(International Print/Online Journal)

SJIF IMPACT FACTOR: 4.617
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 2, Issue 5, Page No: 206-212
September-October 2019

IJMSCR

A study to compare the efficacy of Mannitol alone along with combination with Glycerol and Furosemide on GCS score and effect on serum electrolytes and creatinine levels in patients of traumatic brain injury

[1]Dr Manish Yadav, [2]Dr. Vijayveer Singh, [3]Dr. Divyam Sharma, [4]Dr. Sunil Garg
[1,2]M.Ch Trainee (Neurosurgery), [3]Senior Resident Neurosurgeon DNB (Neurosurgery)
[4]M.Ch (Neurosurgery) Senior Professor
Dr. S.N Medical College and associated M.D.M Hospital Jodhpur, Rajasthan

Corresponding Author
Dr. Divyam Sharma (Department of Neurosurgery)
Dr. S.N Medical College and associated M.D.M Hospital Jodhpur (Rajasthan)

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

ABSTRACT

Introduction: Mannitol is widely used to reduce cerebral edema and raised intracranial pressure following brain injury. Along with this Glycerol and Furosemide are also the commonly used agents to reduce the intracranial pressure. The authors did a study the efficacy of mannitol alone and in combination with glycerol and furosemide in reducing the intracranial pressure and effect on serum electrolytes and creatinine levels in patients of traumatic brain injury.

Methods: This was a prospective observational study which was done in the department of neurosurgery in MDM hospital, Jodhpur, India. A total of 36 patients, divided into equal groups of all ages and both sexes who presented with traumatic brain injury were included in this study. Group 1- received 100 ml of 20% mannitol intravenously six hourly , Group 2 -received 20% mannitol 100 ml eight hourly intravenously plus 30ml of 95%glycerol syrup (through Ryle's tube) thrice daily and Group 3 -received 100ml of 20% mannitol eight hourly intravenously plus 20 mg Inj. furosemide intravenous (i.v) 12 hourly**.** Non Contrast Computed tomography (NCCT) Head was done and surgical intervention was done if required. Follow up of Glasgow Coma Scale (GCS), serum osmolality, serum creatinine, serum sodium and potassium was done for five days and the results were noted.

Results: A total of 36 patients were included in the study. Minimum age was 7 years and maximum age was 75 years. The mean age of patients was 33.13years. There were 31 male patients and 5 female patients. GCS improved in 92% patients in Group 1 while in 8% patients GCS remained same on fifth day, as on admission. No major change was seen in serum sodium, potassium and creatinine levels. Serum osmolality increased progressively to normal levels till 5th day in all patients. In group 2, GCS improved in 75% patients while no significant change seen in 8.33% patients and deteriorated in 16.6% patients. No significant change was seen in serum sodium, potassium and creatinine. While serum osmolality deteriorated in 62.5% patients, no significant change seen in 8.26% patients, improved in 17.52%. In group 3, GCS improved in 66.67 % patients while remained same in 25% patients and deteriorated in 0.83 % patients. No significant change was seen in serum potassium. Serum sodium increased in 16.66% patients due to free water clearance and Serum creatinine increased in one patient. While serum osmolality deteriorated in 37.5% patients, improved in 25% patients, while no significant change seen in 37.5%.

Conclusion: Mannitol alone was found to be the most effective and safest decongestant agent for decreasing intracranial pressure in patients with traumatic brain injury.

Keywords: Traumatic brain injury; Mannitol; Glasgow coma scale; Mannitol plus Glycerol; Mannitol plus furosemide; Raised intracranial pressure.

INTRODUCTION

Mannitol is widely used to reduce cerebral edema and raised intracranial pressure following brain injury. Other agents are hypertonic saline, barbiturates, glycerol or glycerol plus mannitol. Both mannitol and glycerol are osmotic diuretics. Mannitol increases plasma osmolality, so water moves from brain into blood along an osmotic gradient. In this way mannitol reduces brain water content, intracranial pressure and edema, improving neurological outcomes.[1-3] Rebound edema has been observed after long term administration of intravenous (iv) mannitol. The combination of glycerol to mannitol avoids rebound edema.[4] Furosemide is a distal loop diuretic. Furosemide alone does not have any effect on plasma osmolality and brain water content. Furosemide in combination with mannitol produce more increase in plasma osmolality and a larger decrease in brain water than mannitol alone.[5] After our research, we haven't found any study which compared the effect of mannitol plus glycerol and mannitol plus furosemide iv combination and 20% mannitol in patients with severe traumatic brain injury (TBI). This study aims to compare the efficacy of the above-mentioned three drugs in reducing brain edema in patients with traumatic brain injury.

MATERIAL AND METHOD

This prospective study was done in the Department of Neurosurgery, Dr. S.N Medical college and associated MDM hospital, Jodhpur, Rajasthan. Total 36 patients of all age groups and both sexes were included in this study. Patients were selected according to anti-edema therapy initiated by neurosurgical unit (12 in each group)

Group 1- received 100ml of 20% mannitol six hourly intravenously (i.v).

Group 2 -received 20% mannitol 100ml eight hourly i.v plus 30ml of 95% glycerol syrup (through ryle's tube).

Group 3 -received 100ml of 20% mannitol eight hourly i.v plus 20 mg Inj. furosemide i.v 12 hourly**.**

All traumatic brain injury patients were stabilized in emergency department. NCCT Head was done and surgical intervention done if required. Patients were transferred to surgical intensive care unit. Patients received analgesia, inotropic support or ventilator support according to requirement. Baseline GCS, vitals and investigations like serum sodium, potassium, creatinine, plasma osmolality, blood gas analysis, blood sugar, hemoglobin, and prothrombin time recorded.

All patients managed conservatively or surgically and received mannitol or combination according to the group. Follow up of the patients done for five days and investigated daily. Comparison was done at the end of fifth day based on change in GCS, serum sodium and potassium, plasma osmolality and serum creatinine. Data entry was done in Microsoft excel and Data analysis was done using stata 12. Demographic and clinical data were described as percentages. Comparison was analyzed using paired t test. A p- value of less than 0.05 was considered significant.

RESULTS

A total of 36 patients were recruited in this study; minimum age was 7 years and maximum age was 75 years. The mean age of patients was 33.13years. Road traffic accidents were the most common mode of injury and intracranial contusions were the most common presentation. Thirteen patients (36 %) underwent surgical intervention when indicated and were continued on the preoperative decongestant regimen. (Table 1)

In group 1- GCS improved in 92% patients while in 8% patients GCS remained same on fifth day, as on admission. No significant change was seen in serum sodium, potassium and creatinine. While serum osmolality increased progressively to normal levels till 5th day in all patients (Table 2). Mean increase in osmolality was 13.2mosmol/kg.

In group 2- GCS improved in 75% patients while no change seen in 8.33% patients and deteriorated in 16.6% patients. No significant change was seen in serum sodium, potassium and serum creatinine. While serum osmolality deteriorated in 62.5% patients, no significant change seen in 8.26% patients, improved in 17.52%. Mean increase in osmolality was 30.5mosmol/kg, decrease was15.5mosmol/kg.

In group 3- GCS improved in 66.67 % patients while remained same in 25 % patients and deteriorated in 0.83 % patients. No significant change was seen in serum potassium. Serum sodium increased in 16.66% patients due to free water clearance, remains normal in rest. Serum creatinine increased in one patient. While serum osmolality deteriorated in 37.5% patients, improved in 25% patients, while no seen in 37.5%. Mean increase in osmolality was 12, decrement was 32.7mosmol/kg.

Comparison of GCS score was done amongst the three groups on day 0 and day 5 of admission and mean score of GCS scale improved in all three groups. On analysis with paired t test it was found

Volume 2, Issue 5; September-October 2019; Page No.206-212

statistically significant [p value < 0.05] (Table 3 and Figure 1)

When Serum sodium was compared across different groups, it was found that there was no statistical significant difference seen among the three groups (Table 4 and Figure 2).

Serum osmolarity (Table 5, Figure 3) and Serum creatinine (Table 6, Figure 4) when compared in the three different groups also showed no statistical significant difference.

TABLE 1: Mode of Injury with pathology

Mode of Injury	CT/MRI Findings	Intervention done
Road traffic accident-30 patients	EDH with brain edema- 4	Surgical intervention- 13
Fall from height- 6	SDH- 4	Conservative management- 23
	Diffuse axonal injury-7	
	Contusions- 11	
	SAH- 1	
	Multiple- 9	

TABLE 2: Assessment after 5 days

	Group 1(Mannitol)	Group 2(Mannitol + Glycerol)	Group 3(Mannitol +Furosemide)
GCS Improvement	92% Patients	75% Patients	66.67% Patients
GCS Deterioration		16.6%	8.3 %
GCS Same	8%	8.33%	25%
Serum Sodium	No significant change	No significant change	Increased in 2 patients
Serum Potassium	Normal	Normal	Normal
Serum creatinine	Normal	Normal	Increased in 1 patient
Serum Osmolality Improvement	58.31% patients	8.33% patients	16.33% patients
Serum Osmolality Deterioration	0 % patients	41.65% patients	50% patients
Serum Osmolality Same	-	8.33%	-

TABLE 3: Comparison of GCS score from Day 0 to Day 5 among three different groups

	GCS scale (Mean ± SD)		
	Day 0	**Day 5**	**p value**
Group1	4.92±1.40	7.17±1.75	0.002
Group 2	4.50±1.16	7.08±2.47	0.012
Group 3	4.83±1.19	6.00±1.86	0.041

TABLE 4: Comparison of Serum Na. from Day 0 to Day 5 among three different groups

	S. Na (Mean ± SD)		p value
	Day 0	**Day5**	
Group 1	134.91 ± 4.93	133.91 ± 6.92	0.708
Group 2	135.58 ± 7.90	131.83 ± 4.04	0.164
Group 3	136.00 ± 4.99	138.08 ± 9.90	0.477

TABLE 5: Comparison of Serum Osmolality from Day 0 to Day 5 among three different groups

Groups	S. Osmolality (Mean ± SD)		p value
	Day 0	Day 5	
Gp1	279.34±11.11	285.84± 5.88	0.100
Gp2	278.73± 20.20	274.30 ± 10.85	0.581
Gp3	283.06 ± 8.9	278.80 ± 13.99	0.174

TABLE 6: Showing comparison of Serum Creatinine from Day 0 to Day 5 among three different groups

Groups	S. Creatinine (Mean ± SD)		p value
	Day 0	Day 5	
Gp1	0.78± 0.13	0.78 ± 0.17	1.000
Gp2	0.78 ± 0.21	0.85± 0.15	0.370
Gp3	0.89 ± 0.25	1.60± 2.68	0.379

Figure 1: Chart showing the comparison of GCS score from day 0 to day 5

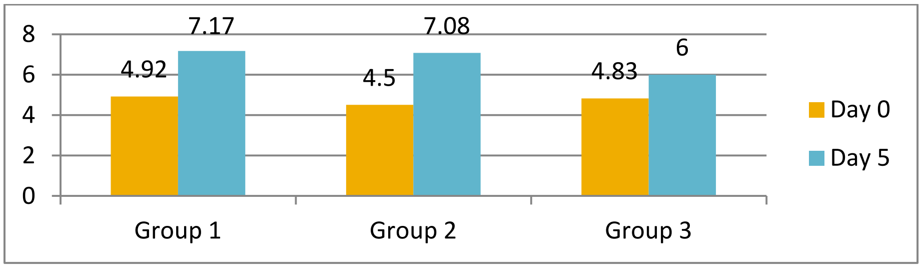


Figure 2: Chart showing the comparison of Serum sodium from day 0 to day 5

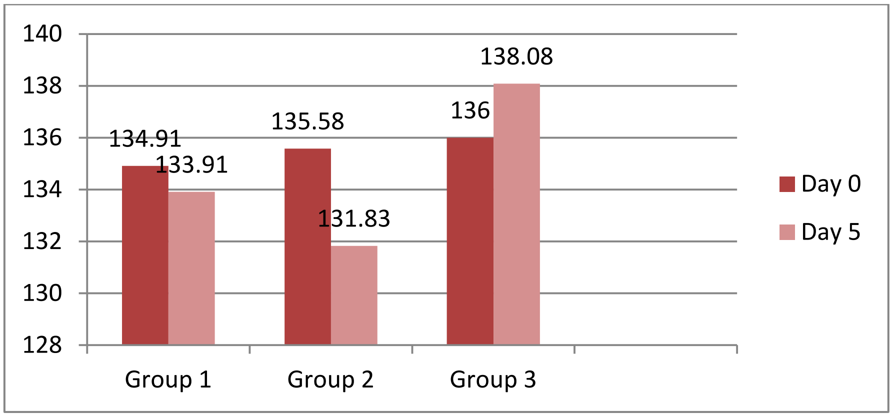


Figure 3: Chart showing the comparison of Serum osmolarity from day 0 to day 5

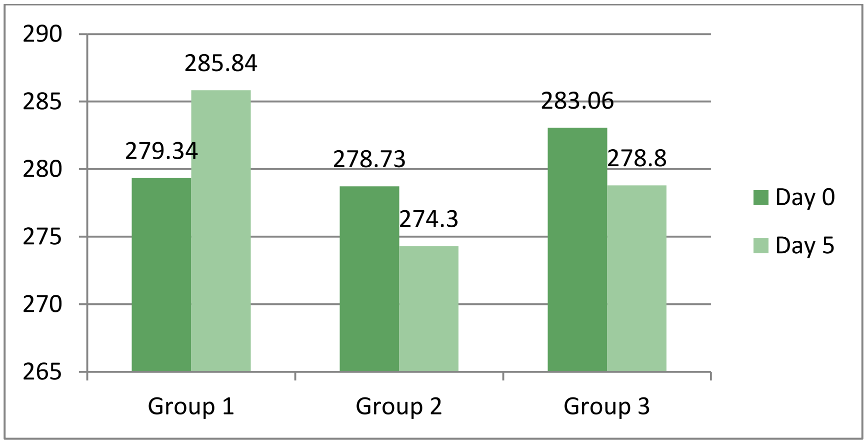
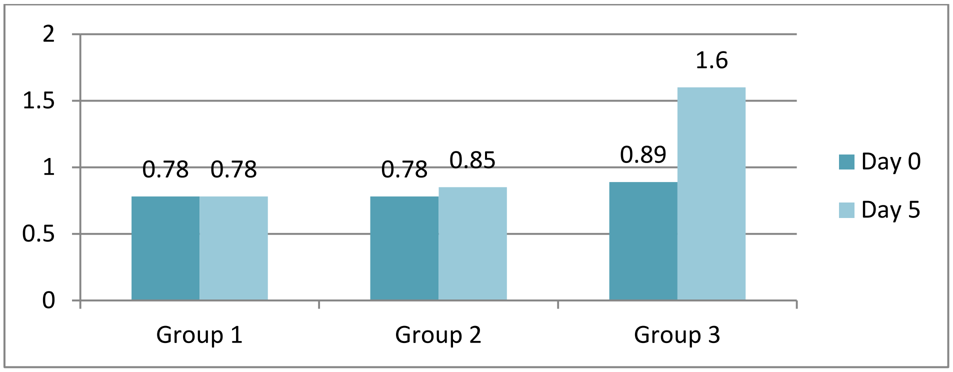


Figure 4: Chart showing the comparison of Serum creatinine from day 0 to day 5



DISCUSSION

Traumatic brain injury is very common in India due to road side accidents, assault or fall from height. Many agents are used to decrease cerebral edema and ICP, to improve neurological outcomes. The treatment with hypertonic fluids is still an attractive means of decreasing the intracranial pressure (ICP) without having a negative effect on the CPP. Various clinical and experimental studies have demonstrated that single doses of mannitol can substantially reduce increased ICP.[5] However, the long-term beneficial effects of mannitol are still controversial, and there are few reports of aggravated brain edema after repeated mannitol treatment. Glycerol (glycerine) is another attractive agent that has been found to exert beneficial effects in controlling ICP in edema and other pathologic conditions. Apart from their hypertonic nature, they also act as a free radical scavenger, antioxidant, and activator of plasma prostaglandin resulting in vasodilation. Either glycerol or mannitol can be administered individually; however, the addition of glycerol to mannitol avoids rebound edema, which is likely to be observed with the intravenous administration of only mannitol.[4-7]

The effects of furosemide on brain edema have been inconsistent; some have shown no drug-induced reductions in water content hence any reduction in edema[8-10], whereas other studies have shown reductions in edema.[11-13]

Patil H et al compared the efficacy of 3% hypertonic saline, 20% mannitol, and 10% mannitol plus 10% glycerol combination in reducing the raised ICP and change in Glasgow Coma Scale in patients with severe traumatic brain injury. The maximum change in the GCS was seen after the bolus dose of 3% hypertonic saline, followed by 10% mannitol plus 10% glycerol combination and then 20% mannitol. But no clear benefit in neurological outcome was seen compared with 20% mannitol.[14] In contrast to above, in our study more improvement regards to GCS and plasma osmolality observed in mannitol group as compared to mannitol plus glycerol combination. Also they had a limitation that did not analyze the late effects of osmotic agents and effects of repeated infusion or maintenance dose and side effects of the drugs.

Harbaugh et al first described therapy with a combination of mannitol and furosemide in rabbits subjected to a cortical freezing injury. They demonstrated a reduction of ICP but no advantage of the combination as compared with mannitol alone was observed.[12] another study was done to examine the effects of furosemide and mannitol, alone and in combination, on brain water content in brain-injured rats. They found out that mannitol increased plasma osmolality and reduced water content of the injured and contralateral hemispheres of rat brain, whereas no effect of furosemide when given either alone or in combination with mannitol was observed on brain water content.[15] Similarly in our study no advantage of mannitol plus furosemide combination seen regards to GCS and plasma osmolality as compared to mannitol alone.

Our study has shown that mannitol is associated with linear improvement in GCS, serum osmolality and no significant effect on serum sodium, potassium and creatinine. While GCS improved in less number of patients in group 2 (mannitol + glycerol) and group 3(mannitol + furosemide). There was significant difference seen in the GCS amongst all the groups, but the best improvement was seen in group 1.

No significant change was in serum sodium, potassium and creatinine in group 1 and group 2. Serum sodium increased in two patients in group 3, probably due to free water clearance. Serum creatinine increased in one patient, probably due to dehydration. Serum osmolality deteriorated in some patients in group 2 & 3, however all these changes were not statistically significant.

There are some limitations in our study. This was a simple prospective observational study of GCS score as a measure of clinical assessment which has its own fallacies [17]. Also no definitive intracranial pressure measurement such as subdural bolt or intraventricular pressure monitoring was done due to financial limitations.

CONCLUSION

The improvement in the GCS score was seen maximum in the patients who received mannitol alone followed by mannitol + glycerol followed by mannitol + furosemide. Mannitol+ furosemide also showed the greatest variations in the serum sodium and osmolality levels when compared with the other groups. Thus according to our study, mannitol was found to be the most effective and safest decongestant agent for decreasing intracranial pressure in patients with traumatic brain injury. However this was only an observational study and further randomized control studies are needed in future to provide better comparison and guidelines regarding the use of these three decongestant agents for the management of traumatic head injury.

REFERENCES

1. Paczynski RP, He YY, Diringer MN, and Hsu CY: Multiple-dose mannitol reduces brain water content in a rat model of cortical infarction. Stroke 1997; 28:1437–44.
2. Hartwell RC, Sutton LN: Mannitol, intracranial pressure, and vasogenic edema. Neurosurgery 1993; 32:444–50.

Volume 2, Issue 5; September-October 2019; Page No.206-212

3. Donato T, Shapira Y, Artru A, Powers K: Effect of mannitol on cerebrospinal fluid dynamics and brain tissue edema. Anesth Analg 1994; 78:58–66.
4. Soustiel JF, Mahamid E, Chistyakov A, Shik V, Benenson R, Zaaroor M. Comparison of moderate hyperventilation and mannitol for control of intracranial pressure control in patients with severe traumatic brain injury—a study of cerebral blood flow and metabolism. Acta Neurochir (Wien).2006; 148:845-851.
5. Sheikh AA, Matsuoka T, Wisner DH. Cerebral effects of resuscitation with hypertonic saline and a new low-sodium hypertonic fluid in hemorrhagic shock and head injury. Crit Care Med. 1996; 24:1226-1232.
6. Berger S, Schurer L, Hartl R, Messmer K, Baethmann A. Reduction of post-traumatic intracranial hypertension by hypertonic/hyperoncotic saline/dextran and hypertonic Mannitol. Neurosurgery. 1995;37:98-107
7. Kaufmann AM, Cardoso ER. Aggravation of vasogenic cerebral edema by multiple-dose mannitol. J Neurosurg. 1992; 77:584-589.
8. Gaab M, Knoblich OE, Herrmann F, Fuhrmeister U: Effect of furosemide (Lasix) on acute severe experimental cerebral edema. J Neurol 1979; 220:185–97
9. Millson C, James HE, Shapiro HM, Laurin R: Intracranial hypertension and brain oedema in albino rabbits: II. Effects of acute therapy with diuretics. Acta Neurochir 1981; 56:167–81.
10. Harbaugh RD, James HE, Marshall LF, Shapiro HM, Laurin R: Acute therapeutic modalities for experimental vasogenic edema. Neurosurgery 1979; 5:656–65.
11. James HE, Bruce DA, Welsh F: Cytotoxic edema produced by 6-aminonicotinamide And its response to therapy. Neurosurgery 1978; 3:196–200.
12. Tornheim PA, McLaurin RL, Sawaya R: Effect of furosemide on experimental Traumatic cerebral edema. Neurosurgery 1979; 4:48–52.
13. Clasen RA, Pandolfi S, Casey D: Furosemide and pentobarbital in cryogenic cerebral injury and edema. Neurology 1974; 24:642–8.
14. Patil H,Gupta R. A Comparative Study of Bolus Dose of Hypertonic Saline, Mannitol, and Mannitol plus Glycerol Combination in Patients with Severe Traumatic Brain Injury. World Neurosurg. 2019; 125:e221-e228.
15. Harbaugh RD, James HE, Marshall LF, Shapiro HM, Laurin R: Acute therapeutic modalities for experimental vasogenic edema. Neurosurgery 1979; 5:656–65.
16. Todd MM, Cutkomp J,Brian JE. Influence of Mannitol and Furosemide, Alone and in Combination, on Brain Water Content after Fluid Percussion Injury. Anesthesiology 2006; 105:1176–81.
17. Sternbach GL. The Glasgow coma scale J Emerg Med. 2000;19(1):67-71