Section: Anaesthesiology

Original Research Article

COMPARATIVE STUDY OF THE EFFICACY OF 20% MANNITOL VS 3% SALINE IN PATIENTS WITH TRAUMATIC BRAIN INJURY UNDERGOING EMERGENCY CRANIOTOMY

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ABSTRACT

Background: Traumatic brain injury commonly causes early cerebral oedema and raised intracranial pressure (ICP), requiring rapid osmotic therapy during emergency craniotomy. Hypertonic saline (HTS) and mannitol are standard options, yet their intraoperative physiological effects differ. This study aimed to compare the efficacy of 20% mannitol and 3% HTS in traumatic brain injury patients undergoing emergency craniotomy. **Materials and Methods:** A prospective randomised study was conducted at Government Vellore Medical College and Hospital on sixty adults undergoing emergency craniotomy. Adults aged 18–60 years with traumatic brain injury were included, while those with hemodynamic instability or major organ dysfunction were excluded. Patients received either 3% HTS or 20% mannitol, and perioperative hemodynamics, electrolytes, lactate, glucose, fluid balance, urine output, vasopressor use, and brain relaxation were recorded. The primary outcome was intraoperative brain relaxation, with secondary measures including hemodynamics, electrolytes, lactate, glucose, fluid balance, and vasopressor requirement. Group comparisons were performed using chi-square tests and unpaired t-tests, with $p<0.05$ considered statistically significant. **Result:** Heart rate increased with mannitol at 45 and 60 minutes (91.57 vs 85.30 bpm; 91.30 vs 84.20 bpm). Systolic pressure was lower at the same intervals with mannitol (123.33 vs 128.33 mmHg; 121.33 vs 128.63 mmHg). Mannitol also showed reduced diastolic and mean arterial pressures at several points. Total fluid requirement was higher with mannitol (1818.9 vs 1373.1 mL), as was urine output (1413.3 vs 1130 mL). Vasopressors were used more often in the mannitol group (20% vs 10%). HTS raised serum sodium and maintained potassium levels, while mannitol caused sodium decline, potassium rise, and higher lactate. Brain relaxation was better with hypertonic saline, with optimal scores in 43.3% compared with 20% in the mannitol group. **Conclusion:** HTS produced steadier physiology, better electrolyte control, and improved operative brain relaxation compared with mannitol. These findings support its use when maintaining perfusion and surgical conditions are essential during emergency craniotomy.

INTRODUCTION

Traumatic brain injury remains a major global cause of morbidity and mortality. Management focuses on preventing secondary injury, preserving cerebral perfusion pressure, and maintaining adequate cerebral oxygenation. These priorities guide acute care because cerebral oedema appears early after injury and increases intracranial pressure (ICP). Elevated ICP limits cerebral blood flow and contributes to poor neurological outcomes. Mannitol is widely used for osmotic reduction of ICP, and its rapid onset makes it suitable for emergency neurosurgical settings. Hypertonic saline (HTS) was first described by Weed and McKibben as an alternative osmotic agent that alters brain volume by shifting water from the intracellular to the intravascular space. Both agents are now integrated into neurosurgical practice, and their comparative effects remain an active clinical and research focus.[1-3] HTS is used in concentrations ranging from

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3% to 23.4%, with typical doses between 1 and 4 mL/kg.[4]

The osmotic gradient determines therapeutic effectiveness, and inadequate concentration limits ICP reduction. Studies from severe head injury does not clearly support one hyperosmolar therapy over another.[5,6] Several meta-analyses report that HTS produces a higher reduction in ICP than mannitol at multiple time intervals after administration.[1,2] Paediatric studies show class II evidence suggesting 3% HTS for intracranial hypertension, supporting reliable sodium-driven osmotic shifts that increase serum tonicity.[6] HTS produces less diuresis than mannitol, which may help maintain circulating volume during emergency craniotomy. Its relative intravascular expansion may contribute to more stable intraoperative hemodynamic.[3,7] Mannitol induces brisk diuresis, and this can reduce preload and increase vasopressor requirements, particularly in patients with borderline hemodynamic profiles.

Current guidelines for severe TBI report insufficient comparative evidence to recommend a specific hyperosmolar agent. The guideline position highlights the need for studies evaluating intraoperative variables linked to surgical conditions and systemic stability. The differences in electrolyte changes, vasopressor use, or intraoperative brain relaxation in adult emergency neurosurgical populations are in limited data.[8-10] Brain relaxation is a practical surgical endpoint, suggesting tissue turgor and intracranial compliance at dural opening. HTS may improve this parameter through osmotic dehydration of neural tissue and secondary microcirculatory effects. Mannitol also reduces brain water content, but its hemodynamic impact may affect overall effectiveness during prolonged procedures.

Emergency craniotomy requires agents that lower ICP while preserving perfusion pressure. Monitoring serum sodium, potassium, glucose, lactate, urine output, and hemodynamic changes helps assess the physiological response to each solution. These perioperative variables give understanding into the differential mechanisms and clinical profiles of 20% mannitol and 3% HTS in traumatic brain injury. Therefore, this study aimed to compare the efficacy of 20% mannitol and 3% HTS in traumatic brain injury patients undergoing emergency craniotomy.

MATERIALS AND METHODS

This prospective, randomised study was conducted in the Department of Anaesthesiology on 60 patients at Government Vellore Medical College and Hospital between April 2023 and August 2024. The study was performed after obtaining approval from the institutional ethics committee (Ref: No.VMC/PI/00013/2023), and informed consent was obtained from all patients.

Sample size calculation: Sample size was determined using the difference in expected proportions between mannitol and hypertonic saline groups, with $\alpha = 0.05$ and power = 80%. Proportion estimates (p_1 and p_2) were taken from prior studies evaluating osmotherapy response in TBI patients. The number of subjects required in each group was obtained using the standard formula: $n = (Z\alpha/2 + Z\beta)^2 \times [p_1 (1 - p_1) + p_2 (1 - p_2)] / (p_1 - p_2)^2$. The study included a total sample size of 60 participants, with equal allocation to the two treatment groups. The sample size was calculated from the expected proportion of subjects receiving 20% mannitol and the proportion receiving 3% hypertonic saline.

Inclusion and exclusion criteria

Adults aged 18–60 years with head injury who were scheduled for emergency craniotomy and classified as ASA I or ASA II with a Glasgow Coma Scale score >10 were included. Patients aged <18 years or >60 years, had hemodynamic instability, or had significant end-organ disease such as congestive cardiac failure, chronic kidney disease, or peripheral vascular disease were excluded.

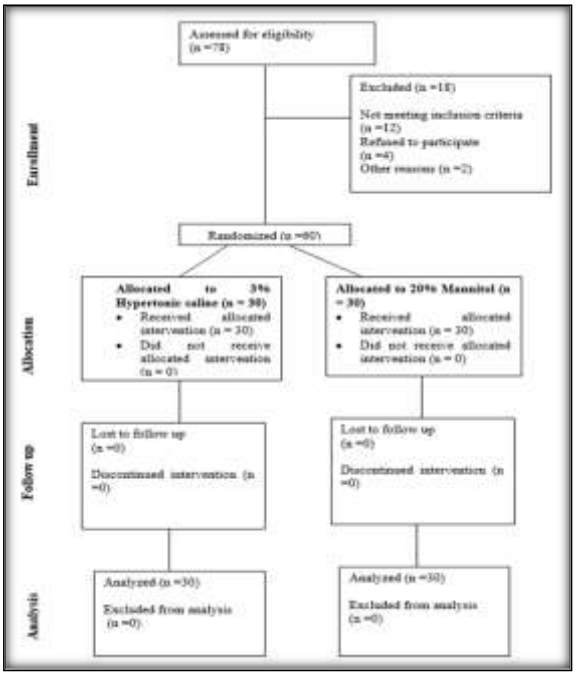

Figure 1: Consort diagram

Methods: Participants were recruited consecutively based on eligibility. Randomisation was performed using a computer-generated sequence, and allocation was concealed from both the anaesthetist and the neurosurgeon. Sixty patients undergoing emergency craniotomy received general anaesthesia and were assigned to mannitol (n = 30) or HTS (n = 30). After induction, the assigned study drug (20% mannitol or 3% hypertonic saline) was infused and continued for up to 12 hours as per protocol. Hemodynamic variables, serum electrolytes, lactate, glucose, and intraoperative volume status were measured at fixed intervals from induction to 120 minutes, then every 30 minutes postoperatively until recovery; samples were drawn through present arterial or venous lines. Electrolytes, glucose, and lactate were analysed using

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the hospital central laboratory auto-analyzer. Invasive arterial lines were used for continuous blood pressure monitoring. Brain relaxation was scored at dural opening on a 4-point scale ranging from a relaxed brain to a bulging brain. The procedure followed institutional anaesthesia protocols, and both the attending anaesthetist and the neurosurgeon were blinded to group allocation. Recovery time was recorded from discontinuation of anaesthesia to full neurologic responsiveness.

The primary outcome was intraoperative brain relaxation assessed using a validated 4-point scale. Secondary outcomes included changes in hemodynamic variables, serum sodium, potassium, lactate, glucose, urine output, and vasopressor requirement. Hypotension was defined as MAP <65 mmHg; hypernatremia as serum sodium >145 mmol/L.

Statistical analysis: Data were analysed using SPSS version 26.0. Data were presented as means and standard deviations for continuous variables and as percentages for categorical variables. The chi-square test or Fisher's exact test was used to find out the association between categorical variables. An unpaired t-test was done to compare the two group means; $p<0.05$ was considered significant. Results were reported with corresponding p-values, and 95% confidence intervals were generated where applicable. No imputation was used for missing data.

RESULTS

A total of 60 patients were analysed, with comparable demographic and baseline clinical profiles between the HTS and mannitol groups. Females were 20% vs. 23.3%, and males 80% vs. 76.7% in the HTS and mannitol groups, respectively. ASA I was more common in the HTS group (66.7% vs. 40%), whereas ASA II occurred more in the mannitol group (33.3% vs. 60%). Preoperative oedema was present in 86.7% vs. 90%, and midline shift in 23.3% vs. 16.7% [Table 1]. Clinical symptoms including headache, blurred vision, nausea/vomiting, drowsiness, altered consciousness, and ENT bleeding were similar between groups [Table 1].

Table 1: Baseline demographic and clinical characteristics of the study groups

Parameter		Hypertonic saline	Mannitol	P value
Age (years)		38.9 ± 6.85	42.53 ± 8.09	0.23
Gender	Female	6 (20%)	7 (23.3%)	0.992
	Male	24 (80%)	23 (76.7%)	
BMI (kg/m²)		29.59 ± 3.20	29.78 ± 3.11	0.816
ASA I		20 (66.7%)	12 (40%)	0.069
ASA II		10 (33.3%)	18 (60%)	
Preoperative oedema	Yes	26 (86.7%)	27 (90%)	0.983
	No	4 (13.3%)	3 (10%)	
Preoperative midline shift	Yes	7 (23.3%)	5 (16.7%)	0.748
	No	23 (76.7%)	25 (83.3%)	
Headache		16 (56.6%)	17 (53.3%)	0.832
Blurred vision		14 (53.3%)	16 (43.3%)	0.732
Nausea/Vomiting		12 (43.3%)	13 (46.6%)	0.583
Drowsiness		14 (46.6%)	14 (40%)	0.632
Altered consciousness		11 (40%)	12 (26.6%)	0.263
ENT bleed		7 (26.6%)	8 (28.3%)	0.532

Heart rate remained similar at baseline and early time points but was significantly higher in the mannitol group at 45 minutes (91.57 vs. 85.30 bpm, p = 0.001) and 60 minutes (91.30 vs. 84.20 bpm, p = 0.029) [Figure 2].

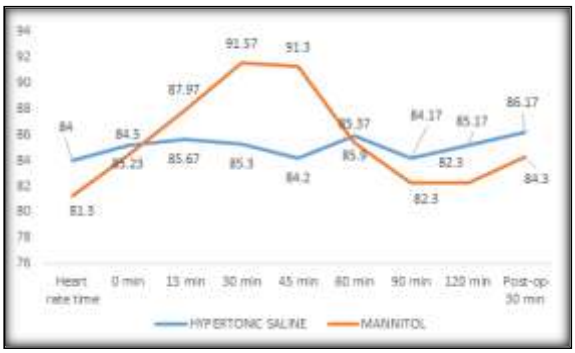

Figure 2: Intra and early postoperative heart rate between groups

Hemodynamic variables: Systolic blood pressure (SBP) was comparable at most intervals; however, SBP was significantly lower with mannitol at 45 minutes (123.33 vs. 128.33 mmHg, p = 0.031) and 60 minutes (121.33 vs. 128.63 mmHg, p = 0.039). Diastolic pressure and mean arterial pressure (MAP) followed a similar pattern, with mannitol showed significantly lower values at 45, 60, and 90 minutes ($p < 0.05$ for all) [Figure 3-5].

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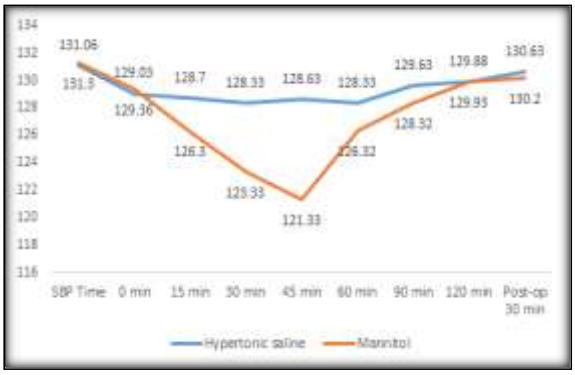

Figure 3: Intra and early postoperative SBP between groups

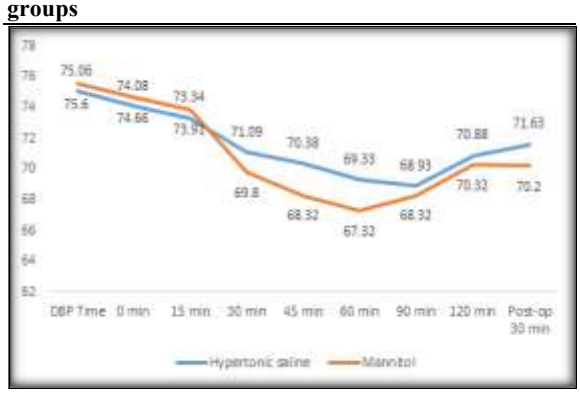

Figure 4: Intra and early postoperative diastolic blood pressure between groups

Intraoperative fluid balance and vasopressor use
The HTS group required vasopressors less (10% vs. 20%, p = 0.043). Total intraoperative fluid intake was significantly lower in the HTS group (1373.1 ± 155.4 mL vs. 1818.9 ± 106.8 mL, p = 0.001). Total urine output was also lower with HTS (1130 ± 155.9 mL vs. 1413.3 ± 108.6 mL, p = 0.001) [Table 2].

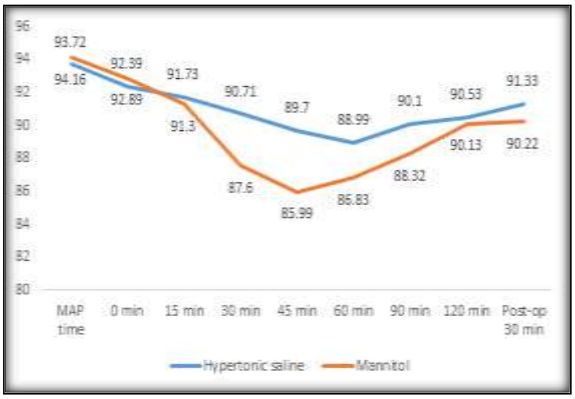

Figure 5: Intra and early postoperative MAP between groups

Table 2: Intraoperative hemodynamic support and fluid balance between groups

Parameter		Hypertonic saline	Mannitol	p value
Vasopressor need	Yes	3 (10%)	6 (20%)	0.043
	No	27 (90%)	24 (80%)	
Total fluid intake (mL)		1373.1 ± 155.4	1818.9 ± 106.8	0.001
Total urine output (mL)		1130 ± 155.9	1413.3 ± 108.6	0.001

Electrolytes, lactate, and glucose: Serum sodium increased significantly in the HTS group (135.7 → 140.9 mEq/L) but decreased in the mannitol group (136.1 → 133.8 mEq/L) (p = 0.001). Serum potassium decreased with HTS (4.63 → 4.245 mEq/L) and increased with mannitol (4.69 → 5.067 mEq/L) (p = 0.001). Serum lactate rose in both groups but significantly lower with HTS at 1 hour (2.763 vs. 2.926 mmol/L, p = 0.002). Blood glucose increased in both groups but did not differ significantly (p = 0.214) [Table 3].

Table 3: Perioperative changes in electrolytes, lactate, and blood glucose between groups

Parameter		Hypertonic saline	Mannitol
Serum sodium (mEq/L)	Baseline	135.7 ± 3.554017	136.1 ± 3.32545
	1 hour	140.9 ± 3.942256	133.8 ± 3.428079
Serum potassium (mEq/L)	Baseline	4.63 ± 0.614284	4.693333 ± 0.483474
	1 hour	4.245 ± 0.612562	5.067 ± 0.470239
Serum lactate (mmol/L)	Baseline	2.353333 ± 0.156983	2.533333 ± 0.257782
	1 hour	2.763333 ± 0.156433	3.02 ± 0.260415
Random blood sugar (mg/dL)	Baseline	131.0667 ± 8.362203	133.3333 ± 6.655738
	1 hour	139.7 ± 8.379573	142.6667 ± 6.645368

Brain relaxation score: Brain relaxation was significantly better in the HTS group. A score of 1 ("perfectly relaxed") was achieved in 43.3% of HTS patients compared with 20% in the mannitol group (p = 0.023). Higher (worse) relaxation scores (3–4) were more frequent with mannitol. The need for an additional hyperosmolar dose was similar between groups (20% vs. 30%, p = 0.278) [Table 4].

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Table 4: Intraoperative brain relaxation scores and need for additional hyperosmolar therapy

Parameter		Hypertonic saline	Mannitol	P value
Brain relaxation score	Score 1	13 (43.3%)	6 (20%)	0.023
	Score 2	10 (33.3%)	11 (36.7%)	
	Score 3	5 (16.7%)	8 (26.7%)	
	Score 4	2 (6.7%)	5 (16.7%)	
Need for an additional dose of a hyperosmolar agent	Yes	6 (20%)	9 (30%)	0.278
	No	24 (80%)	21 (70%)	

DISCUSSION

HTS provided more stable intraoperative physiology and better surgical conditions than mannitol during emergency craniotomy. Mannitol caused mid-procedure hypotension and greater osmotic diuresis, increasing fluid requirements and vasopressor use. HTS maintained more consistent hemodynamics with reduced urine output. Electrolyte changes favoured hypertonic saline, which preserved osmotic balance, while mannitol produced sodium decrease, potassium increase, and higher lactate, indicating greater metabolic stress. Brain relaxation was superior with hypertonic saline, yielding softer, more compliant operative fields.

Mannitol caused transient hemodynamic instability, producing a higher heart rate and lower blood pressure. Similarly, Shariat Moharari et al. found that systolic, diastolic, and MAP values were significantly lower with mannitol at 20–60 min (SBP 97.7 ± 12.9 vs 128.3 ± 31.0 mmHg; DBP 55.0 ± 9.3 vs 78.0 ± 18.7 mmHg; MAP 69.2 ± 12.2 vs 96.5 ± 27.0 mmHg; all p=0.001), while heart rate remained comparable (74.4 ± 8.0 vs 68.8 ± 13.1; p>0.05).[11] Ray et al. showed that heart rate was similar at baseline (82 ± 12 vs 84 ± 11; p>0.05) and at most intervals, with a small difference at 10 minutes (p=0.02). MAP remained comparable across the study, and the pattern showed an early increase in cardiovascular output followed by a decrease around 40–45 minutes.[12] These support our findings because mannitol consistently produces mid-procedure hypotension with a stable heart rate across comparable clinical settings.

The HTS group required vasopressors less often and received a smaller total fluid volume, with correspondingly lower urine output. Similarly, Singla et al. found that mannitol caused higher urine output at 1 h (450 ± 132 vs 222 ± 71 mL), 2 h (465 ± 218 vs 254 ± 63 mL), and 3 h (378 ± 115 vs 209 ± 62 mL; p ≤ 0.002).[13] Thongrong et al. found that urine output was higher with mannitol at 3.8 mL/kg/hr (IQR 2.4–4.5) compared with 2.3 mL/kg/hr (IQR 1.6–3.0) in the HTS group (p=0.003).[10] Therefore, other studies support our study that mannitol induces more osmotic diuresis, increasing fluid loss and vasopressor requirements.

HTS stabilised electrolytes, while mannitol produced sodium decline, potassium rise, and higher lactate levels. Similarly, Tsaousi et al. reported that HTS significantly increased serum sodium vs mannitol, producing higher post-infusion Na^+ levels ($P < 0.001$).[14] Dutta et al. found that Mannitol produced higher lactate (5.45 ± 1.61) than HTS (2.16 ± 1.45 mmol/L), indicating more metabolic stress.[15] Thus, HTS reliably maintains osmotic balance, whereas mannitol causes electrolyte shifts and heightened metabolic stress.

HTS yielded better brain relaxation, while mannitol showed more tension despite similar rescue dosing needs. Similarly, Wu et al. showed that HTS achieved better relaxation (58/43/21) than mannitol (39/42/35), a significant improvement (P = 0.02).16 Dostal et al. found that HTS showed superior relaxation (10/17/2/7) compared with mannitol (3/18/3/14, P = 0.0281).[17] Malik et al. reported that HTS improved relaxation (28/20/5/3) vs mannitol (17/21/11/9), showing superiority ($P < 0.05$).18 Therefore, HTS provides superior intraoperative brain relaxation compared with mannitol across similar surgical setting.

Strengths: This study benefited from a prospective randomised design, clearly defined eligibility criteria, and blinded surgical assessment, which help reduce selection and observer bias. Standardised anaesthesia protocols and consistent intraoperative monitoring strengthened the reliability of physiological measurements and brain relaxation scoring.

Limitations: The single-centre design, small sample, and limited blinding reduce generalisability. Short monitoring intervals missed delayed metabolic changes, and the absence of direct ICP measurements restricts interpretation. Differences in injury severity and surgical complexity may also have influenced outcomes. Future studies should include larger multicentre cohorts and incorporate direct intracranial pressure monitoring to improve external validity. Evaluating long-term neurological outcomes, equiosmolar dosing strategies, and dose–response relationships between hypertonic saline and mannitol will clarify optimal perioperative osmotherapy practices.

Clinical implications: HTS offers steadier physiology and better brain relaxation, strengthening its clinical role as a preferred osmotic agent in emergency craniotomy.

CONCLUSION

HTS offers more stable haemodynamics, better electrolyte control, and improved brain relaxation compared with mannitol during emergency craniotomy for traumatic brain injury. Its ability to limit diuresis and reduce vasopressor needs supports its usefulness in maintaining perfusion during

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surgery. The results indicate a more predictable physiological response with hypertonic saline, which may help create safer operative conditions. Larger multicentre studies with direct ICP monitoring and extended postoperative follow-up are needed to confirm these findings and refine dosing approaches.

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