ARC Journal of Neuroscience
Volume 8, Issue 2 2025, PP 32-42
ISSN 2456-057X
https://doi.org/10.20431/2456-057X.0802005
www.arcjournals.org

Comparison of 20% Mannitol and 3% Hypertonic Saline (NaCl) in Per Operative Brain Relaxation during Elective Supratentorial Craniotomy for Intra-Axial Brain Tumors

***Dr. Urmeeta Dutta[1], Dr. Md. Ashraful Islam[2], Dr. K. M. Zobair Alam[3], Dr. Tayeb Ahmmed[4], Prof. Dr. Dhiman Chowdhury[5], Prof. Dr. Akhlaque Hossain Khan[6]**

[1]Neurosurgeon, Department of Neurosurgery, Bangladesh Medical University, Dhaka, Bangladesh

[2]Neurosurgeon, Department of Neurosurgery, Bangladesh Medical University, Dhaka, Bangladesh

[3]Neurosurgeon, Department of Neurosurgery, Bangladesh Medical University, Dhaka, Bangladesh

[4]Neurosurgeon, Department of Neurosurgery, Bangladesh Medical University, Dhaka, Bangladesh

[5]Professor and Chairman, Department of Neurosurgery, Bangladesh Medical University, Dhaka, Bangladesh

[6]Professor and Ex-Chairman, Department of Neurosurgery, Bangladesh Medical University, Dhaka, Bangladesh

Received: 01 October 2025 Accepted: 17 October 2025 Published: 22 October 2025

Corresponding Author:** ***Dr. Urmeeta Dutta, *Neurosurgeon, Department of Neurosurgery, Bangladesh Medical University, Dhaka, Bangladesh*

Abstract

Background: *Hyperosmolar agents like Mannitol and Hypertonic saline (HS) reduce intracranial pressure and improve brain relaxation for tumor exposure. Mannitol is often considered as the first choice despite side effects. This study aimed to compare 20% Mannitol and 3% HS (NaCl) in per operative brain relaxation during supratentorial craniotomy for intra axial brain tumors.*

Methods: *A cross-sectional study was conducted from September 2023 to March 2025 in the Department of Neurosurgery, Bangladesh Medical University. Thirty-two patients undergoing supratentorial craniotomy for intra axial brain tumors were assigned to receive per operative hyper osmolar agent, either 3% HS (Group A) or 20% Mannitol (Group B) as per surgeon's choice (16 patients per group). Brain relaxation was evaluated after dural opening by per operative brain relaxation score and depth of brain surface in relation to skull bone thickness. Grading for the surgeon's brain relaxation score was 1= for perfectly relaxed, 2= for satisfactory, 3= for firm, and 4= for bulging. Brain depth: Grade A- beneath inner cortex of skull, Grade B- in between inner and outer cortex, Grade C- Bulging over outer cortex of skull. Hemodynamic parameters—mean arterial pressure (MAP) and heart rate (HR)—were recorded at intervals. Serum sodium and lactate were measured before infusion (T0) and 60 minutes after infusion (T60), and urine output was documented at T60. Data were analyzed using SPSS v26.0 with significance at $p < 0.05$.*

Result: *Mean age was 40.4 ±17.1 and 35.1 ±14.6 years in Groups A and B, with predominantly male participants. Glioblastoma was the most common (43.8%) among the intra axial tumors. In Group A, 81.3% had Grade-1 brain relaxation and 18.7% Grade-2. In Group B, 50% had Grade-1 and 43.8% Grade-2 relaxation, without a significant difference. Moreover, 87.5% patients in Group A had Grade A brain depth, and 12.5% had Grade B. Conversely, in Group B, each half of total patients showed Grade A and Grade B brain depth, though did not reach statistical significance. MAP and HR showed no significant differences. Group B had higher urine output. Initial serum sodium and lactate were similar, but T60 showed significant differences ($p<0.001$). Group B showed serum sodium reduction and lactate increase, while Group A remained stable in both parameters.*

Conclusion: *During supratentorial intra axial brain tumor surgery, both 3% HS and 20% Mannitol produced equivalent per operative brain relaxation and hemodynamic effects, though Mannitol caused significant biochemical changes and higher urine output.*

Keywords: *3% Hypertonic saline, 20% Mannitol, Brain relaxation, Supratentorial Craniotomy,* Intracranial *pressure.*

1. INTRODUCTION

Brain swelling following dural opening during supratentorial craniotomy is a frequent challenge in neurosurgical procedures for intra-axial brain tumors. Effective per operative brain relaxation is essential to facilitate surgical exposure, minimize retractor-induced brain parenchymal injury, and prevents transdural herniation, consequent cerebral ischemia and postoperative neurological deficits [1,2]. Hyperosmolar agents—principally 20% Mannitol and 3% Hypertonic Saline (HS)—are widely employed to achieve these objectives by reducing intracranial pressure (ICP) and cerebral edema [3]. Their ability to transiently shrink brain volume through osmotic dehydration has made them indispensable in neurosurgical practice [4]. Intra-axial brain tumors encompass a diverse spectrum of neoplasms with variable histopathological grades and biological behaviors, ranging from benign (i.e. cerebellar dysplastic gangliocytoma) to highly malignant lesions such as glioblastoma [5]. Surgical resection through supratentorial craniotomy remains the mainstay of treatment. When preoperative imaging reveals significant mass effect—such as midline shift, effacement of basal cisterns, or sulcal effacement—surgeons often administer hyperosmolar agents before dural opening to optimize brain relaxation and exposure [2,6].

The therapeutic effects of hyperosmolar substances are mediated through two principal mechanisms: a rapid onset hemodynamic effect resulting from plasma expansion and a delayed osmotic effect via establishment of a transendothelial osmotic gradient across the blood–brain barrier (BBB), promoting fluid movement from brain parenchyma to the intravascular compartment [3,7]. Mannitol, a six-carbon sugar alcohol, has long been regarded as the gold standard osmotic diuretic for ICP reduction [8]. Administered intravenously in doses of 0.25–1 g/kg, it increases plasma tonicity without crossing the intact BBB, thereby extracting both interstitial and intracellular water from cerebral tissue [9]. However, its use is not devoid of complications. Rebound intracranial hypertension, dyselectrolytaemia, hypovolemia, and nephrotoxicity have been reported, especially with repeated or high-dose administration [10,11]. Additionally, in diabetic or renal-compromised patients, mannitol may exacerbate osmotic nephropathy or metabolic acidosis [9].

Hypertonic saline, initially introduced as a resuscitative solution for hypovolemic shock, has gained recognition as an alternative osmotic agent for ICP management [12]. Clinical studies demonstrate that 3% HS produces more sustained ICP reduction, with less diuresis, metabolic acidosis and hemodynamic instability compared to mannitol [13,14]. Its higher reflection coefficient (RC = 1.0) relative to mannitol (RC = 0.9) signifies superior impermeability to the BBB, enhancing osmotic efficiency and minimizing the rebound phenomenon [2,15]. Furthermore, HS exerts additional hemodynamic benefits by augmenting cardiac output, reducing extravascular lung water, and improving systemic oxygenation [8].

Comparative investigations have shown that HS can achieve equivalent or superior ICP control, while maintaining circulatory and metabolic stability and intravascular volume [7,13]. Among the various concentrations, 3% HS is frequently preferred for per operative use because it can be safely administered through peripheral lines and produces a balanced osmotic effect without severe hypernatremia [14]. Nonetheless, despite increasing clinical adoption, there remains limited consensus regarding the relative superiority of 3% HS over 20% Mannitol for per operative brain relaxation during elective tumor surgery, particularly in resource-limited settings [2].

In the context of supratentorial intra axial brain tumors, choosing the optimal osmotic agent has important implications for surgical exposure, patient safety, and postoperative outcomes. Although both agents share similar mechanisms, differences in pharmacodynamics and systemic effects necessitate head-to-head evaluation under controlled clinical conditions. To date, comparative data from South Asian neurosurgical practice, including Bangladesh, remain scarce.

Therefore, this study aims to compare the efficacy and biochemical effects of equivolume and equiosmolar 20% Mannitol and 3% Hypertonic Saline (NaCl) in achieving per operative brain relaxation during elective supratentorial craniotomy for intra axial brain tumors. The findings are expected to provide clinically relevant evidence to guide anesthesiologists and neurosurgeons in selecting the most effective hyperosmolar agent for optimal surgical management.

2. METHODOLOGY & MATERIALS

This analytic observational study employed a cross-sectional comparative design. It was conducted in the Department of Neurosurgery, Bangladesh Medical University (BMU), Dhaka, one of the country's premier neurosurgical centers that performs a wide range of intracranial surgical procedures. The study spanned eighteen months (September 2023–March 2025). After receiving Institutional Review Board (IRB) approval, patient enrollment and data collection was commenced and continued until the required sample size was achieved. The study population comprised adult patients undergoing elective supratentorial craniotomy for intra axial brain tumors at BMU. Participants were divided into two groups based on the hyperosmolar agent used intraoperatively for brain relaxation:

- **Group A:** Received 3% Hypertonic Saline (NaCl)
- **Group B:** Received 20% Mannitol

2.1. Sample Selection

A purposive sampling technique was applied. Eligible patients who met all inclusion criteria and provided informed consent were enrolled consecutively until each group reached 16 participants, resulting in a total sample size of 32 patients.

2.2. Inclusion Criteria

- Patients aged 18–70 years
- Patients scheduled for elective supratentorial craniotomy for intra-axial brain tumors
- Patients selected by the operating surgeon to receive either 3% Hypertonic Saline or 20% Mannitol for per operative brain relaxation

2.3. Exclusion Criteria

- Preoperative electrolyte imbalance
- Treatment with hyperosmolar agents before surgery
- Per operative CSF drainage via lumbar drain
- Co-morbidities, i.e. Ischemic heart disease, uncontrolled hypertension, uncontrolled diabetes mellitus, or chronic kidney disease
- Recurrent or residual brain tumors
- Patients or guardians who declined consent for participation

2.4. Data Collection and Study Procedure

Data were collected prospectively using a semi-structured data collection sheet specifically developed and validated for this study. Eligible patients were identified preoperatively through MRI or CT confirmation of intra axial brain tumors with radiological signs of raised intracranial pressure (e.g., midline shift >5 mm, obliteration of basal cisterns, or loss of normal sulcal pattern). Following written informed consent, baseline demographic and clinical information was recorded.

Patients were assigned to Group A (3% HS) or Group B (20% Mannitol) according to the operating surgeon's preference. Standardized anesthetic protocols were followed for all patients. Induction was achieved with fentanyl (1 µg/kg) and propofol (2 mg/kg), followed by suxamethonium (1.5 mg/kg) to facilitate intubation. Anesthesia was maintained using nitrous oxide (70%) and oxygen (30%) with isoflurane (MAC 0.5–0.6) and vecuronium bromide for muscle relaxation. Induced hypotension (mean arterial pressure [MAP] 55–80 mmHg) was maintained to optimize the surgical field. Depth of anesthesia was monitored by any change in heart rate and MAP.

Hyperosmolar therapy began at the time of scalp incision:

- Group A: 3 mL/kg of 3% NaCl (osmolarity 1026 mOsm/L).
- Group B: 3 mL/kg of 20% mannitol (0.6 g/kg; osmolarity 1098 mOsm/L).

Intravenous infusion of hyperosmolar agent was administered at the rate of 25 d/min. Upon dural opening, the brain relaxation score and depth of brain surface relative to skull bone thickness were assessed by the operating surgeon using standardized grading systems i.e: Surgeon's Brain Relaxation score (Grade 1-Perfectly relaxed, Grade 2- Satisfactorily relaxed, Grade 3-Firm brain, Grade 4- Bulging brain) and Depth of brain surface relative to skull thickness (Grade A-Beneath inner cortical layer of skull, Grade B- In between inner and outer cortex of skull, Grade C-Bulging over the outer cortex of skull) [1,2]. Haemodynamic parameters—including MAP, heart rate (HR) were recorded at baseline, upon dural opening and 60 minutes after starting infusion, urine output (in first hour); Biochemical parameters- serum sodium, serum lactate—were recorded at baseline (T_0) and 60 minutes after infusion (T_{60}).

To ensure reliability, all monitoring devices were calibrated, and biochemical assays were conducted in the hospital's central laboratory

using standard analyzers. Data were checked for completeness, consistency, and accuracy after each operation.

2.5. Ethical Considerations

The study protocol received ethical approval from the Institutional Review Board (IRB) of Bangladesh Medical University (Memo No. BSMMU/2024/6834, Reg. No. 5059). All participants or their legal guardians were thoroughly informed about the study's purpose, procedures, potential risks, and benefits before signing written consent. Patient confidentiality was strictly maintained using anonymized identification codes. Participation was voluntary, and patients could withdraw at any point without affecting their treatment. The study was conducted in full compliance with the principles of the Declaration of Helsinki (2013 revision).

2.6. Statistical Analysis

Data were entered and analyzed using SPSS version 26.0 and Microsoft Excel 2019. Descriptive statistics were presented as mean ± standard deviation (SD) for continuous variables and frequency (percentage) for categorical data. The Shapiro–Wilk test assessed data normality.

Independent-sample t-test and paired-sample t-test were used for continuous variables (e.g., serum sodium and lactate). Mann-Whitney U test was applied for ordinal variables (brain relaxation grades). Fisher's exact test was used for categorical comparisons (tumor histology). Repeated measures ANOVA analyzed hemodynamic variables (MAP and HR) at different time points. All statistical tests were two-tailed, and a p-value < 0.05 was considered statistically significant, with 95% confidence intervals (CI) reported where applicable.

3. RESULTS

This cross-sectional comparative study was conducted in the Department of Neurosurgery, Bangladesh Medical University. A total of 32 patients who underwent elective supratentorial craniotomy for intra axial brain tumors were enrolled in the study and divided into two groups. Group A received per operatively 3% HS (NaCl) and Group B received per operatively 20% Mannitol.

Table 1. *Distribution of the patients according to age group (n=32)*

Age group (years)	Group A (n=16)	Group B (n=16)	p-value
	n (%)	n (%)	0.085
<35	8 (50)	9 (56.2)	
≥35	8 (50)	7 (43.8)	
Mean ±SD	40.4±17.1	35.1±14.6	0.346

The mean age of the patients was slightly higher in Group A (40.4 ± 17.1 years) than in Group B (35.1 ± 14.6 years), but the difference was not statistically significant.

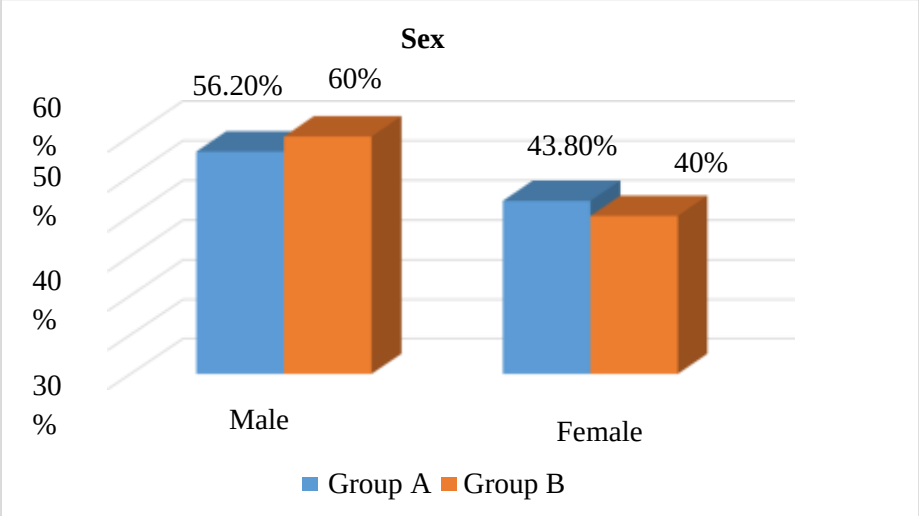

Figure 1. *Bar diagram showing distribution of the patients according to Sex (n=32)*

In both Group A and Group B majority were male (56.2% vs 60%), followed by female (43.8% vs 40%). The difference between the two groups was not statistically significant.

Table 2. *Histopathological types of the brain tumors among the patients (n=32)*

	Group A (n=16)	Group B (n=16)	p-value
	n (%)	n (%)	
Astrocytoma	3 (18.8)	6 (37.5)	0.561
Glioblastoma	8 (43.8)	6 (37.5)	
Metastatic Carcinoma	1 (6.3)	2 (12.5)	
Oligodendroglioma	3 (18.8)	2 (12.5)	
Cavernoma	1 (6.3)	0 (0)	

The most common diagnosis in both groups was glioblastoma, observed in 43.8% of Group A and 37.5% of Group B. Astrocytoma was present in 18.8% of Group A and 37.5% of Group B. Other histopathological findings included oligodendroglioma (18.8% in Group A and 12.5% in Group B), metastatic carcinoma (6.3% vs. 12.5% respectively), and cavernoma (6.3% in Group A only; This patient was included by radiological features that mimicked Glioma, but final diagnosis was made by Histopathology). No statistically significant difference was found between the groups.

Table 3. *Per operative brain relaxation grading among the study patients (n=32)*

	Group A (n=16)	Group B (n=16)	p-value
	n (%)	n (%)	
Grade 1	13 (81.3)	8 (50)	0.119
Grade 2	3 (18.7)	7 (43.8)	
Grade 3	0 (0)	1 (6.2)	
Grade 4	0 (0)	0 (0)	

In Group A, the majority of patients (81.3%) had Grade 1 brain relaxation, while 18.7% were classified as Grade 2, and none had Grade 3 relaxation. In contrast, Group B had a lower proportion of patients with Grade 1 relaxation (50%), while 43.8% had Grade 2, and 6.2% had Grade 3 relaxation. None had Grade 4 relaxation in this study. Although Group A showed a higher proportion of patients with better brain relaxation (Grade 1) compared to Group B, the difference was not statistically significant.

Table 4. *Distribution of the study patients according to the Depth of the Brain surface in relation to skull bone thickness (n=32)*

	Group A (n=16)	Group B (n=16)	p-value
	n (%)	n (%)	
Grade A	14 (87.5)	8 (50)	0.073
Grade B	2 (12.5)	8 (50)	
Grade C	0 (0)	0 (0)	

Regarding the depth of the brain surface in relation to skull bone thickness, the majority of patients in Group A (87.5%) were classified as Grade A, while only 12.5% fell into the Grade B category. Conversely, in Group B, an equal distribution was observed, with 50% of patients categorized in each grade (Grade A & Grade B). No patient in this study had a Grade C category brain depth. Although a higher proportion of patients in Group A had a deeper brain surface compared to Group B, indicating better brain relaxation, the difference did not reach statistical significance.

Table 5. *Distribution of the patients according to hemodynamic parameters of both treatment groups (n=32)*

	Group A (n=16)	Group B (n=16)	p-value
	Mean ± SD	Mean ± SD	
Pre-induction			
MAP (mmHg)	70.31 ± 12.57	68.31 ± 10.12	0.624
HR (beats/min)	84.38 ± 6.08	86.25 ± 7.62	0.448
Upon dural opening			
MAP (mmHg)	70.69 ± 9.22	65.94 ± 6.64	0.105

HR (beats/min)	81.69 ± 4.73	81.25 ± 7.59	0.846
T60			
MAP (mmHg)	69 ± 10.98	67.56 ± 6.68	0.658
HR (beats/min)	81.75 ± 4.84	79.25 ± 7.01	0.25

Group A and Group B showed no statistically significant differences in mean arterial pressure and heart rate at different time points. Pre-induction MAP was 70.31 ± 12.57 mmHg in Group A and 68.31 ± 10.12 mmHg in Group B, while HR was 84.38 ± 6.08 beats/min and 86.25 ± 7.62 beats/min, respectively. Upon dural opening, MAP was slightly lower in Group B (65.94 ± 6.64 mmHg) compared to Group A (70.69 ± 9.22 mmHg) but with no statistically significant difference, whereas HR remained comparable (81.69 ± 4.73 beats/min vs. 81.25 ± 7.59 beats/min). At T60, MAP was 69± 10.98 mmHg in Group A and 67.56 ± 6.68 mmHg in Group B, with HR values of 81.75 ± 4.84 beats/min and 79.25 ± 7.01 beats/min, respectively.

Table 6. *Distribution of the patients according to Biochemical parameters and urine output of both treatment groups (n=32)*

	Group A (n=16)	**Group B (n =16)**	**p-value**
	Mean ± SD	Mean ± SD	
T0			
Serum sodium level (mmol/L)	136.19 ± 2.69	138.81 ± 3.35	0.118
Serum lactate level (mmol/L)	1.39 ± 0.92	1.55 ± 0.74	0.589
T60			
Serum sodium level (mmol/L)	141.56 ± 3.79	131.13 ± 4.43	<0.001
Serum lactate level (mmol/L)	2.16 ± 1.45	5.45 ± 1.61	<0.001
Urine output (mL)	83.75 ± 33.19	294.38 ± 89.79	<0.001

At baseline (T0), serum sodium and serum lactate levels showed no significant difference between Group A (136.19 ± 2.69 mmol/L serum sodium;1.39 ± 0.92 mmol/L serum lactate) and Group B (138.81 ± 3.35 mmol/L serum sodium;1.55 ± 0.74 mmol/L serum lactate). At T60, Group B demonstrated a significantly lower serum sodium level (131.13 ± 4.43 mmol/L) than in Group A (141.56 ± 3.79 mmol/L). Serum lactate levels were markedly elevated in Group B (5.45 ± 1.61 mmol/L) compared to Group A (2.16± 1.45 mmol/L), which was statistically significant. Furthermore, urine output at T60 was significantly higher in Group B (294.38 ± 89.79 mL) than in Group A (83.75 ± 33.19 mL).

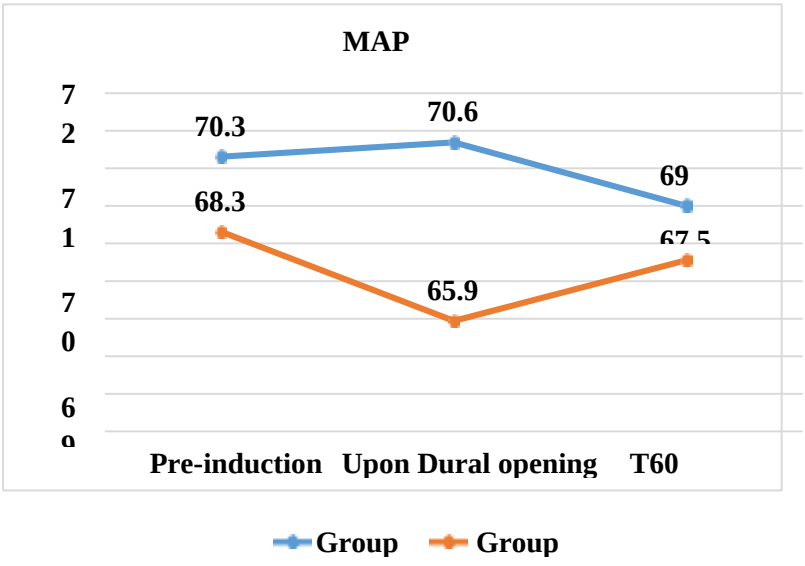

Figure 2. *Line chart showing MAP level in different time intervals in both treatment groups (n=32)*

p-value was determined by Repeated Measures ANOVA Test. (in Group A p= 0.477and in Group B p= 0.271). Both Group A and Group B indicated no significant difference in MAP levels over time during the study period.

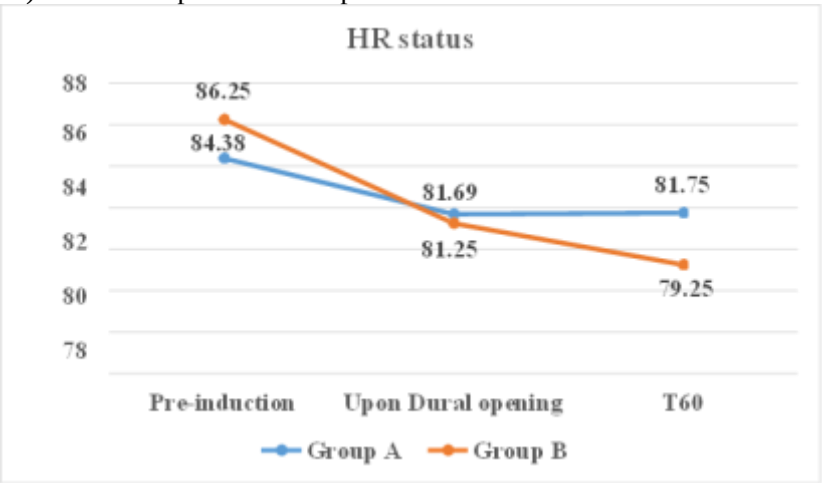

Figure 3. *Line chart showing HR level in different time intervals in both treatment groups (n=32)*

p-value was determined by Repeated Measures ANOVA Test (in Group A p=0.271 and in Group B p=0.441). Both Group A and Group B suggested no significant change in HR levels throughout the study period.

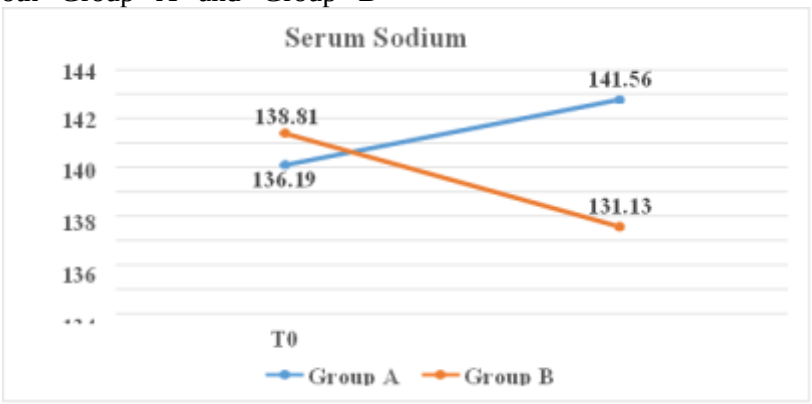

Figure 4. *Line chart showing serum sodium level in different time intervals in both treatment groups (n=32)*

p-value was determined by Paired sample t test (In Group A, p = 0.069 and Group B, p<0.001). A significant difference was found within the 20% Mannitol group regarding serum sodium level, indicating notable changes over time due to the natriuretic effect of Mannitol, whereas 3% HS caused no statistically significant change in serum sodium level.

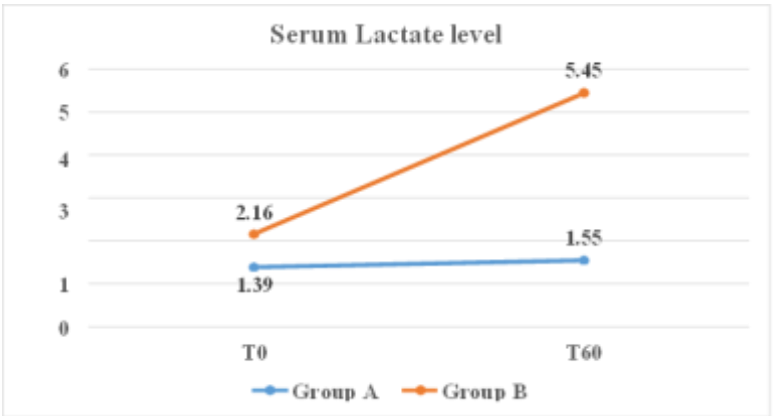

Figure 5. *Line chart showing serum lactate levels in different time intervals in both treatment groups (n=32)*

p-value was determined by Paired sample t test (In both Group A, p = 0.118 and Group B, p<0.001). Serum lactate levels varied significantly over time within the 20% Mannitol group, but not in the case of 3% HS, highlighting the impact of the different agents on lactate metabolism.

4. DISCUSSION

In neurosurgical practice, patients with intra-axial brain tumors commonly present with evidence of raised intracranial pressure (ICP) due to cerebral swelling, cerebral oedema and mass effect [16]. Optimal per operative brain relaxation is therefore a critical component of surgical strategy: a relaxed brain improves surgical exposure, reduces retractor-induced tissue injury, and diminishes the risk of local hypoperfusion and cerebral ischemia [17]. In our study comparing 20% Mannitol with 3% Hypertonic Saline (HS) during elective supratentorial craniotomy for intra axial brain tumors, we sought to determine whether HS offers superior brain relaxation, hemodynamic stability and biochemical effects.

The demographic data in our cohort revealed no statistically significant difference between the two treatment groups in terms of mean age (40.4 ± 17.1 vs 35.1 ± 14.6 years) or gender distribution (male 56.2% vs 60%; p = 0.346 and p = 1.00, respectively). These findings align with the studies of Solanki et al., Ali et al., which reported similar age and sex profiles across treatment arms, and strengthen the internal validity of our results: comparable baseline characteristics reduce potential confounding and allow a more meaningful comparison of outcomes [18,19].

Histopathological data showed that glioblastoma was the most common diagnosis (43.8% overall), followed by astrocytoma (28.1%) and oligodendroglioma (15.6%). These proportions are consistent with published epidemiological patterns of intra-axial tumors [20,21], assuring that our patient sample is representative of routine neurosurgical practice.

With respect to brain relaxation, the proportion of patients achieving Grade 1 ("perfectly relaxed") brain condition was higher in the HS group (81.3%) than in the Mannitol group (50%), whereas the Mannitol group exhibited a greater share of less favorable grades (Grade 2: 43.8%; Grade 3: 6.2%) than HS (Grade 2: 18.7%; Grade 3: 0%). Although this difference did not reach statistical significance (p = 0.135), the trend suggests a potential clinical advantage for HS in producing more favorable intra-operative brain conditions. This pattern parallels the meta-analytical findings of Fang et al., indicating that HS may reduce the incidence of "bulging" brain compared with Mannitol [22].

In terms of the depth of brain surface relative to skull bone thickness—used as an adjunct measure of brain relaxation— we observed that 87.5% of patients in the HS group were in Grade A (deepest surface, indicating best relaxation) versus 50% in the mannitol group, whereas Grade B (shallower brain surface) occurred in 50% of mannitol versus 12.5% of HS patients (p=0.064). While again not statistically significant, this supports a possible modest benefit of HS. Notably, larger randomized trials have reported significant differences in brain relaxation favoring HS over Mannitol [1]. The absence of statistical significance in our study may reflect the relatively small sample size (n=32), limiting power.

Hemodynamic variables—pre-induction MAP and heart rate were similar between groups, and whereas the Mannitol group demonstrated a slightly lower MAP at dural opening compared with HS, this trend did not reach statistical significance (p = 0.105). This finding aligns with several prior studies in which no significant difference in intra-operative MAP or heart rate was detected between osmotherapy groups [4,7]. Importantly, one study reported significantly lower central venous pressure in mannitol patients, suggesting that monitoring CVP may be more sensitive than MAP in detecting subtle hemodynamic differences [1]. In our series, the lack of significant hemodynamic divergence indicates that either agent may be acceptable from a stability viewpoint under standard anesthetic management.

The biochemical analysis revealed a striking difference in serum sodium at T60: a significantly lower mean sodium in the Mannitol group (131.13 ± 4.43 mmol/L) compared with the HS group (141.56 ± 3.79 mmol/L). This likely reflects the natriuretic-diuretic effects of Mannitol, and the hypernatremic, intravascular-expanding effect of HS. This is consistent with the literature, which shows HS increases serum sodium and osmolality without significant diuresis, whereas mannitol induces marked diuresis and potential hypovolemia [24,25]. Similarly, serum lactate was markedly higher in the Mannitol group (5.45 ± 1.61 mmol/L)

compared with HS (2.16 ± 1.45 mmol/L). Elevated lactate may indicate relative tissue hypoperfusion or anaerobic metabolism, perhaps secondary to mannitol-induced diuresis and volume contraction. Though not widely reported in neurosurgical osmotherapy literature, this finding may point to a clinically meaningful difference in metabolic stress between agents.

Urine output at T60 was significantly greater in the Mannitol group (294.38 ± 89.79 mL) compared with HS (83.75 ± 33.19 mL), reflecting the known osmotic diuresis of mannitol [18]. While diuresis may aid brain relaxation through volume reduction, it can also lead to hypovolemia, electrolyte imbalance and rebound cerebral oedema [4]. HS, by contrast, provides osmotic dehydration without excessive fluid loss, which may preserve hemodynamic and cerebral perfusion stability.

Taken together, our data suggest that both 3% HS and 20% Mannitol are effective in achieving adequate per operative brain relaxation. However, 3% HS may offer advantages in terms of less diuresis, more stable serum sodium levels. These findings accord with a growing body of evidence favoring 3% HS in neurosurgical osmotherapy [23,26].

5. Limitations of the Study

This study has several limitations.

- The purposive sampling technique was used in the current study to include the patients; therefore, there was a chance of selection bias.
- A single surgeon operating all the cases would assess per operative brain relaxation score more homogenous and acceptably. As inter-observer variation and lack of inter-rater agreement could lead to bias.
- Intra axial tumors of different histopathological types were included (Glioma, Metastasis) that could cause a variable amount of vasogenic edema and mass effect, therefore could affect per operative brain relaxation.

6. Conclusion

This study demonstrated that 3% Hypertonic Saline (HS) and 20% Mannitol provide comparable per operative brain relaxation and hemodynamic stability during elective supratentorial craniotomy for intra axial brain tumors. Although both agents were equally effective in achieving optimal surgical conditions, Mannitol was associated with significantly greater diuresis, reduced serum sodium, and elevated serum lactate levels. In contrast, 3% HS maintained biochemical stability with fewer systemic side effects. Therefore, while 3% HS is not superior to 20% Mannitol in terms of brain relaxation efficacy, it appears to be a safer alternative for intraoperative osmotherapy due to its more favorable metabolic profile.

7. Acknowledgment

I would like to express my sincere gratitude for the invaluable support and cooperation provided by the staff, participants, and my co-authors/colleagues who contributed to this study.

Conflicts of interest

There are no conflicts of interest.

Ethical approval

The study was approved by the Institutional Ethics Committee.

References

[1] Dostal P, Dostalova V, Schreiberova J, Tyll T, Habalova J, Cerny V, Rehak S, Cesak T. A comparison of equivolume, equiosmolar solutions of hypertonic saline and mannitol for brain relaxation in patients undergoing elective intracranial tumor surgery: a randomized clinical trial. Journal of Neurosurgical Anesthesiology. 2015 Jan 1;27(1):51-6.

[2] Johansyah TK, Jonathan J, Yusari IA, Nolan J, Alamsyah AH, Ramadhana GA. Equiosmolar doses of hypertonic saline versus mannitol for brain relaxation in patients undergoing elective craniotomies: an updated systematic review and meta-analysis. The Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2022 Dec 2;58(1):142.

[3] Barik AK, Agrawal S, Gupta P, Kumari R. Evaluation of equiosmolar 20% mannitol, 3% hypertonic saline and 8.4% sodium bicarbonate on intraoperative brain relaxation and hemodynamic parameters in patients undergoing craniotomy for supratentorial tumors: a prospective randomized study. Minerva Anestesiologica. 2021 Sep 1;87(9):997-1005.

[4] Hernández-Palazón J, Fuentes-García D, Doménech-Asensi P, Piqueras-Pérez C, Falcón-Araña L, Burguillos-López S. A comparison of equivolume, equiosmolar solutions of hypertonic saline and mannitol for brain relaxation during elective supratentorial craniotomy. British Journal of Neurosurgery. 2016 Jan 2;30(1):70-5.

[5] Rapalino O, Batchelor T, González RG. Intra-axial brain tumors. InHandbook of clinical neurology 2016 Jan 1 (Vol. 135, pp. 253-274). Elsevier.

[6] Taylor MD, Bernstein M. Awake craniotomy with brain mapping as the routine surgical approach to treating patients with supratentorial intraaxial tumors: a prospective trial of 200 cases. Journal of neurosurgery. 1999 Jan 1;90(1):35-41.

[7] Raghava A, Bidkar PU, Prakash MS, Hemavathy B. Comparison of equiosmolar concentrations of hypertonic saline and mannitol for intraoperative lax brain in patients undergoing craniotomy. Surgical neurology international. 2015 May 8; 6:73.

[8] Rossi S, Picetti E, Zoerle T, Carbonara M, Zanier ER, Stocchetti N. Fluid management in acute brain injury. Current Neurology and Neuroscience Reports. 2018 Nov;18(11):74.

[9] Eldahab HA, Awad W, Wagh O. Should hypertonic saline 3% replace mannitol 20% for reduction of intracranial pressure in craniotomy for supratentorial tumors. A comparative study. Egypt J Anaesth. 2009; 25:413-28.

[10] Wakai A, Roberts IG, Schierhout G. Mannitol for acute traumatic brain injury. Cochrane Database of Systematic Reviews. 2005(4).

[11] Strandvik GF. Hypertonic saline in critical care: a review of the literature and guidelines for use in hypotensive states and raised intracranial pressure. Anaesthesia. 2009 Sep;64(9):990-1003.

[12] Ware ML, Nemani VM, Meeker M, Lee C, Morabito DJ, Manley GT. Effects of 23.4% sodium chloride solution in reducing intracranial pressure in patients with traumatic brain injury: a preliminary study. Neurosurgery. 2005 Oct 1;57(4):727-36.

[13] Shi J, Tan L, Ye J, Hu L. Hypertonic saline and mannitol in patients with traumatic brain injury: A systematic and meta-analysis. Medicine. 2020 Aug 28;99(35): e21655.

[14] Iqbal U, Kumar A, Arsal SA, Shafique MA, Amin SB, Raja A, Aqeel R, Waqas S. Efficacy of hypertonic saline and mannitol in patients with traumatic brain injury and cerebral edema: a systematic review and meta-analysis. Egyptian Journal of Neurosurgery. 2023 Oct 2;38(1):54.

[15] Schwarz S, Schwab S, Bertram M, Aschoff A, Hacke W. Effects of hypertonic saline hydroxyethyl starch solution and mannitol in patients with increased intracranial pressure after stroke. Stroke. 1998 Aug;29(8):1550-5.

[16] Comelli I, Lippi G, Campana V, Servadei F, Cervellin G. Clinical presentation and epidemiology of brain tumors firstly diagnosed in adults in the Emergency Department: a 10-year, single center retrospective study. Annals of translational medicine. 2017 Jul;5(13):269.

[17] Prabhakar H, Singh GP, Anand V, Kalaivani M. Mannitol versus hypertonic saline for brain relaxation in patients undergoing craniotomy. Cochrane Database of Systematic Reviews. 2014(7).

[18] R N Solanki, T V Tank, J M Thakkar, Farista Pegu, K M Solanki. Hypertonic saline (3%): A safe alternative to mannitol (20%) for brain relaxation in elective craniotomy for supratentorial brain tumor. MedPulse International Journal of Anesthesiology. March 2020; 13(3): 154-157.

[19] Ali A, Tetik A, Sabanci PA, Altun D, Sivrikoz N, Abdullah T, Aydoseli A, Sencer A, Akinci IO. Comparison of 3% hypertonic saline and 20% mannitol for reducing intracranial pressure in patients undergoing supratentorial brain tumor surgery: a randomized, double-blind clinical trial. Journal of Neurosurgical Anesthesiology. 2018 Apr 1;30(2):171-8.

[20] Mohile NA, Thomas AA, editors. Brain Tumors: A Pocket Guide. Springer Nature; 2023 Nov 27.

[21] Dolecek TA, Propp JM, Stroup NE, Kruchko C. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2005–2009. Neuro-oncology. 2012 Nov 1;14(suppl_5): v1-49.

[22] Fang J, Yang Y, Wang W, Liu Y, An T, Zou M, Cheng G. Comparison of equiosmolar hypertonic saline and mannitol for brain relaxation during craniotomies: a meta-analysis of randomized controlled trials. Neurosurgical Review. 2018 Oct;41(4):945-56.

[23] Abdulhamid AS, Ghaddaf AA, Bokhari AF, Alghamdi YA, Alhakami MF, Alaboud AK, Lary A. Equiosmolar hypertonic saline and mannitol for brain relaxation in patients undergoing supratentorial tumor surgery: a systematic review and meta-analysis. Surgical Neurology International. 2022 Mar 31; 13:120.

[24] Shao L, Hong F, Zou Y, Hao X, Hou H, Tian M. Hypertonic saline for brain relaxation and intracranial pressure in patients undergoing neurosurgical procedures: a meta-analysis of randomized controlled trials. PLoS One. 2015 Jan 30;10(1): e0117314.

[25] Choudhury A, Bairwa M, Jithesh G, Kumar S, Kumar N. Efficacy of intravenous 20% mannitol vs 3% hypertonic saline in reducing intracranial pressure in nontraumatic brain injury: A systematic review and meta-analysis. Indian

Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine. 2024 Jun 29;28(7):686.

[26] Shi J, Tan L, Ye J, Hu L. Hypertonic saline and mannitol in patients with traumatic brain injury: A systematic and meta-analysis. Medicine. 2020 Aug 28;99(35):e21655.

Citation: *Dr. Urmeeta Dutta et al. "Comparison of 20% Mannitol and 3% Hypertonic Saline (NaCl) in Per Operative Brain Relaxation during Elective Supratentorial Craniotomy for Intra-Axial Brain Tumors". ARC Journal of Neuroscience, 2025; 8(2): 32-42. DOI: https://doi.org/10.20431/2456-057X.0802005.*