvement in CPP and cerebral metabolism but no difference in GOS scores at 3 and 6 months.
- Phase III trial : awaits funding

Clinical trials

- **Decompressive craniectomy**
- **TABLE** . Summary of phase III trial for decompressive Craniectomy in Severe TBI

trial	Methodology	Projected Study Size	Comparisons	Primary
RESCUEicp	Multicentre RCT	6oo	decompressive craniectomy(<6 hrs of randomization) Vs. standard icu care including ventriculostomy	GOS at discharge and GOS-extended at 6m

Message

- The recent trends in the management are more focused on the electro-physiological monitoring of the traumatized brain

- The prognosis in TBI especially severe TBI has remarkably improved owing to newer modalities of treatment and monitoring.

But

the degree of reliability and validity of these tests and treatments still needs further evaluation.

THANK YOU