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Research Article

# Safety of Hypertonic Saline and Mannitol with HES in Supratentorial Brain Tumor Surgeries: A Comparative Study on Coagulation Parameters

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**ABSTRACT**

**Background:** Managing intracranial pressure and brain swelling during supratentorial brain tumor surgery often involves hyperosmolar solutions like hypertonic saline and mannitol. However, using these solutions alongside hydroxyethyl starch (HES) could potentially affect blood clotting. This study aimed to compare the impact of hypertonic saline and mannitol, when combined with HES, on blood coagulation in patients undergoing these surgeries.

**Methods:** This clinical trial compared 20% mannitol and 3% hypertonic saline in patients undergoing brain tumor surgery. Patients were divided into two groups, each receiving one of these osmotic agents along with hydroxyethyl starch. The study focused on assessing any blood clotting abnormalities.

**Results:** The study included 30 patients (15 in each group). Their initial characteristics were similar. The study found no significant differences in blood coagulation tests between the groups. Additionally, osmolality levels and measures of brain tension were comparable in both groups. There were also no significant differences in intraoperative hemodynamic parameters.

**Conclusion:** Both hypertonic saline and mannitol, when used with HES, effectively manage intracranial pressure without significantly affecting blood clotting during supratentorial tumor surgeries. Further research is needed to refine fluid management strategies and minimize potential clotting risks in these procedures.

## Introduction

Fluid management in neurosurgery is a debated topic among anesthesiologists, as maintaining normovolemia and hemodynamic stability during intracranial surgeries is crucial to prevent complications. Mannitol and hypertonic saline (HTS) are commonly used in neurosurgery to reduce intracranial pressure by leveraging their hyperosmolarity and the blood-brain barrier's impermeability, facilitating water movement from brain tissue to blood vessels. Hypertonic saline and mannitol both decrease intracranial pressure through osmotic effects. However, hypertonic saline has benefits such as not inducing diuresis and preventing rebound edema [1-2].

HTS creates an osmotic gradient that draws water out of the brain, reducing intracranial pressure (ICP). Mannitol also reduces ICP but may lead to rebound effects due to osmotic compensation, making agent selection and dosing critical in treatment [3]. Several

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clinical trials have compared the efficacy of HTS and mannitol on brain relaxation and ICP in surgical and intensive care settings. Mannitol increases cerebral blood flow, whereas HTS provides faster onset and more sustained effects [3-4].

In stroke, HTS has a reflection coefficient of 1.0, better excluded from the brain than mannitol (0.9). It creates a steep osmotic gradient, shifting fluid from intracellular to intravascular compartments, thus reducing intracranial pressure and improving microcirculation [5].

Hyperosmolar therapy using HTS or mannitol is a primary treatment for intracranial hypertension. Proposed mechanisms of impaired hemostasis include dilutional coagulopathy, platelet dysfunction, diminished clot propagation, and clot strength, as well as impaired fibrin formation. Despite concerns about potential coagulation impairment, a study found no significant impact on coagulation function in patients with moderate traumatic brain injury. Both 3% HTS and 20% mannitol were safe to use for controlling intracranial pressure without increasing the risk of intracranial rebleeding [6].

Given the essential need for hyperosmolar solutions to control ICP and cerebral edema during cranial surgeries and the potential for hyperosmolar solution-associated coagulopathy, the selection of the optimal fluid management strategy is paramount. The present study aimed to investigate the coagulation abnormalities of HTS and mannitol solutions when administered in combination with HES in patients undergoing supratentorial tumor surgeries.

## Methods

This clinical trial was a prospective, double-blinded, randomized study conducted at an academic teaching hospital from January to June 2020. The study received approval from the ethics committee of Shahid Beheshti University (IR.SBMU.RETECH.REC.1397.621) and was registered at the Iranian Registry of Clinical Trials as IRCT (IRCT20210506051200N2).

This study included patients with a first occurrence of supratentorial brain tumors who were at least 18 years old. However, certain conditions disqualified individuals from participating. These exclusions included a history of chronic or acute health issues, such as coagulation disorders or organ failure affecting the kidneys or liver. Additionally, patients who had taken medications that could influence coagulation within a week prior to the study were not eligible. Other exclusions include hypersensitivity to the prescribed drugs, pregnancy, and those whose surgical procedures were performed in positions other than supine.

This research used a double-blinded, randomized methodology with two parallel groups (receiving either mannitol or HTS). A non-participating anesthesiologist, who was not directly responsible for patient care, did the randomization. prior to anesthesia, this was done with dice. Then, the treatment that had been assigned was prepared and given to the group. To keep the blinding going, the anesthesiologist who was taking care of the patient wrote down important information and sent it to the researcher in a sealed, opaque envelope.

Patients' baseline characteristics, including age, sex, and neurologic status, were documented. Routine blood tests, along with PFA-100, fibrinogen levels, and serum osmolality, were also conducted. In this study, thromboelastography devices were not available for use.

Anesthesia was induced with midazolam (0.05 mg/kg), fentanyl (5 µg/kg), lidocaine (1 mg/kg), propofol (2 mg/kg), and atracurium (0.5 mg/kg). Norepinephrine, if needed, to maintain cerebral perfusion pressure (60-70 mmHg). Propofol (200-250 µg/kg/min) and fentanyl (1 µg/kg/h) were used for maintenance. Dexamethasone (0.25 mg/kg) was administered. Systolic volume variability was kept below 12%, measured by the Vigilio device.

After the induction of general anesthesia, patients in the mannitol group were administered 20% mannitol at a dose of 1 g/kg over 30 minutes. In contrast, the HTS group received 3% saline at a volume of 5 mL/kg. Blood samples for coagulation parameters were collected immediately before and after the infusion of these agents. Subsequently, as per the hospital's local protocol, 500 mL of HES was infused over 20 minutes. A follow-up blood sample was obtained 30 minutes after the completion of the HES infusion.

Throughout the intervention, hemodynamic parameters, including heart rate, systolic and diastolic blood pressure, mean arterial pressure, central venous pressure, cardiac index, and systolic volume variability, were monitored from the beginning of anesthesia.

The dural tension score (DTS) was used to estimate the degree of brain relaxation. It was determined immediately after the opening of the dura by the neurosurgeons, who were blinded to the group assignments. The scores were assigned using the following scale as described by Shao et al. [7]: I. Normal dural tension: the neurosurgeon easily opened the dura mater; II. Increased dural tension: the dura mater could be opened without additional procedures to lower the ICP; III. Markedly increased dural tension: additional procedures were necessary to lower the ICP to open the dura mater. Also, the brain relaxation score (BRS) was used based on the Mousa et al. study [8]. The four-point scale score of brain relaxation is as follows: 1 = perfectly relaxed, 2 = satisfactorily relaxed, 3 = firm (leveled) brain or bulging brain.

The sample size was estimated based on a preliminary assessment, targeting a clinically significant difference of 20 seconds in mean PFA-100 values between groups, with an assumed standard deviation of 20 seconds for each. Employing a confidence level of 95% ($\alpha = 0.05$)

and a power of 80% (β = 0.20), the calculated sample size was 30.

The Shapiro-Wilk test (to check the normality of data distribution), the chi-square test, the Mann-Whitney U test, or the Friedman test was utilized for statistical analysis using SPSS version 22. Statistical significance was determined at a P value of less than 0.05.

## Results

This study, carried out from January to June 2020, explored how HTS compares to mannitol in its effects during surgery. Patients were enrolled and evenly divided into two groups (n=15 per group) based on predefined inclusion criteria. A CONSORT flow diagram was used to illustrate participant flow throughout the study. All 30 enrolled patients completed the study (Figure 1).

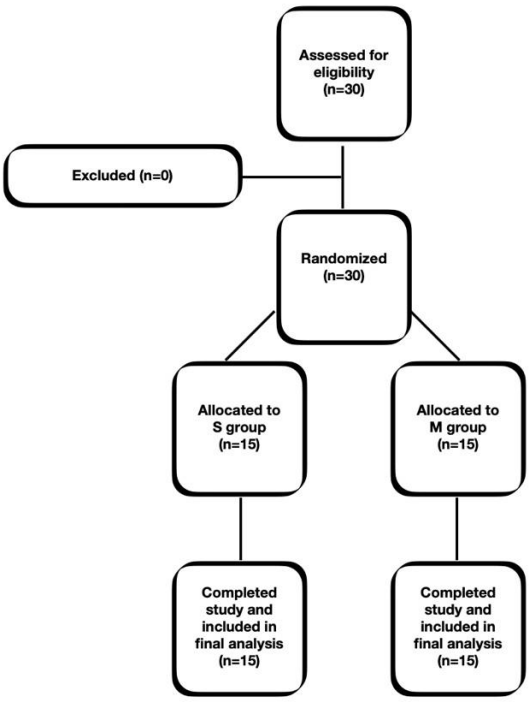


**Figure 1- CONSORT Flow Diagram**

Age was normally distributed in both groups. The near-identical mean values and nonsignificant between-group difference (p = 0.954) demonstrated effective age-matching. Analysis revealed no statistically significant difference in gender distribution between groups (p = 0.439). Although a minor numerical imbalance was observed, with a slightly higher proportion of males in the mannitol group, this difference is not expected to exert a meaningful influence on the study outcomes. Both groups had BMIs in the upper normal range (approaching overweight). There was no statistically significant difference in body mass index (BMI) between the groups. The mean difference was negligible (Δ = 0.15 kg/m²; p = 0.766). Both BUN and creatinine were comparable between groups, with values within normal physiologic ranges (Table 1).

No significant difference (p = 0.935) in surgery duration, indicating similar procedural complexity. The large standard deviations indicate differences in tumor size and location, yet they also show that the surgical complexity was well balanced between the two groups. The duration of ICU stay was similar (p = 0.397), suggesting that neither osmotic agent increased the need for prolonged critical care. Also, the length of hospitalization was comparable (p = 0.486), indicating that patients in both groups had similar recovery courses. The HTS group's slightly longer stay (10.7 vs. 10.3 days) is unlikely to reflect osmotic agent effects (Table 1).

Despite a numerical difference (~124 mL more in the HTS group), bleeding volumes were statistically similar (p = 0.307) and a medium effect size (Cohen's d = 0.5). PC transfusion rates were low and equivalent (p = 0.436). The HTS group required marginally fewer transfusions (0.27 vs. 0.47 events). The majority of patients in both groups did not require any blood transfusions—73% in the HTS group and 67% in the mannitol group (Table 1).

The comparison of Cardiac Index (CI) between the mannitol and HTS groups revealed no significant differences in the study. This findings indicate that both groups maintained similar cardiac output levels throughout the study. As indicated in Table 2, Analysis of CVP revealed no significant differences, suggesting comparable changes in intravascular volume and fluid balance between the groups. Likewise, Stroke Volume Variation (SVV) showed no significant difference, indicating that both groups demonstrated similar fluid responsiveness.

Hemoglobin levels remained almost unchanged throughout the study. Although the mannitol group tended to have slightly higher average Hb than the HTS group, this difference was not statistically significant (p = 0.187, independent-samples t-test).

Similarly, as shown in Table 3, calcium, sodium, and potassium levels measured at three different time points were comparable between the groups (all p > 0.05, Mann–Whitney U test), suggesting that mannitol and HTS have similar effects on maintaining electrolyte balance.

The analysis of coagulation parameters and platelet function showed no significant differences between the hypertonic saline (HTS) and mannitol groups at any of the measured time points. Platelet counts showed no statistically significant differences between the hypertonic saline and mannitol groups. The effect sizes (Cohen's d) ranged from -0.148 to -0.076, suggesting only negligible to small differences. This suggests that neither HTS nor mannitol significantly influenced platelet quantity during the perioperative period.

Prothrombin Time (PT), a measure of the extrinsic coagulation pathway, showed P values between 0.529 and 0.563, with effect sizes ranging from -0.233 to -0.214. Although these values indicate small differences between the groups, they were not statistically significant, confirming that both osmotic agents maintain similar coagulation dynamics in this aspect. Partial Thromboplastin Time (PTT) showed no significant differences, with P values ranging from 0.471 to 0.563 and effect sizes from -0.267 to -0.214, suggest that the intrinsic coagulation cascade remained largely unaffected by either HTS or mannitol. The International Normalized Ratio (INR), an additional measure of coagulation status, exhibited P values between 0.549 and 0.985 and effect sizes ranging from -0.222 to -0.007, indicating negligible to small differences between the groups. This further supports the finding that both treatments have a similar influence on overall coagulation. Finally, platelet function assessed using the PFA-100 analyzer showed P values ranging from 0.217 to 1.000, with Mann–Whitney U effect sizes ranging from 82.500 to 112.500. The platelet functionality, including adhesion and aggregation capacity, was comparable between the HTS and mannitol groups, with no clinically meaningful differences observed. All these results indicate that both hypertonic saline and mannitol, when administered with HES during surgery, exert similar effects on coagulation parameters and platelet function (Table 3).

The evaluation of osmolality levels at various time intervals indicated no statistically significant differences between the mannitol and HTS groups. The independent samples t-test revealed no significant difference at the initial measurement (p = 0.870). The Mann-Whitney U test at the second measurement also showed that there was no significant difference (p = 0.100), but the mannitol group had a higher osmolality than the HTS group. At the third measurement, there was non-significant difference (p = 0.212), with the mannitol group exhibiting higher osmolality. The comparison of dural tension scores (DTS) revealed no significant difference between the two groups (p = 0.586, Mann-Whitney U test). Brain Relaxation Scores (BRS) also showed no statistically significant differences (p = 0.838, Mann-Whitney U test), which means that both agents had the same effect on intraoperative brain relaxation and dural tension (Table 4).

No postoperative complications related to coagulation disorders or other surgical issues were observed in the patient population, and there were no reported mortalities during the study period.

**Table 1- Baseline clinical data by group**

| Variables | HTS 3% | Mannitol 20% | P value |
|---|---|---|---|
| Gender, male number (%) | 9 (60.0%) | 11 (73.3%) | 0.700 |
| Age year Mean (SD) | 47.40±12.83 | 47.13±12.15 | 0.954 |
| BMI kg/m$^2$ Mean (SD) | 25.58±5.56 | 25.43±4.76 | 0.766 |
| BUN, mg/dL Mean (SD) | 29.14 (6.15) | 28.50 (5.44) | 0.765 |
| Cr, mg/dl Median (IQR) | 0.86 (0.04) | 0.82 (0.14) | 0.214 |
| Duration of surgery, min Median (IQR) | 251.00 (157) | 229 (83) | 0.934 |
| Length of stay in ICU, hours Mean (SD) | 72.80 (25.09) | 64.47 (27.88) | 0.397 |
| Duration of hospitalization, day Median (IQR) | 10.00 (3) | 9.00 (3) | 0.459 |
| Intraoperative bleeding, mL Mean (SD) | 1054.53 (321.855) | 930.87 (328.441) | 0.307 |
| Units of blood transfused, n Median (IQR) | 0.00 (0) | 0.00 (1) | 0.274 |

HTS: hypertonic saline; BMI: body mass index; ICU: intensive care unit; BUN: blood urea nitrogen; Cr: creatinine; SD: standard deviation; IQR: interquartile range

**Table 2- Compare mean CI, CVP, and SVV between groups during the study**

| Variables | Time | HTS 3% | Mannitol 20% | P value |
|---|---|---|---|---|
| Cardiac Index Median (IQR) | Baseline | 2.95 (0.20) | 2.98 (0.14) | 1.000 |
| | After saline/mannitol infusion | 3.01 (0.13) | 3.04 (0.14) | 0.466 |
| | After HES infusion | 3.04 (0.13) | 3.07 (0.14) | 0.466 |
| Central Venous Pressure Median (IQR) | Baseline | 4.24 (1.90) | 4.20 (1.90) | 0.924 |
| | After saline/mannitol infusion | 4.32 (1.96) | 4.28 (1.94) | 0.923 |
| | After HES infusion | 4.37 (1.98) | 4.33 (1.96) | 0.924 |
| Stroke Volume Variability Median (IQR) | Baseline | 11.01 (3.30) | 10.90 (3.30) | 0.878 |
| | After saline/mannitol infusion | 11.23 (3.40) | 11.12 (3.36) | 0.878 |
| | After HES infusion | 11.34 (3.44) | 11.23 (3.40) | 0.877 |

HTS: Hypertonic saline; HES: hydroxyethyl starch; SD: standard deviation; IQR: interquartile range

**Table 3- Mean and Median Lab and Blood Coagulation Parameters by Group and Time Point**

| Variables | Time | HTS 3% | Mannitol 20% | P value |
|---|---|---|---|---|
| Hb, g/dl Mean (SD) | Baseline | 12.59 (1.61) | 13.44 (1.84) | 0.187 |
| | After saline/mannitol infusion | 11.39 (1.43) | 12.09 (1.65) | 0.220 |

| | | | | |
|---|---|---|---|---|
| | After HES infusion | 10.79 (1.35) | 11.42 (1.56) | 0.239 |
| Ca, mEq/L Median (IQR) | Baseline | 9.80 (0.90) | 9.10 (1.30) | 0.135 |
| | After saline/mannitol infusion | 9.30 (1.20) | 9.50 (1.20) | 0.771 |
| | After HES infusion | 9.60 (1.00) | 9.10 (1.40) | 0.280 |
| Na, mEq/L Mean (SD) | Baseline | 139.32 (1.52) | 139.04 (1.29) | 0.591 |
| | After saline/mannitol infusion | 138.87 (1.22) | 138.74 (1.46) | 0.788 |
| | After HES infusion | 139.40 (1.67) | 138.95 (1.50) | 0.447 |
| K, mEq/L Mean (SD) | Baseline | 4.12 (0.35) | 4.05 (0.42) | 0.644 |
| | After saline/mannitol infusion | 4.02 (0.34) | 4.14 (0.36) | 0.358 |
| | After HES infusion | 4.23 (0.42) | 4.13 (0.39) | 0.535 |
| PLT×$10^3$ Mean (SD) | Baseline | 302.33 (62.19) | 307.00 (60.29) | 0.836 |
| | After saline/mannitol infusion | 268.60 (53.70) | 276.25 (54.26) | 0.699 |
| | After HES infusion | 228.07 (45.46) | 234.86 (46.12) | 0.688 |
| PT, s Mean (SD) | Baseline | 10.87 (1.09) | 11.13 (1.09) | 0.529 |
| | After saline/mannitol infusion | 11.48 (1.18) | 11.72 (1.19) | 0.587 |
| | After HES infusion | 11.83 (1.20) | 12.06 (1.21) | 0.603 |
| PTT, s Mean (SD) | Baseline | 30.57 (3.99) | 31.63 (3.99) | 0.471 |
| | After saline/mannitol infusion | 32.39 (4.23) | 33.28 (4.15) | 0.563 |
| | After HES infusion | 33.33 (4.39) | 34.29 (4.25) | 0.549 |
| INR Mean (SD) | Baseline | 1.09 (0.11) | 1.11 (0.12) | 0.557 |
| | After saline/mannitol infusion | 1.17 (0.12) | 1.17 (0.13) | 0.985 |
| | After HES infusion | 1.20 (0.12) | 1.20 (0.14) | 0.964 |
| Positive PFA-100 Median (IQR) | Baseline | 0 (0) | 0 (0) | 1.00 |
| | After saline/mannitol infusion | 0 (0) | 0 (1) | 0.035 |
| | After HES infusion | 0 (1) | 1 (1) | 0.472 |
| Fib, mg/dl Median (IQR) | Baseline | 290.00 (90) | 305.00 (85) | 0.468 |
| | After saline/mannitol infusion | 246.00 (76) | 259.00 (73) | 0.419 |
| | After HES infusion | 197.00 (54) | 207.00 (51) | 0.407 |

HTS: Hypertonic saline; Hb: hemoglobin; Fib: fibrinogen; Ca: calcium; Na: sodium; K: potassium; HES: hydroxyethyl starch; SD: standard deviation; IQR: Interquartile Range; PLT: platelet; PT: prothrombin time; PTT: partial thromboplastin time; INR: International Normalization Ratio; PFA-100: Platelet Function Analyzer; S: second

**Table 4- Compare median osmolality and dural tension-relaxation scores**

| Variables | Time | HTS | Mannitol | P value |
|---|---|---|---|---|
| Osmolality, mOsm/kg Median (IQR) | Baseline | 288.00 (6.00) | 289.00 (8.00) | 0.493 |
| | After saline/mannitol infusion | 312.40 (9.40) | 317.90 (9.90) | 0.051 |
| | After HES infusion | 310.79 (8.62) | 311.94 (8.62) | 0.290 |
| DTS Median (IQR) | | 1.00 (0) | 1.00 (0) | 0.586 |
| BRS Median (IQR) | | 2.00 (2) | 2.00 (2) | 0.826 |

HTS: Hypertonic saline; DTS: Dural Tension Score; BRS: Brain Relaxation Score; HES: Hydroxyethyl starch; IQR: Interquartile Range

## Discussion

This study examined the coagulation effects of combining HTS (3%) or mannitol (20%) with hydroxyethyl starch (HES) in patients undergoing supratentorial brain tumor resection. The results indicate that both HTS and mannitol, when administered alongside HES, appear to have no significant adverse effects on coagulation parameters. These findings offer important insights into the comparative efficacy and safety of these two hyperosmolar agents, which are frequently employed to manage intracranial pressure (ICP) during neurosurgical interventions.

In neurosurgical practice, HTS and mannitol are commonly utilized to reduce cerebral edema and ICP, thereby facilitating surgical procedures. Both agents are effective in lowering intracranial pressure (ICP), but HTS may work for a longer time. Meningioma surgeries often involve significant intraoperative hemorrhage, generally addressed with colloids like hydroxyethyl starch (HES) [3–4]. It has been shown that combining HTS with HES can improve fluid balance and lower dural tension during neurosurgery, which could make the surgery safer and easier to control [9–10].

The use of HES carries a theoretical risk of coagulopathy, as it may reduce the activity of several coagulation factors, including fibrinogen, factor II, factor XIII, and factor X, to a greater extent than what would be expected from hemodilution alone. Nevertheless, the endogenous thrombin potential remains unaffected [11–13]. Among HES formulations, Voluven (HES 130/0.4) is associated with fewer coagulation-related complications compared to other hydroxyethyl starches, largely due to its lower molecular weight and degree of

substitution, which mitigate its impact on coagulation factors. Despite these advantages, it is important to note that Voluven can still influence coagulation parameters [14-15].

Hydroxyethyl starch can cause hypersensitivity reactions [16-17]. Due to the limited reports on the effects of mannitol and HTS in combination with HES on coagulation parameters, it is hard to draw a firm conclusion on the clinical use of HES. This study did not reveal a significant coagulopathy in either the mannitol-HES or HTS-HES groups. Based on these results, Voluven-HTS 3% and Voluven-mannitol may be safely used in elective supratentorial brain tumor surgeries.

Research examining the effects of HTS and mannitol on coagulation has yielded mixed results. Tan et al. indicated that elevated concentrations of HTS (7.5%) might demonstrate anticoagulant properties when used to substitute a significant volume of blood [18]. Conversely, Wang et al. observed no significant effect with the same concentration of HTS utilized in our study [6]. Additionally, Hanke et al. demonstrated that HTS combined with hydroxyethyl starch (HyperHaes), containing a 7.2% concentration of HTS, impairs platelet function even at low dilution levels [19]. It is important to recognize that some studies, including those by Teemu Luostarinen et al., have reported greater coagulopathy with mannitol compared to HTS. Although the observed changes in coagulation parameters were statistically significant, all values remained within the normal range. The discrepancies in findings among studies may be due to limited sample sizes and the interaction between fibrinogen and fibrin, which could signify a crucial mechanism underlying the coagulopathy linked to HTS and mannitol [20-21]. Another study indicates that 3% HTS is the ideal concentration, with a therapeutic dosage ranging from 1.4 to 2.5 mL/kg, administered as a bolus [22]. In our study, which utilized 3% of HTS, no significant differences were observed in coagulation parameters or intraoperative blood loss between the HTS and mannitol groups. The present study observed no significant differences in fibrinogen levels, platelet counts, prothrombin time (PT), partial thromboplastin time (PTT), or international normalized ratio (INR) between the two groups. These findings suggest that neither HTS nor mannitol significantly impairs coagulation when used in combination with HES. Also, the PFA-100 analyzes platelet function by simulating adhesion and aggregation under high shear stress. It helps identify inherited, acquired, or drug-related platelet disorders [23-24]. The PFA-100 is affected by various factors that can impair platelet function, leading to an extended closure time (CT). These factors include a low platelet count and hematocrit, which are often linked to thrombocytopathies. Clinicians should consider these limitations when interpreting the results [25]. In our study, PFA-100 testing showed no signs of coagulopathy in either group at any time, indicating that neither osmotic agent caused clinically significant changes in platelet function.

A thorough evaluation of hemodynamic parameters revealed no significant differences between the HTS and mannitol groups. Overall, these results indicate that both agents exert comparable effects on intravascular volume and fluid balance, maintaining stable systemic hemodynamics throughout the perioperative period. When proper monitoring is in place, either agent can be safely used without causing significant hemodynamic disturbances. This indicates that either agent can be used safely without significant hemodynamic compromise, provided that appropriate monitoring is maintained.

These observations align with prior research indicating that hypertonic saline (HTS) typically produces a more rapid onset and a longer-lasting reduction in intracranial pressure (ICP) than mannitol, while not compromising hemodynamic stability [9, 26]. Supporting evidence from another study demonstrated that 7.5% HTS was associated with notable increases in CI, stroke volume index (SVI), and ejection fraction (EF), with only small, non-significant rises in mean arterial pressure and CVP [27].

Both HTS and mannitol significantly decreased ICP, as demonstrated by the similar dural tension scores (DTS) and brain relaxation scores (BRS) observed in both groups. This aligns with previous studies that have demonstrated the efficacy of both agents in decreasing ICP through osmotic effects [22, 28]. Eslam et al. demonstrated that, in comparison to the use of mannitol alone, lower prescribed doses of mannitol combined with hypertonic saline (HTS) resulted in improved intraoperative brain relaxation and greater surgeon satisfaction during supratentorial brain tumor surgery [29]. Another study showed that 3% hypertonic saline is better than mannitol at relaxing the brain and may also help with fluid management and sodium (Na+) balance [30]. Our study did not reveal a statistically significant difference in the level of brain relaxation between the two groups, indicating that both HTS and mannitol are equally effective in attaining the requisite surgical conditions. The research faces certain constraints, such as a limited number of participants and a brief observation period. For more conclusive results, upcoming studies should incorporate larger, multi-center trials with extended monitoring and employ more sophisticated laboratory equipment. This will help verify the current findings and investigate other outcomes, including long-term neurological recovery and the occurrence of complications after surgery.

## Conclusion

The study has several limitations especially a relatively small sample size and a short follow-up period. A critical

limitation is the absence of Thromboelastography (TEG) and Rotational Thromboelastometry (ROTEM) data. Future research should involve larger, multi-center trials with longer follow-up periods and utilize more advanced laboratory devices, such as TEG and ROTEM.

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