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Effects of Application of 3% Hypertonic Saline with 20% Mannitol on Intraoperative Brain Relaxation in Patients Undergoing Craniotomy

Dr.Medidi Veerababu[*1,]Dr G Pradeep[2], Dr.Boddu Venkat Mukesh Yadav[3,]Dr GummarekulaHarika[4]

[*1](Postgraduate, Department of Anaesthesiology, Great Eastern Medical School & Hospital, Srikakulam Andhra Pradesh, India)
[2](Assistant Professor,Department of Anaesthesiology,Govt. Medical College, Srikakulam, Andhra Pradesh, India)
[2](Postgraduate, Department of Anaesthesiology,Great Eastern Medical School & Hospital, Srikakulam, Andhra Pradesh, India)
[3](Postgraduate, Department of Anaesthesiology, Great Eastern Medical School & Hospital, Srikakulam, Andhra Pradesh, India)

Abstract:
Background: *Brain relaxation is essential in anesthesia for intracranial surgery and it has been considered a neuroprotective measure as it can reduce surgical compression, local hypo perfusion, cerebral ischemia, and blood loss. Mannitol is considered a standard and a first-choice hyperosmotic agent for the treatment of increased ICP in a variety of intracranial diseases. In recent years, hypertonic saline (HS) has emerged as an attractive alternative in hyperosmotic management to get satisfactory brain relaxation and ICP in a variety of neurosurgical practices.*
Aim:*Aim of the study is to compare the effects of the application of 3% hypertonic saline with 20% mannitol on intraoperative brain relaxation in patients undergoing elective craniotomy.*
Materials and Methods:*The current study was done on 50 patients belonging to American Society of Anaesthesiologists (ASA) grade I and 2 posted for elective craniotomywho were allotted randomly into two groupsRandomization was done by computer generated software. Group H patients received 3% hypertonic saline (3ml/kg) via peripheral intravenous (IV) line over 30min. Group M patients received 20% mannitol (0.75 g/kg) via peripheral IV line over 30 min before dural opening.*
Results:*There is no significant difference in the mean age of patients. Most of the patients were males. There is no significant difference in the mean brain relaxation score. Fluid intake was significantly less in group H patients. Blood loss was significantly less in H group patients. The mean urine output was less in M group patients.*
Conclusion: *HS can be routinely used in place of mannitol to achieve perfectly relaxed brain relaxation, superior neurosurgical access, and better hemodynamic stability in elective supratentorial craniotomies.*
Key Words: *Brain relaxation, Craniotomy, Intracranial pressure, Hypertonic saline, Mannitol*

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I. Introduction

Patients with brain tumor commonly have increased intracranial pressure due to swelling of brain tissue. To ease removal of surgical tumor, measures are taken to reduce brain swelling, referred as brain relaxation. Brain relaxation is essential in anesthesia for intracranial surgery and it has been considered a neuroprotective measure as it can reduce surgical compression, local hypo perfusion, cerebral ischemia, and blood loss[1]. Administration of osmotherapy at the onset of craniotomy before opening the duramater is one of the interventions used to produce cerebral relaxation in elective neurosurgeries[2]. Supratentorial brain tumors produce a circumscribed mass lesion, with a surrounding area of cerebral edema. A progressively widening band of edema indicates loss of normal intracranial compliance and also probable impairment of cerebrovascular autoregulation[3].Thus, there is increasing investigation worldwide exploring the ideal therapy to get satisfactory brain relaxation and intracranial pressure (ICP) during neurosurgical procedures[4]. Mannitol is considered as standard and a first-choice hyperosmotic agent for the treatment of increased ICP in a variety of intracranial diseases. However, a wealth of clinical studies has reported that many patients with raised ICP are refractory to the mannitol[5]. And vigorous and repeated administration of mannitol may lead to obvious side effects involving excessive diuresis, electrolyte abnormalities and secondary hypovolemia, while the latter is undesirable in patients undergoing neurosurgical procedures because it may result in intraoperative hypovolemia.[6,7] In recent years, hypertonic saline (HS) has emerged as an attractive alternative in hyperosmotic management to get satisfactory brain relaxation and ICP in a variety of neurosurgical practices.[8,9]

Mannitol is a six-carbon sugar compound. It exerts its intracranial pressure-lowering effects via two mechanisms- an immediate effect because of plasma expansion and a slightly delayed effect related to its osmotic action. The early plasma expansion reduces blood viscosity and this, in turn, improves regional cerebral microvascular flow and oxygenation[10].Use of mannitol is frequently associated with serious adverse effects, such as intravascular volume depletion, hyponatremia, rebound ICP elevation, and renal failure[11]. The effects of hypertonic saline were first described by Weed and Mckibban in 1919. In addition to an osmotic action, hypertonic saline has hemodynamic, vasoregulatory, immunological, and neurochemical effects, relaxes arteriolar vascular smooth muscle and in association with a reduction in cerebral endothelial cell edema, improves cerebral microcirculatory flow.[12] It also expands intravascular volume, thereby potentially augmenting cerebral perfusion pressure.[13, 14]

Aim:
Aim of the study is to compare the effects of the application of 3% hypertonic saline with 20% mannitol on intraoperative brain relaxation in patients undergoing elective craniotomy.

II. Material And Methods

This study was carried out at a tertiary care centre in India from January 2022 to June2022.
Study Design: Interventionalstudy
Study Location: This study was done at a tertiary care teaching institute in the Department of anaesthesia at Great Eastern Medical School and Hospital, Srikakulam, Andhra Pradesh, India.
Study Duration: January 2022 to June2022
Sample size: 50 Patients
Simple random sampling was the sampling procedure used.

Sample size calculation:
As per the previous study,[15]with a difference of 1 point in brain relaxation between groups to be clinically significant, at 95% confidence intervals, with abeta- error of 10% showed a sample size of 24 in each group. So, we included 50 patients in each group.

Subjects & selection method:
Patients were randomized into group H and group M by computer generated table.
GROUP H (n=25), patients received 3% hypertonic saline (3ml/kg) via peripheral intravenous (IV) line over 30min
GROUP M (n=25), patients received 20% mannitol (0.75 g/kg) via peripheral IV line over 30 min before dural opening.

Eligibility criteria:

Inclusion criteria:
1. Patients aged 18 to 60 years.
2. Patients who provided informed consent to participate in the study.
3. Patients with ASA grade I and II.

Exclusion criteria:
1. Pregnant and lactating women
2. Glasgow coma scale<13
3. American Association of Anesthesiologists physical status class 4 or 5
4. Hypo or Hypernatremia (serum sodium below 135 or above 150 meq/l)
5. Osmotherapy (either mannitol or hypertonic saline) given in the last 24 hours
6. Congestive heart failure (LVEF<40% or restrictive diastolic dysfunction on echocardiography)
7. Chronic renal failure (creatinine clearance<30ml/min).

III. Methodology:

In the operation room, peripheral intravenous line was secured and 0.9% normal saline was given for fluid management. The standard monitors including electrocardiogram (ECG), noninvasive blood pressure (NIBP), and pulse oximeter were attached and baseline heart rate (HR), NIBP, and SPO_2readings were recorded. After preoxygenation with 100% O_2 for 3 min, general anaesthesia was induced with 2 mcg/kg fentanyl hydrochloride and 5 mg/kg thiopentone sodium. Muscle relaxation was achieved using 0.1 mg/kg vecuronium bromide. Post-induction radial artery was cannulated and central venous catheter was placed depending on the need of surgery. Every patient received 4mg dexamethasone IV before skin incision. Foley's catheterization was done for all patients to monitor urine output.Intraoperative anesthesia was maintained using oxygen–nitrous oxide mixture (40:60) with 0.7–1 minimal alveolar concentration (MAC) of isoflurane. Opioids for analgesia and vecuronium bromide for muscle relaxation were repeated as needed. PaCO2 was maintained between 30 and 35 mmHg. HR and invasive arterial blood pressure were kept within ± 20% of the baseline values. Normal saline (0.9%) was used as maintenance fluid at 2 ml/kg/h with additional replacement for urine output, third space loss, and blood loss. Brain relaxation was assessed by the operating neurosurgeon, who was blinded to the study drug upon opening the dura on four-point scale (ROZET QUENTIN scale): [15]

Scale 1: Perfectly relaxed (shrunken Dura with prominent veins)
Scale 2: Satisfactorily relaxed (only prominent veins)
Scale 3: Firm brain
Scale 4: Bulging brain

Parameters assessed:

- Age
- Gender
- Brain relaxation score
- Fluid intake
- Blood loss
- Urine output

Statistical analysis:
Data was analyzed using SPSS software version 24.0. Results were expressed as percentages and mean with standard deviation. Students t test was used to compare numerical parameters between two groups. P value below 0.05 is considered significant.

Ethical considerations:
Informed consent was taken from every patient participated in the study.Ethical committee approval was taken before conducting the study.

IV. Results

The current study included 50 patients scheduled for elective craniotomy.

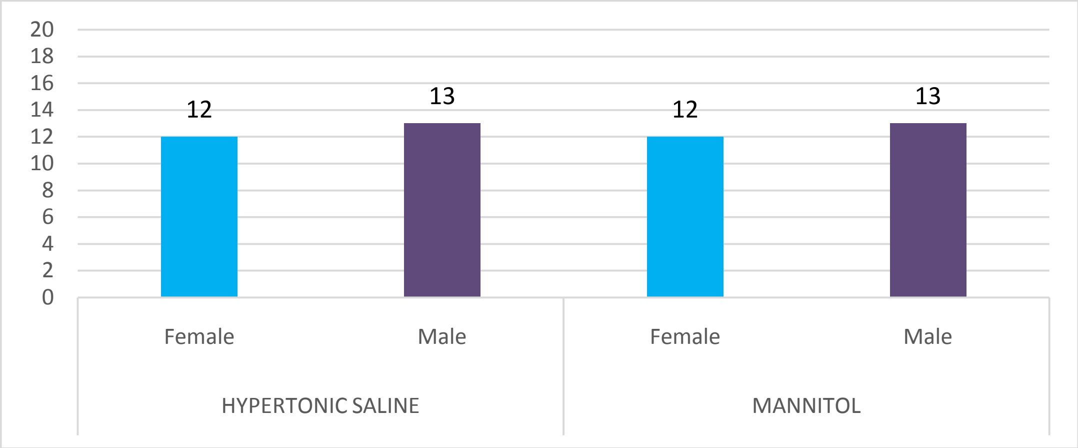
Age:
There is no significant difference in the mean age of patients between two groups(p=0.11).

Table 1 shows mean age of patients

Group	Mean age	P value
H	36.5±10.24	0.29
M	39.6±10.49	

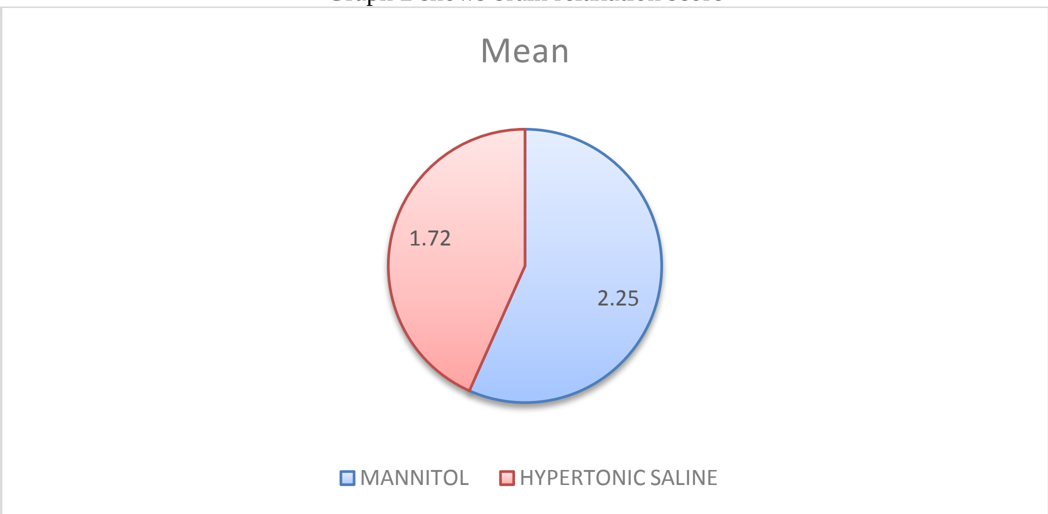
Gender distribution: Most of the patients were males in the current study.

Graph 1 shows gender distribution of patients



Brain relaxation score: There is no significant difference in the mean brain relaxation score between two groups. (p=0.10)

Graph 2 shows brain relaxation score



Fluid intake: There is significant difference in the mean fluid intake between two groups(p=0.0001). It was less in group H patients.

Table 2 shows mean fluid intake among patients of two groups

Group	Mean(ml)	Std. Deviation	P value
M	5214.0	723.4	<0.001 Significant
H	4281.0	341.8	

Blood loss:

There issignificant difference in the pain mean blood loss between two groups. It was more in M group patients.

Table 3 shows blood loss among patients

Group	Mean(ml)	Std. Deviation	P value
M	782.00	328.6	<0.001 Significant
H	841.00	241.8	

Urine output:

There is significant difference in the mean urine output between two groups at various intervals. The mean urine output was more in M group patients.

Table 4 shows mean urine output among two groups at various intervals

Intervals(min)	Group	Mean(ml)	Std. Deviation	P value
Urine Output 60	M	470.00	92.421	<0.001 Significant
	H	324.00	69.402	
Urine Output 120	M	568.00	107.897	<0.001 Significant
	H	284.00	55.377	
Urine Output 180	M	552.00	87.178	<0.001 Significant
	H	234.00	53.463	
Urine Output 240	M	340.00	85.391	<0.001 Significant
	H	206.00	56.495	

V. Discussion

The current study was done on 50 patients belonging to American Society of Anaesthesiologists (ASA) grade I and 2 posted for elective craniotomy who were allotted randomly into two groups. Results showed that there is no significant difference in the mean age of patients. Most of the patients were males. There is no significant difference in the mean brain relaxation score. Fluid intake was significantly less in group H patients. Blood loss was significantly less in H group patients. The mean urine output was less in M group patients in our study.

Girija P. Rath et al[16] and **A.Raghava et al**[17]found that urine output was significantly higher in mannitol group.

In the current study, while comparing the urine output in hypertonic saline group and Mannitol group at different time intervals of 60, 120 ,180 and 240 min, the urine output in mannitol group is higher than hypertonic saline group at all the time intervals and thismean difference is statistically significant, similar to the study conducted by **Liujiazi Shao et al**[18]**.**

Irene Rozet, et al[19] did a prospective, randomized, double-blinded study, and included patients scheduled to undergo craniotomy for various neurosurgical pathologies, requiring intraoperative lumbar cerebrospinal fluid (CSF) drainage. Exclusion criteria were age younger than 18 yr, preoperative hyponatremia or hypernatremia (serum Na <130 or >150 mEq/l), treatment with any hyperosmotic fluid (mannitol or HS) in the previous 24 h, or history of congestive heart failure or kidney disease. After randomization using sealed envelopes, patients were assigned to receive 5 ml/kg of either 20% mannitol (1 g/kg, osmolarity = 1,098 mOsm/l; mannitol group) or 3% HS (osmolarity = 1,024 mOsm/l; HS group) for intraoperative brain relaxation. Both fluids were administered over 15 min using an infusion pump with the type of fluid blinded to both surgeon and anesthesiologist.

Sokhal N et al[20]compared the changes in ICP and systemic hemodynamics after infusion of equiosmolar solutions of both agents in patients undergoing craniotomy for supratentorial tumors.The patients were randomized to receive equiosmolar solutions of either 20% mannitol (5ml/kg) or 3% HS (5.35ml/kg) for brain relaxation. They found that brain relaxation score was comparable in both the groups.

VI. Conclusion

Hypertonic saline provided more acceptable brain relaxation compared to mannitol and hypertonic saline, which resulted in a significant increase in osmolarity compared with mannitol, without diuretic effect. Thus, we conclude that HS can be routinely used in place of mannitol to achieve perfectly relaxed brain relaxation, superior neurosurgical access, and better hemodynamic stability in elective supratentorial craniotomies.

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