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**P: In patients with traumatic brain injury**  
**I: Does the use of hypertonic fluid**  
**C: Compared to mannitol or isotonic fluid**  
**O: Result in better patient outcome**

| Study  | Patient Group   | Study Type                                       | Key Outcomes  | Key Results   | Limitations   |
|--|---|--|---|---|---|
| Vialet, R.<br>Isovolume hypertonic solutes in the treatment of refractory posttraumatic intracranial hypertension.<br><u>Crit Care Med</u> 2003; 31(6)<br>France | 20 patients<br><br>2 groups: HSS v. mannitol<br><br>Patients with persistent coma requiring ICP monitoring and with ICP resistant to standard therapy<br><br>If ICP >25 for >= 5 minutes, patients received 2 ml/kg of 20% mannitol (2.3 mOsm/kg) or 7.5% HSS (4.8 mOsm/kg) over 20 minutes | Prospective<br><br>Randomized<br><br>Non-blinded | Mortality<br><br>Neurological outcome<br><br>Episodes of ↑ICP<br><br>Treatment failures- inability to ↑CPP > 70 or ↓ICP < 35 with 2 infusions | Mortality (5 mannitol, 4 HSS) and neurological outcome did not differ<br><br>Mannitol group had more episodes of ↑ICP per day (p<0.02)<br><br>Mannitol group had more treatment failures (p<0.01) | Limited study size<br><br>Osmotherapy not used as first line    |
| Francony, G.<br>Equimolar doses of mannitol and hypertonic saline in the treatment of increased ICP.<br><u>Crit Care Med</u> 2008; 36(3)<br>France               | 20 patients (17 TBI, 3 CVA)<br><br>If ICP >20 for >= 10 minutes one equimolar (255 mOsm) dose of 20% mannitol (231 ml) or 7.45% HSS (100 ml) given over 20 minutes<br><br>ICP monitored intra-parenchymally   | RCT  | ICP<br><br>Cerebral oxygenation   | ICP reduced by 45% in mannitol group and 35% in HSS group<br><br>ICP reductions lasted >= 2 hours<br><br>No changes in cerebral oxygenation   | Only pts with stable vital signs and adequate CPP were included |
| Ware, M.<br>Effects of 23.4% sodium  | 13 TBI patients<br><br>When ICP > 20  | Retrospective chart review                       | ICP<br>CPP<br>MAP   | Significant ↓ICP both mannitol and HSS (p<0.001) but no   | Limited patient population                                      |

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|--|---|---|-----|---|---------------------------------|
| chloride solution in reducing ICP in patients with TBI: A preliminary study. <u>Neurosurg</u> 2005; 57(4) USA  | for 5 minutes: CSF drained then mannitol administered<br><br>If mannitol ineffective 30mL 23.4% NaCl (8008 mOsm/L) given over 2 minutes   |   |     | significant difference between agents<br><br>Duration of effect longer for HSS than mannitol (p<0.02)                 | HSS administered after mannitol |
| Shackford S. Hypertonic saline resuscitation of patients with head injury: A prospective, randomized clinical trial. <u>J Trauma</u> 1998; 44(1) USA | 34 patients<br><br>2 groups: HSS v. LR<br><br>Pts received either 1.6% saline or LR bolus for hemodynamic instability in the ER, OR and 1 <sup>st</sup> 5 ICU days<br>Endpoint- SBP >90 and UOP | Prospective<br><br>RCT<br><br>2 hospitals | ICP | ICP not significantly different between 2 groups<br><br>HSS group required more interventions to control ICP (p<0.01) | Sample size                     |

**Clinical Bottom Line:** While evidence suggests that HSS lowers ICP as well as or better than mannitol, there is no agreement as to the type and amount of HSS that should be used. Our focus in the ED would be on the patient with TBI and hemodynamic instability who needs resuscitative fluids to increase MAP with minimal detriment to ICP. There does not appear to be any harm in using HSS; however the type and amount need to be better characterized.

CPP = MAP – ICP

MAP between 60 and 110 allows cerebral autoregulation

TBI affects nearly 1.5 million patients per year.

Many of these patients have cerebral edema or space occupying lesions that increase ICP.

Elevation of ICP plays a major role in worsening Neurologic status by impairing brain perfusion.

Conventional treatment of ICP includes: osmotic therapy, hyperventilation, head elevation, barbiturates.

Mannitol has been 1<sup>st</sup> line agent for years to reduce ICP

- Recent Cochrane review demonstrated unclear effectiveness of mannitol on mortality.
- Repeated administrations of mannitol introduce risk of renal failure and accumulation of mannitol in brain
- Also is a systemic diuretic

HSS thought to work by

- reducing volume of cerebral cells and decreasing ICP- however it is not known if this happens preferentially in injured or non-injured regions
- vascular expansion, causing increase in MAP, which triggers cerebral vasospasm, lowering ICP

Limited number of studies investigated HSS v. mannitol in ability to reduce ICP.

- Infusions are not all equimolar
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