Original Research Article

Hypertonic saline (3%): A safe alternative to mannitol (20%) for brain relaxation in elective craniotomy for supratentorial brain tumor

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Abstract

Background: Brain tumor patients presents with increased intracranial pressure due to brain swelling. Osmotherapy is one of the measures to reduce brain swelling, called brain relaxation in elective craniotomies. Objective is to investigate effect of equal volumes (5ml/kg) of 3% hypertonic saline (HS) and 20% mannitol (M) on brain relaxation, serum osmolarity, serum sodium and hemodynamics in elective neurosurgeries. **Methods:** This prospective, randomized and double-blind study was conducted in 60 adult patients posted for elective craniotomy for supratentorial brain tumors. About 30 min before skull opening, all patients received 5 ml/kg of either hypertonic saline (3%) in HS group or mannitol (20%) in M group. Evaluation of brain relaxation as soft, adequate or tight was done by neurosurgeon. Serum osmolarity, serum sodium were tested before and immediately after surgery. Other outcomes were urine output, fluid input and hemodynamic variables. **Result:** Brain relaxation conditions were comparable in both the groups. They were (soft/adequate/tight) 15/10/5 in HS group and 14/9/7 in M group in numbers respectively (P>0.05). Average urine output was higher in group M (1365.0±114.2 ml) than in group HS (992±124.3 ml) p<0.001. The levels of serum osmolarity, serum sodium were higher in group HS as compared to group M at the end of surgery. (P<0.001) There was no significant difference in fluid input and hemodynamics between the 2 groups. **Conclusion:** Hypertonic saline might be an alternative to mannitol for providing brain relaxation.

Key Words: Brain relaxation; brain tumor; elective craniotomy; hypertonic saline; mannitol

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Received Date: 12/11/2019 Revised Date: 10/12/2019 Accepted Date: 16/01/2020
DOI: https://doi.org/10.26611/101513234

Access this article online

Quick Response Code:

Website: www.medpulse.in

Accessed Date: 01 March 2020

INTRODUCTION

Patients with brain tumor usually have swollen brain tissue and thus increased intracranial pressure before surgery. So to ease surgical removal of brain, various methods like hyperventilation, drainage of cerebrospinal fluid (CSF), and hyperosmotic agents like mannitol, hypertonic saline etc. have been used during neurosurgery to control brain relaxation and ICP.[1,2] It has been observed that during elective craniotomies, osmotherapy at the onset of craniotomy before opening the dura mater produces cerebral relaxation. For that purpose mannitol is the first-choice hyperosmotic agent which reduces ICP by withdrawing water from the brain parenchyma to the intravascular space with intact blood–brain barrier (BBB) and thus reduces blood viscosity and transiently increases cerebral blood flow leading to reflex cerebral vasoconstriction.[3]Hypertonic saline (HS) has osmotic action, 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. It also expands intravascular volume, thereby potentially augmenting cerebral perfusion pressure. cerebrospinal fluid pressure is found to be less with HS[4,5].Several studies comparing the effects of HS and mannitol on intracranial pressure (ICP) suggest that HS is at least as effective as mannitol or better than mannitol to achieve brain relaxation during neurosurgeries and traumatic brain injury patients also.[6,8] Our study aims to compare cerebral relaxation after the

How to cite this article: 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.

administration of hypertonic saline (3%) and mannitol (20%) in patients undergoing elective craniotomy.

MATERIAL AND METHOD

After getting ethical committee approval and written informed consent,60 adult patients between 18-60 years of age, ASA physical status II and III, undergoing elective supratentorial brain tumor surgery were randomly selected. Patients excluded were ASA grade IV,V, signs of increased ICP, Glassgow Coma Scale Score<13, history of treatment with hypertonic saline or mannitol within 24 hrs before craniotomy, history of congestive heart failure or severe renal function impairment and preoperative serum sodium level <135 or >150 meq/l. All patients were given injection Dexamethasone 8 mg 8 hourly for 48 hours before brain tumor resection. Patients were randomly divided into two groups, 30 patients in each group (HS and M) in this prospective study. Using peripheral intravenous line, equal volume (5ml/kg) of 3% hypertonic saline in HS Group and 20% mannitol in M Group were infused 30 min before dural opening over 30 min time period. In the operating room, after standard preparation and monitors attachment, patients were preoxygenated for 3 minutes. Injection Glycopyrrolate 0.004 mg/kg, injection Fentanyl 2mcg/kg and injection Lignocaine2% 1.5mg/kg were given intravenously. Induction was done with injection Propofol 2mg/kg and injection Vecuronium 0.12mg/kg intravenously. Tracheal intubation was done using proper size flexometallic endotracheal tube. A radial arterial line was inserted. Anesthesia was maintained with Sevoflurane 1% and injection Vecuronium 0.01mg/kg/hour infusion. If needed intravenous bolus of injection Fentanyl and Propofol were given to maintain hemodynamic stability within ±20% of baseline values. Injection Dexamethasone 4mg intravenous was given before skin incision. Fluid input was maintained with Ringer lactate solution and 0.9% saline with additional fluid for urine output and blood transfusion was given according to clinical condition of patients with haemoglobin value<10 mg%. Assessment of the degree of brain relaxation was done by neurosurgeon blinded to the anesthetic technique and using 3 point scale of brain relaxation- soft (1), adequate (2), tight (3) immediately after opening dura. Patients without satisfactory brain relaxation were given another bolus of same osmotic agent and if needed hyperventilation were initiated to maintain PaCO2 between 30-35 mmHg. Other variables measured were total urine output, fluid input, blood loss, blood transfusion, serum osmolarity, serum Na concentration, arterial blood gases.

OBSERVATION AND RESULT

Analysis of demographic data of the studied patients in both the groups were comparable regarding age, sex, weight, height and ASA status (Table-1). Mannitol and Hypertonic saline had similar effects on brain relaxation (Table-2). On neurosurgeon request, 5 patients in Group HS and 7 patients in Group M were given additional bolus of study solution. Whereas 3 patients in Group HS and 5 patients in Group M needed hyperventilation and were comparable in both groups (P>0.05). Urine output was significantly less in Group HS than Group M (P<0.01) at the end of surgery. Serum osmolarity and serum Na were significantly on higher side in Group HS compared to Group M at the end of surgery (P<0.01). There was no significant difference in duration of surgery, fluid input, blood loss, blood transfusion and hemodynamic variables (Table-3).

Table 1: Patient Characteristics

	Group HS (n=30)	Group M (n=30)	P value
Age (years)	44.5±13.8	46.3±12.7	0.6
Sex (M/F)	18/12	16/14	0.3
Weight (kilograms)	59.7±10.7	59.3±8.8	0.84
Height (Centimeter)	158.16 ± 6.45	160.83 ± 5.66	0.09
ASA physical status (II/III)	14/16	13/17	

Data are presented as mean ± Standard Deviation, ASA – American Society of Anesthesiologists, HS – Hypertonic Saline, M – Mannitol, M/F – Male/Female

Table 2: Brain Relaxation Data

Brain Relaxation	Group HS (n-30)	Group M (n-30)	P value
Soft	15	14	0.9533
Adequate	10	9	0.9726
Tight	5	7	0.9533

Table 3: Intraoperative Data

Parameter	Group HS (n-30)	Group M (n-30)	P value
Duration of surgery (minutes)	261±51	250±45	0.37
Total fluid input (ml)	2184±120	2305±136	0.52
Blood loss (ml)	720±396	740±430	0.85
Blood transfused (ml)	410±430	390±380	0.84
Urine output (ml)	992.0±124.3	1365.0±114.2	<0.0001
No. Patients required additional solution	5	7	0.7480
No. Patients required hyperventilation	3	5	0.7065
Serum osmolarity (mmol/l)			
Baseline	294.4±3.8	292.2±5.3	>0.06
At the end of surgery	304.8±2.5	297.8±3.6	<0.0001
Serum Na (meq/l)			
Baseline	138.6±3.0	137.5±11.6	>0.27
At the end of surgery	144.8±6.2	138.9±6.4	0.0006

Data are presented as mean ± Standard Deviation, HS – Hypertonic Saline, M – Mannitol, ml – milliliter, Na – Sodium

STATISTICS

Graphpad software was used for statistical analysis. All data were presented as the Mean±SD. Categorical data were evaluated by Fischer's exact test (Brain relaxation score, number of patients requiring hyperventilation or additional solution). Unpaired student t-test was used to evaluate clinical variable differences between groups (Age, Weight, Height, Operative duration, Fluid input, Blood loss, Blood transfusion, and Urine output). Multivariate analysis of variance was used to compare difference in hemodynamic and laboratory variables (Serum Na, Serum osmolarity). P<0.05 was considered statistically significant.

DISCUSSION

To make surgical access and removal of brain tumor easy, osmotherapy is being used preoperatively since many decades and mannitol was the first choice. Hypertonic saline as a hyperosmotic agent was first described by Weed and Mckibban in 1919[9]. Recently in many studies hypertonic saline was found a comparable or better choice for brain relaxation in neuropatients.[10-15] Principle mechanism by which both act is that when they are infused intravascularly, they create an osmotic gradient in vascular space between blood and brain and draw fluid from brain tissue into intravascular space and reduce brain volume and thus causes brain relaxation. The cause is being impermeability of blood brain barrier to sodium and mannitol.[3,4,5]

In our prospective randomized controlled study, we found that

1. Brain relaxation was similar in both study groups.
2. M group has higher urine output owing to its diuretic property.
3. HS group has higher serum osmolarity and serum Na levels at the end of surgery

In our study brain relaxation was statistically insignificant between two groups (P>0.05) similar to Rozet *et al*[7] and A Raghava *et al*[19].Patients requiring additional bolus of study solution and hyperventilation were also not significant in this study. De Vivo *et al* [17] and Gemma *et al* [1] in their study reported satisfactory brain relaxation with equal volumes of non-equiosmolar solutions of 7.5% HS and 20% mannitol. Wu *et al* [18] found HS superior over mannitol for satisfactory brain relaxation. However in our study groups, 50% patients in Group HS and 47% patients in Group M had soft brain condition. This can be because of RC (Reflection Coefficient) of HS 1 versus 0.9 of mannitol which means HS remains intravascularly and created osmotic gradient more effectively and extracted more water than mannitol. We maintained PaCO2 between 30-35 mmHg and arterial blood pressure within baseline values± 20% throughout surgery to avoid their effects on brain bulk and for better assessment of brain relaxation. In a systemic review and meta analysis done by Min Li *et al*., comparison between mannitol and hypertonic saline for treating elevated intracranial pressure after traumatic brain injury demonstrates superiority of saline over mannitol in terms of reducing ICP with comparable osmolarity in both the groups.[8] There are other human as well as animal studies also mentioning benefits of HS over Mannitol for reducing ICP, brain water content and superior brain relaxation. Justification given is that intact blood brain barrier is less permeable to saline than mannitol.[16,21,22] All patients of both groups had no significant changes in hemodynamic parameters like heart rate, systolic, diastolic and mean blood pressure and arterial blood gases throughout the study. Mishra *et al* also did not observe significant haemodynamic changes in their study.[20] Li J *et al*. observed decrease in heart rate with HS and no change in mannitol group but there was transient decrease in blood pressure after 10 minutes infusion of mannitol.[2] In some studies HS is found to have favorable effects on both cerebral and systemic hemodynamics.[5,13] In a study done by J da Silva *et al*. HS is found to decrease ICP with rise in cerebral perfusion pressure as well as mean arterial blood pressure.[4] Urine output was 1365.0±114.2 ml in Group M and 992.0±124.3 ml in Group HS which was statistically highly significant (P<0.0001).It is owing to osmotic diuretic effect of mannitol. Rozet *et al*. in their study had similar results.[7] Francony G also noted more urine output without any difficulty in vascular filling with mannitol.[10] HS increased serum sodium concentration, which stimulates release of anti diuretic hormone and thus more free water absorption from kidney explains comparatively less urine output in Group HS. In a study done by A Raghva *et al*., HS group had less urine output.[19] Intraoperative fluid input, blood loss and blood transfused during surgery were statistically insignificant between two groups (P>0.05).Same findings were observed in studies done by Wu *et al*[18] and Mishra *et al*[20].Serum osmolarity, serum Na concentration were comparable before surgery (P>0.05) .HS group has higher serum osmolarity and serum Na concentration at the end of surgery (P<0.0001).in many studies high Na concentration in HTS group is observed[7,12,18,23] while serum osmolarity was same for both groups in a study done by Rozet *et al*[7].One study has observed rise in serum sodium level 120 min after HS infusion.[10] De Vivo P found HS as a safe alternative to mannitol in neurosurgery especially when multiple doses are required because in their study they observed decrease ICP without reducing CVP, serum osmolarity and serum Na levels with the use of Hs in comparison to mannitol.[17]

CONCLUSION

Acceptable brain relaxation under a uniform type of neurosurgery can be achieved with both hypertonic saline as well as mannitol. Mannitol resulted in more diuretic effect and HS resulted in significant rise in serum osmolarity and na concentration without affecting hemodynamics. So, we can conclude that HS can be used as an alternative to Mannitol to achieve brain relaxation in elective supratentorial craniotomies.

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Source of Support: None Declared
Conflict of Interest: None Declared