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Research Article

ANESTHESIA AND CRITICAL CARE

ISSN: 2687-7996

Comparison of Effect of Various Doses of Mannitol Infusion on Brain Relaxation and Cardiac Function in Patients Undergoing Craniotomy for Supratentorial Brain Tumors

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Abstract

Introduction: Most of the brain tumors are supratentorial tumors accounting for 79% of all tumors. The most common of which gliomas, meningiomas and pituitary tumors. They produce significant mass effects in the brain and certain types are accompanied by significant peritumoral edema that leads to increased intracranial pressure. Mannitol is widely used to reduce intracranial pressure (ICP) in patients with cerebral edema. The use of mannitol for the type of surgery that patients in our study will undergo has been found overall to be beneficial; however, the appropriate dose of mannitol is controversial, particularly since large multiple doses can have negative effects. In the present study, we prospectively assessed the effect of different doses of mannitol on intraoperative brain relaxation and adverse effects in patients undergoing craniotomy for the removal of supratentorial brain tumors. We also sought to determine the mannitol dose to provide adequate brain relaxation with the fewest adverse effects. **Objectives:** To assess brain relaxation in using different doses of mannitol during craniotomy.

Materials and Method: The present study will be conducted in the Department of Anesthesiology, Shyam Shah Medical College and associated Sanjay Gandhi and Gandhi Memorial Hospitals, Rewa, Madhya Pradesh from SEP 2022 to SEP 2023 on 90 patients posted for Craniotomy. patients will be divided into three groups as group-A group-B and group-C. Depending on the dose of mannitol given. Each group was aimed as follows. GROUP A: 20% mannitol 0.5gm/kg GROUP B: 20% mannitol 1.0 gm/kg GROUP C: 20% mannitol 1.5gm/kg A detailed history of all selected patients will be taken. A thorough pre-anaesthetic evaluation including the airway, assessment will be performed. The patients will be explained about the entire procedure, informed consent. Intravenous line will be secured. Monitors will be attached and baseline parameters viz heart rate, systolic and diastolic blood pressure, mean arterial pressure, SpO2, ECG tracings will be recorded. Brain relaxation at the opening of the duramater assessed by a neurosurgeon on scale (ROZET QUENTIN SCALE) from 1 to 4.

Result: We found a positive correlation between increased brain relaxation and mannitol dose. The incidence of satisfactory brain relaxation was significantly greater at higher doses of mannitol (1.0 and 1.5 g/kg) compared with the lowest dose (0.5g/kg). Our results showed that although a 0.5- g/kg dose of mannitol caused minimal electrolyte disturbance, the incidence of satisfactory brain relaxation was low at this dose as compared with that using higher doses. Based on our results, the 1.0-g/kg dose of mannitol can be regarded as the optimal dose producing the satisfactory brain relaxation with the minimal adverse effects.in patient undergoing elective supratentorial brain tumor surgery.

Conclusion: The study is ongoing, and the conclusion will be discussed at time of presentation.

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Citation: Ashutosh Garg, Rajeev Dwivedi, Shailja Tiwari, Abhay Raj Yadav. Comparison of Effect of Various Doses of Mannitol Infusion on Brain Relaxation and Cardiac Function in Patients Undergoing Craniotomy for Supratentorial Brain Tumors. Anesthesia and Critical care7 (2025): 35-41.

Received: June 10, 2025
Accepted: June 17, 2025
Published: June 24, 2025

Garg A, et al., Anesth Crit Care 2025
DOI:10.26502/acc.080

Keywords: Supratentorial brain tumors; Mannitol; Brain relaxation; Craniotomy

Introduction

The supratentorial tumors account for 79% of all brain tumors. The most common of which are gliomas, meningiomas and pituitary tumors. They produce significant mass effects in the brain and some are accompanied by significant peritumoral oedema that leads to increased intracranial pressure. Bedford et al. [1] demonstrated a strong correlation between the severity of peritumoral edema before surgery and the subsequent elevation in intracranial pressure following the operation. Rasmussen et al. [2] revealed that the risk of dura opening was very high in patients with glioma having midline shift undergoing craniotomy. Dehydration aids in ensuring proper brain relaxation and facilitates tumor exposure. Mannitol is widely used to reduce intracranial pressure (ICP) in patients with cerebral edema [3,4]. Dehydration of the brain tissue is caused by Increased osmotic pressure within the blood vessels following mannitol infusion, which forces water molecules out of the brain tissue and into the blood vessels [3]. If the blood brain barrier is damaged, mannitol will extravasate and will transfer water molecules into brain tissue, which will aggravate cerebral oedema and increased intracranial pressure. Certain patients might have some degree of disruption of the blood-brain barrier, which could prevent the desired effects of mannitol; however, the magnitude of this disruption is unknown and frequently impacted by multiple-dose mannitol administration. Mannitol reduces ICP by decreasing brain water content, improving cerebral microcirculation, reducing cerebral blood flow via vasoconstriction, and decreasing cerebrospinal fluid volume [5]. But mannitol has several adverse effects, including hypochloremic metabolic alkalosis associated with volume contraction and diuresis, hypernatremia, hypokalemia, and renal failure [6]. Because of tumor size, brain edema, or increased ICP, satisfactory brain relaxation can be required for tumor resection [7]. Satisfactory brain relaxation improves the surgical approach in patients undergoing craniotomy [8]. Mannitol is generally administered intravenously at doses between 0.25 and 1.5 g/kg, [9,10] but the optimal dose has not been established. In the present study, we assessed the effect of different doses of mannitol on intraoperative brain relaxation and adverse effects in patients undergoing craniotomy for the removal of supratentorial brain tumors. We also sought to determine the appropriate dose of mannitol to provide adequate brain relaxation with the minimum adverse effects

Aims and Objectives: To assess brain relaxation in using different doses of mannitol during craniotomy.

Materials and Methods

The present study entitled "Comparison of effect of various doses of mannitol infusion on brain relaxation and cardiac function in patients undergoing craniotomy for supratentorial brain tumors" After getting approval from "Institutional Ethics Committee", present study was conducted in the Department of Anesthesiology, Shyam Shah Medical College and associated Hospitals, Rewa, Madhya Pradesh from SEP 2022 to SEP 2023 on 90 patients posted for Craniotomy. Patients were divided into three groups 30 each depending on the dose of mannitol given.

Each group was aimed as follows.

GROUP A: 30 patients (20% mannitol 0.5gm/kg)

GROUP B: 30 patients (20% mannitol 1.0gm/kg)

GROUP C: 30 patients (20% mannitol 1.5gm/kg)

Inclusion Criteria:

Patients aged >18 years, of either sex, undergoing elective craniotomy for supratentorial tumors under GA.

- ASA-I, II

Exclusion criteria:

Patient refusal

- Chronic Renal Failure.
- Recent use (+ 24 hrs before surgery) of mannitol or other hypertonic solution.
- Glasgow Coma Scale < 13
- Severe hyponatremia or hypernatremia (Na+ < 120 mmol/L or > 155 mmol/L
- Cardiac dysfunction (i.e., congestive heart failure, left ventricle ejection fraction < 40%)

Probability Sampling:

90 Patients were randomized (30 in each group) from the people who were willing to take part in the study. All the patients stand an equal chance of getting into any group.

Methodology

In the PAC room detailed history taken routine investigation collected and physical examination done. All the patients were explaining about study informed written and video consent were taken.

In the operating room all patients were premedicated with IV. Inj. glycopyrrolate 0.2 mg 30 minutes before surgery. Monitors were connected. Baseline data like pulse rate, blood pressure, mean arterial pressure, spO2, temperature, serum electrolytes, preoperative arterial blood gases were recorded.

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Intravenous cannula secured and connected to IV. fluids. Another IV. cannula secured for infusion of 20% mannitol. Patients were preoxygenated with 100% 02 for 3 minutes. Patients were induced with Inj fentanyl 2 mcg/kg of body weight, Propofol 2 mg/kg of body weight, inj vecronium of 0.08 mg/kg was used, to blunt the haemodyanamic response of intubation inj 2% lignocaine of 1.5mg/kg was given IV. Patients were intubated with appropriate size of endotracheal tube. Bilateral air entry checked and connected to closed circuit. Patient was maintained with N20:02 with inj fentanyl 1 mcg /kg of body weight every 45 minutes and inj vecronium in titrated doses. All patients received iv mannitol according to group at time of skin incision.

ETCO2 was maintained in 25-30 mmHg range throughout the procedure. Haemodyanamic variables like blood pressure, mean arterial pressure, pulse rate and SPO2 were recorded regular interval. Urine output, perioperative fluid balance, blood loss and ABG, electrolytes were measured immediately prior to the infusion of mannitol, at 30 and 60 minutes after the administration of mannitol. Data were recorded according to the time frame. At the time of duramater opening, brain relaxation was assessed by a neurosurgeon on ROZET QUENTIN SCALE from 1 to 4 before, after 30 min and 60 min of mannitol infusion.

At the end of surgery, after adequate attempts of respiration patients were reversed with inj glycopyrolate of 10 mg/kg of body weight and inj neostigmine of 40 mcg/ kg of body weight. Adequate suctioning done. To blunt the haemodyanamic response of extubation inj 2% lignocaine of 1.5mg/ kg was given. Patients were then extubated after attaining adequate muscle power.

Parameters Monitored Intraoperatively

Primary outcome measures, brain relaxation at the opening of the duramater assessed by a neuro surgeon on scale (ROZET QUENTIN SCALE) from 1 to 4.

Scale 1: Perfectly relaxed (shrunken dura with prominent veins)

Scale 2: Satisfactorily relaxed (only prominent veins)

Scale 3: Firm brain

Scale 4: Bulging brain

Secondary outcome measures hemodynamic variables, - mean arterial pressure, heart rate, blood pressure,spo2,urine output arterial blood gas analysis, perioperative fluid balance and blood loss time frame - immediately prior to the infusion of mannitol, at 30 and 60 minutes after the administration of mannitol.

Results

Table 1 shoes demographic data of different group.

Table 2 shows that brain relaxation score of Patients.

Patients of Group A Shows value 4 ± 0 before, 3.5 ± 0.092 (30 min) after and 3.0 ± 0.126 (1 hr) after mannitol infusion. P value is less than 0.05.Patients of Group B Shows value 4± 0 before, 2.83 ±0.069 (30 min) after and 2.1 ± 0.11 (1 hr) after induction P value is less than 0.05.Patients of Group C Shows value 4.0 ± 0 before, 1.0 ± 0 (30 min) after and 1.0 ± 0 (1 hr) after induction P value is less than 0.05 (Table 3). On comparing patients of patients of Group A with patients of Group B there is statistically significant brain relaxation seen in patients of Group B, while comparing patients of Group B with C there is statistically significant brain relaxation observed in patients of Group C.

Table 3 shows incidences of electrolyte disturbance increase by increasing the doses of mannitol.

Hyponatremia (low sodium levels) was most common in Group C (26 patients), followed by Group B (16) and Group A (10). This shows a trend of increasing frequency across groups.

Hypernatremia (high sodium levels) was rare, occurring in only 1 patient each in Groups A and B, and none in Group C.

Hypokalemia (low potassium levels) was observed across all groups, with the highest number in Group A (15 patients). Groups C and B had 13 and 10 cases, respectively.

Hyperkalemia (high potassium levels) was absent in all groups, indicating no cases were reported.

A high OG was a common finding across all groups. It was most frequent in Group C (30 patients), followed by Group B (28), and Group A (21). This suggests a progressive increase in high OG prevalence from Group A to Group C.

Demographic Data:

Table 1: Demographic data of different groups.

Parameter	GROUP A	GROUP B	Group C
Male	14	14	17
Female	16	16	13
Age (Mean)	39.33	41.36	46.96
BMI	22.5	25.06	24.36

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Table 2: Brain relaxation score of Patients.

Brain Relaxation Score						
Dose	**Before**		**Over (30 min)**		**Over 1 hour**	
	Before	**SEM**	**Over (30 min)**		**Over 1 hour**	
GROUP A 20 % mannitol (0.5 g /Kg body weight)	4	0	3.5	0.092	3	0.126
GROUP B 20 % mannitol (1 g /Kg body weight)	4	0	2.83	0.069	2.1	0.11
GROUP C 20 % mannitol (1.5 g /Kg body weight)	4	0	1	0	1	0
P value (Welch and Brown-Forsythe ANOVA)	>0.05 (NS)		<0.0001 (Sig.)		<0.0001 (Sig.)	

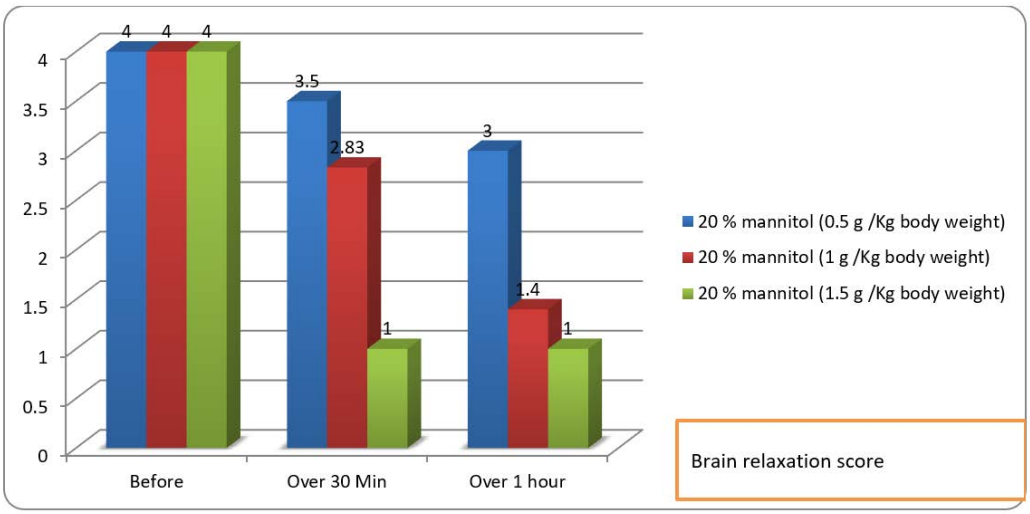
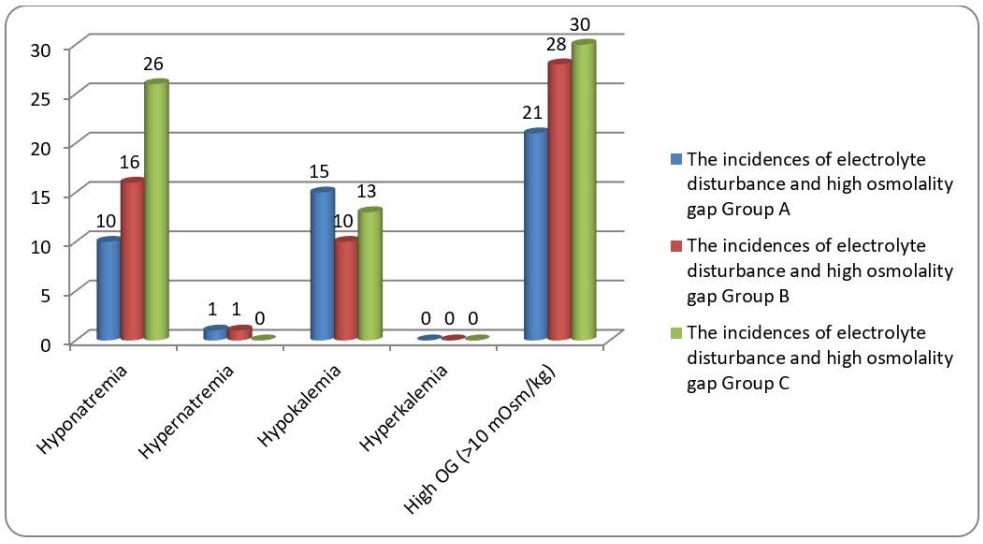


Table 3: The incidences of electrolyte disturbance and high osmolality gap.

The incidences of electrolyte disturbance and high osmolality gap			
Variable	**Patients of Group A**	**Patients of Group B**	**Patients of Group C**
Hyponatremia	10	16	26
Hypernatremia	1	1	0
Hypokalemia	15	10	13
Hyperkalemia	0	0	0
High OG (>10 mOsm/kg)	21	28	30



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Discussion

In demographic data age, sex and BMI shows statistically not significant difference in each group. The demographic data was comparable among all groups [11]. In brain relaxation score Patients of Group A Shows value 4 ± 0 before, 3.5 ± 0.092 (30 min) after and 3.0 ± 0.126 (1hr) after mannitol P value is less than 0.05. Patients of Group B Shows value 4± 0 before, 2.83 ± 0.069 (30 min) after and 2.1 ± 0.11 (1 hr) after induction P value is less than 0.05. Patients of Group C Shows value 4.0 ± 0 before, 1.0 ± 0 (30 min) after and 1.0 ± 0 (1hr) after induction P value is less than 0.05. On comparing patients of group A with group B there is better brain relaxation seen in group B, while comparing group B with C there is significant brain relaxation observed in group C. There is statistically significant change in brain relaxation score with increasing dose of mannitol.Like our study Irene Rozet et al. They studied the impact of a single dose of mannitol (1.0 g/kg) on brain relaxation in patients with diverse intracerebral pathologies, including supratentorial tumors, and observed satisfactory results in brain relaxation. Unlike our study Sorani et al. They conducted a retrospective study to investigate the dose-response relationship between mannitol and intracranial pressure (ICP). Their findings indicated that higher doses of mannitol (>1 g/kg body weight) provided better brain relaxation. However, they also observed significant variability in the degree and occurrence of peritumoral edema among intensive care unit patients with traumatic brain injury.Unlike our study Quentin et al. show that 1.4 g•kg−1 of 20% mannitol results in equivalent brain relaxation scores as 0.7 g•kg−1 in patients. This is contrary to a prior hypothesis. This is because 0.7g /kg is much closer to 1.0 g / kg which was not used by author. However, the authors did not control the number of patients exhibiting a midline shift on the brain CT or MRI, which is an important sign of increased ICP. In a manner similar to our study, Yuming Peng et al. in (2014) investigated the effects of different doses of mannitol (0.7 g/kg, 1.0 g/kg, and 1.4 g/kg) on patients undergoing supratentorial tumor surgery. They aimed to assess how mannitol could potentially enhance tumor exposure and resection by improving brain relaxation. The study included 220 patients with preoperative CT/MRI results showing brain midline shift. Groups A, B, and C received intraoperative dehydration treatment with 20% mannitol solutions at doses of 0.7 g/kg, 1.0 g/kg, and 1.4 g/kg, respectively, administered at a rate of 600 mL/h. The control group did not receive mannitol. Primary outcomes focused on improvements in intraoperative brain relaxation and reduction in dural tension following mannitol dehydration. Secondary outcomes included postoperative results and the occurrence of mannitol-related side effects. The study aimed to determine the optimal dose of 20% mannitol for intraoperative infusion.

Like our study Prasanna K et al. using similar doses like our study and found that better brain relaxation score in mannitol doses of 1.5 g/kg as compare to 0.5g/kg. The incidences of electrolyte disturbance increases by increasing the doses of mannitol .There are increases number of complication with increase doses of mannitol hyponatremia in Patients of group A 10 cases Patients of Group B 16 cases Patients of group C 26 cases , hypernatremia in Patients of group A 1 case Patients of Group B 1 cases Patients of group C 0 cases ,hypokalemia in group Patients of A 15, case Patients of Group B 10 cases, Patients of group C 13 cases , hyperkalemia Zero in each group , High OG (>10 mOsm/kg) in Patients of group A 21 cases Patients of Group B 28 cases Patients of group C 30 cases.Unlike our study Mannian et al. [11]. Mannian observed a notable rise in serum potassium levels, with a maximum mean increase of 1.5 mmol/L, following the administration of high-dose mannitol (1.5 g/kg) in seven patients undergoing cerebral aneurysm clipping. Like our study Prasanna K et al. [12] found similar results in ABG changes urine output.

Similar to our study Bala Krishna Duba et al. [13] Serum electrolytes, blood gases, urine output and haemodynamic stability are better maintained without gross impairment in 1.5 mg/kg of 20% mannitol.Like our study Hyungseok Seo et al [14] compare Group A (67.7% and 64.5% vs 32.2%, $p = 0.011$ and 0.022, respectively). Compared with the other groups, the serum sodium levels in Group D were significantly lower at 30 and 60 minutes but returned to baseline 180 minutes after the administration of the drug. The overall incidence of additional methods for further brain relaxation was comparable among the 4 groups. There was a significant correlation between the degree of brain relaxation and serum osmolality at (30 min) after the end of mannitol administration (correlation coefficient 1.43, $p = 0.036$). Serum osmolality (median [IQR]) measured at (30 min) after the end of mannitol administration was significantly higher in Group D than in other groups (315 [310–317] vs 303 [301–309], 303 [300–307], and 306 [303–310] mOsm/kg in Groups A, B, and C, $p < 0.001$, respectively) and was higher in Group C than in Group B ($p = 0.008$. The serum potassium level (mean [SD]) was higher in Group D than in Group A at (30 min) after the end of mannitol administration (4.1 [0.5] vs 3.7 [0.3] mmol/L, $p = 0.002$) and higher in Group D than in Groups A and B at 60 minutes after the end of mannitol administration (4.2 [0.4] vs 3.9 [0.3] and 3.9 [0.3] mmol/L; $p < 0.001$ and $p = 0.004$, respectively).Like our study JH Kim et al [15]. Regarding potassium levels, extended administration periods commonly result in decreased blood concentrations, but if kidney function is impaired, blood concentrations may instead increase.

Based on our results, the 1.0-g/kg dose of mannitol can be regarded as the optimal dose producing the satisfactory brain relaxation with the minimal adverse effects.in patient undergoing elective supratentorial brain tumor surgery.

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Limitations

Our study has some limitations.

- The mannitol dose was not perfectly blinded in this study, anaesthesiologists knew the dose, although the 3 neurosurgeons who assessed the brain relaxation were completely blinded to the mannitol dose.
- The degree of brain relaxation was evaluated by neurosurgeons blinded to the mannitol dose using a 4-point scale this method is subjective. Subjective variations are possible.
- Quantitative measurements of ICP, such as ventricular or lumbar cerebrospinal fluid drainage, may provide better results; however, but with risks such as bleeding and infection.
- We did not quantitatively measure the extent of peritumoral brain edema. Given the capacity of mannitol to transfer water from brain tissue to plasma, it may be helpful to investigate the relationship between the degree of peritumoral brain edema and mannitol effect.

Conclusion

Based on our results, the 1.0-g/kg dose of mannitol can be regarded as the optimal dose producing the satisfactory brain relaxation with the minimal adverse effects.in patient undergoing elective supratentorial brain tumor surgery.

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