

HYPERBARIC OXYGEN BRAIN INJURY TREATMENT TRIAL: CLINICAL STANDARD GUIDELINES (CSG)

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OBTAINING AN ACCURATE ENROLLMENT GLASGOW COMA SCALE (GCS) SCALE

- The most accurate GCS is post resuscitation (off sedation) just prior to enrollment
- The degree of change in neurologic status from either pre-hospital or first hospital to enrollment is highly significant ($p < 0.001$)
- Patients with lower GCS scores and compromised pupil reactivity have a greater range of improvement over time, while patients less compromised have a greater range for deterioration

Marmarou et al.; J Neurotrauma 24:270-280, 2007

OBTAINING AN ACCURATE ENROLLMENT GCS SCORE

- Short-acting sedative and analgesic agents are recommended
- Propofol is drug of choice as it allows rapid titration and short half life

EVALUATION

- GCS
 - Eye opening
 - Best motor response
 - Verbal response
- Pupillary size, equality, reaction to light
- Symmetry of motor strength

GCS BEST MOTOR RESPONSE

- Follow commands 6
- Localizes to pain 5
- Withdrawal to pain 4
- Flexion posturing (decorticate) 3
- Extensor posturing (decerebrate) 2
- No response 1

IMPACT SCORE

- Age
- Motor score
- Pupillary reactivity
- CT Marshall score
- The IMPACT score will be used in the predictive model of GOS-E outcome at 6 months

CLINICAL STANDARD GUIDELINES

- CSGs formulated by a multidisciplinary standardization team
- Treatment variability among sites can undermine a RCT
- The guidelines do not preclude clinical judgement

PHYSIOLOGIC GOALS

Pulse Ox $\geq 90\%$	ICP < 22 mmHg	Physiologic Na+ 135-145*
PaO ₂ ≥ 100 mmHg	PbtO ₂ ≥ 20 mmHg	INR ≤ 1.4
PaCO ₂ 40-45 mmHg	CPP ≥ 60 mmHg	PLTS $\geq 75 \times 10^3/\text{mm}^3$
MAP ≥ 70 mmHg	Temp 36.0-37.9° C	Hgb ≥ 8 gm/dl
SBP > 100 mmHg if 50 to 69 years old or > 110 mmHg if 15 to 49 or over 70 years old	Glucose 80-180 mg/dL	pH 7.35-7.45

**Hypertonic saline therapy: Na+ range: 145 mmol/L (minimum) to 160 mmol/L (maximum)*

OXYGENATION / VENTILATION

- End tidal CO₂ (ETCO₂) should be monitored preclinical, ED, and during transport to and from HBO₂
- Hyperventilation should be strictly avoided during resuscitation because it increases ischemia
- Therapeutic hyperventilation may be necessary for brief periods for refractory ICP, herniation

BLOOD PRESSURE / VOLUME RESUSCITATION

- Normal saline is initially recommended to maintain euvoemia
- Blood transfusion as needed ($\text{Hgb} \geq 8 \text{ gm/dl}$)
- Vasopressors may be required to maintain $\text{SBP} > 100\text{-}110 \text{ mmHg}$ and/or to maintain $\text{CPP} > 60 \text{ mmHg}$

INTRACRANIAL PRESSURE MONITORING

- A ventriculostomy is the preferred monitoring device for the HOBIT Trial
- The ventriculostomy is zeroed at the tragus of the ear (foramen of Monroe)
- Hypertonic saline (HTS) or mannitol should be used prior to ICP monitoring in patients undergoing uncal herniation or neurologic deterioration
- Intracranial hypertension is defined as ≥ 22 mmHg
- Despite this being National Brain Injury Foundation Guidelines, 22 mmHg is high intraventricular pressure (equals 286 mm H₂O)

ADVANTAGES OF HTS COMPARED TO MANNITOL AS AN OSMOTIC AGENT

- HTS has a more prolonged effect
- HTS expands vascular volume utilizing small volumes while mannitol causes a diuresis and volume/electrolyte depletion with risk of hypotension
- HTS administration results in decreased ICP, increased MAP, increased CPP, with improved $P_{bt}O_2$

Rockswold et al, Neurosurg 65:1035-1042, 2009

ADVANTAGES OF HTS COMPARED TO MANNITOL AS AN OSMOTIC AGENT

- HTS use can be continued despite elevated Na (~ 160) and serum osmolarities (340)
- Mannitol use has to be restricted to serum mOsm > 320 or acute renal failure can result
- HTS has less “rebound” due to a higher reflection coefficient (1.0 vs 0.9)

Rockswold et al, Neurosurg 65:1035-1042, 2009

MANAGEMENT OF INCREASED INTRACRANIAL PRESSURE

GENERAL RECOMMENDATIONS

- Adjust cervical collar placement if applicable
- Repeat CT
 - A repeat CT scan of the brain should be done at 6-12 hours post admission to rule out the evolution or development of a surgical mass or unexpected intracranial lesion and to check for the correct placement of monitors
- Craniotomy for surgical lesions
 - To be discussed later in presentation

TIER I

- Head of patient's bed to be placed at ≥ 30 degrees
- Sedation and analgesia using recommended agents (propofol, fentanyl, and versed)
- Ventriculostomy – extraventricular drain; drain to 10 mmHg for ICP ≥ 22 mmHg sustained for ≥ 5 minutes
- Mannitol: 0.25-1.0 g/kg; IV bolus x 1 dose *OR*
- Hypertonic saline: 30 cc of 23.4% for 30 minutes x 1 dose
- Mild hyperventilation with a PCO_2 goal of 35-40 mmHg

Tier 1 completed within 30-60 minutes, if ICP ≥ 22 mmHg proceed to Tier 2

TIER 2

- HyperOsmolar Therapy

- Mannitol: Intermittent boluses of mannitol (0.25-1 gm/kg body weight) should be administered. The serum sodium and osmolality must be assessed frequently (every 6 hours) and additional doses should be held if the serum osmolality exceeds 320 mOsm/L.
- Hypertonic saline: Boluses of 30 cc of 23.4% over 30 minutes may be used. Serum sodium and osmolality must be assessed frequently (every 6 hours) and additional doses should be held if serum sodium exceeds 160 mEq/L.

TIER 2

- PCO₂ goal 30-35 mmHg, as long as brain hypoxia is not encountered
- Neuromuscular paralysis: Pharmacologic paralysis with a continuous infusion of a neuromuscular blocking agent should be employed if the above measures fail to adequately lower the ICP and restore CPP. Adequate sedation must be utilized if pharmacologic paralysis is employed.

Tier 2 completed within 30-60 minutes, if ICP \geq 22 mmHg proceed to Tier 3

TIER 3

(INCLUDES POTENTIAL SALVAGE THERAPIES)

- Decompressive hemi-craniectomy or bilateral craniectomy should only be performed if Tiers 1 and 2 are not sufficient. Procedure per site surgical protocol. This procedure is **NOT** a contraindication for HBO₂.
- Barbiturate or propofol (anesthesia dosage) coma: It should only be instituted if a test-dose of barbiturates or propofol results in a decrease in ICP. Hypotension is a frequent side effect of high dose therapy.

ANTISEIZURE PROPHYLAXIS

- TBI and HBO₂ can both cause seizures
- All HOBIT patients are intravenously loaded with phenytoin (Dilantin) or levetiracetam (Keppra) and therapeutic levels maintained for 7 days

SURGICAL MANAGEMENT OF TBI

- In general, mass lesions should be evacuated for the following or a combination of indications
 - Midline shift to > 5 mm, especially if the mass is in the temporal lobe
 - Deterioration in the GCS motor score of one level
 - ICP ≥ 22 mmHg
 - Compressed/absent circumcephalic cisterns
 - Clinical judgement is required