Original Article

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Effect of 3% Hypertonic Saline and Mannitol on Brain Relaxation during Supratentorial Brain Tumor Surgery

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Abstract

Introduction: Patients with brain tumor usually have increased intracranial pressure due to swelling of the brain tissue. To ease surgical tumor removal, measures are taken to reduce brain swelling, often referred to as brain relaxation. Administration of osmotherapy is one of the interventions used to produce cerebral relaxation in elective neurosurgeries. The objective of the present study is to compare brain relaxation after the administration of hypertonic saline (3%) and mannitol (20%) in patients undergoing supratentorial brain tumor surgery.

Materials and Methods: A prospective, case-control study included total 60 patients of ASA I and II between age 18 and 70 years were scheduled for supratentorial brain tumor surgery. Two groups were formed; Group HS received 3% hypertonic saline (3 ml/kg), and Group M received 20% mannitol (0.75 g/kg) via peripheral intravenous line over 30 min before dural opening. Outcome measurements were brain relaxation, fluid input, urine output, and blood loss.

Result: Brain relaxation in Group HS was better than those in Group M ($P < 0.0017$). The mean intraoperative urine output in Group HS was lower 881.0 ± 112.1 ml as compared to the Group M 1155.0 ± 145.2 ml ($P < 0.05$). There were no significant differences in fluid input and blood loss in between the two groups.

Conclusion: We conclude that the use of 3% hypertonic saline provides better brain relaxation as compared to 20% mannitol.

Key words: Brain relaxation, Brain tumor, Hypertonic saline, Mannitol

INTRODUCTION

Patients with brain tumor usually have increased intracranial pressure due to swelling of the brain tissue. To ease surgical tumor removal, measures are taken to reduce brain swelling, often referred to as brain relaxation. Brain relaxation is essential in anesthesia for intracranial surgery; it has been considered a neuroprotective measure as it can reduce surgical compression, local hypoperfusion, cerebral ischemia, and blood loss.[1]

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Administration of osmotherapy at the onset of craniotomy before opening the dura mater is one of the interventions used to produce cerebral relaxation in elective neurosurgeries.[2] It has been the cornerstone of the medical management of cerebral edema, irrespective of its etiology, for decades; the mannitol is the most widely used agent.[3]

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.[4]

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

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vascular smooth muscle and in association with a reduction in cerebral endothelial cell edema, improves cerebral microcirculatory flow.[5] It also expands intravascular volume, thereby potentially augmenting cerebral perfusion pressure.[6,7]

The modern day concept of cerebral edema is based on the theory of Klatzo[8] who proposed two different types of edema, cytotoxic, and vasogenic. Edema associated with the brain tumors is considered to be vasogenic. In vasogenic edema, vascular permeability is increased, under normal conditions a sink effect is provided by the ventricles and subarachnoid cerebrospinal fluid to allow steady circulation and replenishment of the extracellular space, this sink effect is overwhelmed in vasogenic edema resulting in extracellular fluid accumulation. Aquaporin 4 (AQP4) is a water channel protein strongly expressed in the brain parenchyma and major fluid compartment, including cerebrospinal fluid and blood AQP4 deletion, aggravates vasogenic brain edema produced by tumor.[9]

On a molecular level morphologically disrupted tight junctions in newly formed brain tumors capillaries are associated with a paucity or lack of proteins such as occludins, claudins, or the junctional adhesion molecules.[10-12] The transmembrane proteins, such as Zo-1, Zo-2, and Zo-3, are in the coupling of tight junctions to the actin cytoskeleton of endothelial cells.[13] Decrease in expression or function of these tight junction proteins leads to opening of the junction and to the formation of edema.[12,13]

The objective of the present study is to compare cerebral relaxation after the administration of hypertonic saline (3%) and mannitol (20%) in patients undergoing supratentorial brain tumor surgery. Blood loss was also evaluated during surgery.

MATERIALS AND METHODS

After obtaining approval of the Ethics Committee, the study was carried out in the Neurosurgery Operation Theatre, Department of Anesthesiology, Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, Madhya Pradesh, India. 60 adults of ASA physical status I and II between ages 18 and 70 years undergoing supratentorial brain tumor surgery were included in this study. A detailed history was taken. Thorough physical examination, routine investigations, and any special investigations if required were done.

It was a prospective case-control study in which two groups were formed, in Group A received 3% hypertonic saline (3 ml/kg) via peripheral intravenous (IV) line over 30 min and those in Group B received 20% mannitol (0.75 g/kg) via peripheral IV line over 30 min before dural opening.

Sample size was derived using a right size sample size calculator. Total 30 cases in each group were selected assuming that the minimum requirement of the cases in each group considered the 95% confidence interval with 5% precision of error.

In the operating room after standard preparation and setting up of monitors and preoxygenation with 100% oxygen for 3 min, anesthetic induction was done using propofol 2 mg/kg. Just before induction IV glycopyrrolate 0.01 mg/kg and fentanyl 2 μg/kg were given. Tracheal intubation was performed 3 min after administration of 0.1 mg/kg vecuronium. Anesthetic maintenance was done with isoflurane at (1.2 minimum alveolar concentration) with oxygen at the rate of 5 L/min and vecuronium was given when required and was repeated according to need. Every patient received 4 mg dexamethasone IV before skin incision. Foley's catheterization was done for all patients to monitor urine output. The impression of neurosurgeon about brain relaxation was assessed on a scale ranging from 1 to 4 where:

1. Perfectly relaxed
2. Satisfactory relaxed
3. Firm brain
4. Bulging brain.

Patients without satisfactory brain relaxation after surgical appraisal received another bolus of the same osmotic agent.

Assessment of blood loss:
Blood loss = Estimated blood volume × ln (hematocrit 1/hematocrit 2).[14]

Where hematocrit 1 is the pre-operative hematocrit and hematocrit 2 is the post-operative hematocrit. Those who required intraoperative blood transfusion were excluded from the study.

Statistical Analysis

Data are presented as the mean ± standard deviation or as the median with ranges. Differences between the HTS and M groups were analyzed using a χ^2 test (demographic variables), a Mann–Whitney *U*-test (brain relaxation scores), and an unpaired Student *t*-test for multiple measurements (fluid input, urine output, blood loss). $P < 0.05$ was considered significant.

OBSERVATIONS AND RESULTS

This prospective case-control study was carried out in the Department of Anesthesiology, NSCB Medical

College. 60 selected cases were included under the study to compare the cerebral relaxation after the administration of hypertonic saline (3%) and mannitol (20%) in patients undergoing supratentorial brain tumor surgery.

Analysis of the demographic characteristics of the studied patients has shown that all groups were matched as regarding age, gender, and weight and it was insignificantly different among the groups (Table 1).

The median of brain relaxation in Group A was 1 and in Group B was 3 by applying Mann-Whitney *U*-test. We found a $P = 0.0017$ which implies a statistically significant difference between the two groups ($P < 0.01$) (Table 2) (Graph 1).

The mean intraoperative fluid input in Group A was 1911.7 ± 131.1 and in Group B was 1891.7 ± 168.2 ml. We did not found any significant different in both studied groups ($P > 0.05$).

The mean intraoperative urine output in Group A was 881.0 ± 112.1 ml and in Group B was 1155.0 ± 145.2 ml, and there was statistically significant different in both groups ($P < 0.05$)

The mean intraoperative blood loss in Group A was 257.1 ± 47.1 ml and in Group B was 266.0 ± 48.2 ml, and there was no statistically significant difference between the two groups ($P > 0.05$) (Table 3).

DISCUSSION

Administration of hypertonic saline or mannitol increases serum osmolarity and decreases intracranial pressure and brain water content in not injured brain areas. The principal mechanism underlying these effects is the induction of water shift from brain tissue to the intravascular space by the hyperosmolarity of hypertonic saline and mannitol because the blood brain barrier is impermeable to sodium and mannitol.

We performed the study as a prospective case control. The demographic data of our study showed that all patients were 18-70 years of age. The mean age of patients in Group A was 38.47 ± 12.9 years and in Group B was 38.03 ± 14.17 years. There was no statistically significant difference in both groups ($P > 0.05$).

We found that 3% hypertonic saline provided better brain relaxation than mannitol. Our study was in agreement with the study of Wu *et al.*[15] in showing the superiority of hypertonic saline over mannitol for providing satisfactory

Table 1: Demographic data

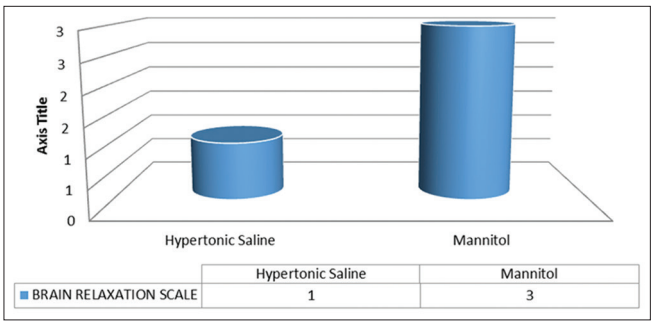
Parameters	Group A (3% HS)	Group B (20% M)	*P* value
Age (years)	38.47±12.9	38.03±14.17	0.89
Sex ratio (male:female)	12:18	18:12	0.19
Weight (kg)	56.5±3.8	55.8±7	0.114
ASA grading (1:2)	7:23	22:8	0.78

Table 2: Brain relaxation scale

Group	Brain relaxation scale
Hypertonic saline	
Median	1
Range	1-4
Mannitol	
Median	3
Range	1-4
P value	0.0017

Table 3: Intraoperative parameters

Parameters	Group A (3% HS)	Group B (20% M)	*P* value
Fluid input (ml)	1911.7±131.1	1891.7±168.2	0.607
Urine output (ml)	881.0±112.1	1155.0±145.	0.045
Blood loss (ml)	257.1±47.1	266.0±48.2	0.460



Graph 1: Brain relaxation scale

brain relaxation. Rozet *et al.*[16] and Li *et al.*[17] found a significant decrease in dural tension score in patients receiving hypertonic saline as compared to mannitol ($P < 0.05$). Our findings concurred with the findings of Li *et al.* in showing the superiority of hypertonic saline over mannitol. However, our study was more significant with respect to the sample size taken. The effectiveness of the hyperosmolar solute depends on the reflection coefficient which determines the relative impermeability of an intact blood-brain barrier to the solute. RC of 1 means an absolutely impermeable solute and RC of 0 means ideally permeable solute. Hypertonic saline may present a theoretical advantage over mannitol because sodium has a higher osmotic RC than does mannitol (1 vs. 0.9), a lower solute leakage may evoke a greater increase in serum osmolarity and a higher transendothelial osmotic gradient

in the vascular compartment may lead to increased brain water extraction into the intravascular space.[15,16]

All the patients in both the groups remained hemodynamically stable, with no significant changes in Heart rate, systolic, diastolic, and mean blood pressure.

The mean intraoperative fluid input in Group A was 1911.7 ± 131.1 ml and in Group B was 1891.7 ± 168.2 ml. We did not found any significant difference between both groups ($P > 0.05$).

Being an osmotic diuretic, infusion of mannitol leads to significant diuresis. We found that the mean intraoperative urine output was more in the mannitol group as compared with HS ($P < 0.05$). These findings are in concordance with earlier studies.[15-18]

Accurate assessment of blood loss is a problem in neurosurgery, estimation of actual blood loss during neurosurgery with traditional methods, such as measuring the loss of blood in suction bottles, drapes, and swab are difficult. Estimated blood loss is not a good predictor of calculated blood loss. Laboratory investigations are better than significant difference with the routine method of visual estimation. Accurate assessment of blood loss is of critical importance in these patients to maintain oxygen delivery to the brain. So, keeping this view in mind in the present study, we did an assessment of blood loss based on laboratory calculations with pre and post-operative hematocrit values. There was no statistically significant difference between both groups ($P > 0.05$). However, blood loss was slightly less in 3% hypertonic saline group as compared to 20% mannitol group. It was compatible with the study did by Romani *et al.*[19] In which median intraoperative blood loss was 200 ml.

CONCLUSION

Administration of the mannitol and HS provided acceptable brain relaxation. HS 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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