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Original Research Article

Comparison of the efficacy of 3% hypertonic saline and 20% mannitol in reducing intracranial pressure in patients with traumatic brain injury

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ABSTRACT

Background: Objective of the study was to compare the effects of 3% hypertonic saline (HTS) solution and 20% mannitol (MTL) solution on intracranial hypertension.
Methods: The prospective study subjects consisted of 60 patients with traumatic brain injury admitted to the Department of Neurosurgery, RIMS, Ranchi between March 2020 to February 2023. The subjects fulfilling the inclusion criteria were selected and divided into two groups: group A (n=30): treated with 3% HTS, and group B (n=30): treated with 20% MTL.
Results: All the findings were noted on Microsoft excel sheet and data were analyzed using the statistical package for the social sciences (SPSS) 21.0 package. Quantitative data were analyzed using student's t-test (paired and unpaired) and categorical data were analyzed by the test of proportion, Chi-square, and Fisher's exact test.
Conclusions: Both 3% HTS and MTL can effectively reduce intracranial pressure, but 3% HTS has a more sustained effect on intracranial pressure and can effectively increase cerebral perfusion pressure.

Keywords: TBI, Hypertonic saline, Mannitol, Intracranial pressure

INTRODUCTION

Severe traumatic brain injury (TBI) is one of the significant causes of morbidity and mortality.[1] Studies from the United States and New Zealand have estimated approximately 500–800 new cases of TBI per 100,000 people each year. As per a report by the Ministry of Road Transport, Government of India, 1.4 lakh road accidents happened in 2007 which killed 40,612 people, and 1.5 lakh people were injured. Hence, India is leading the world in fatalities due to road traffic accidents. Young males are a commonly affected population in TBI.[2]

Intracranial pressure (ICP) is the pressure inside the skull and at rest is normally 7-15 mmHg for an adult in a supine posture while in the standing posture, it does not exceed 15 mmHg. By definition, an ICP that exceeds 20 mm Hg is considered high and is indicative of the need for immediate treatment.[3]

Brain trauma foundation (BTF) guidelines recommended the use of mannitol for the treatment of high ICP. They state that "mannitol is effective in reducing ICP in the management of traumatic intracranial hypertension" and that "current evidence is not strong enough to make recommendations on the use, concentration, and method of administration of hypertonic saline for the treatment of traumatic intracranial hypertension.

Hyperosmolar treatment is one of the most important methods for the treatment of cerebral edema and has been employed since the early 1960's.[4] Urea, glycerol, and mannitol were used for the treatment of this condition in the early years. The use of urea and glycerol was soon abandoned because of their low efficacy. Mannitol (MTL) is still used widely. Side effects of MTL such as rebound effect, serum electrolyte imbalance, and hypovolemia have led to the continued search for other osmotically active agents. One such agent is hypertonic saline (HTS).[5] In addition to its potent osmotic effect, HTS has beneficial effects on vascular tone.

Therefore, a study was conducted to compare the efficacy of 3% HTS and 20% MTS in reducing ICP in patients with TBI.

METHODS

This hospital-based prospective study was conducted with the approval of the institutional ethical committee between March 2020 to Feb 2023. The study subjects consisted of 60 patients with traumatic brain injury admitted to the Department of Neurosurgery, RIMS, Ranchi.

The subjects fulfilling the inclusion criteria were selected and divided into two groups: group A (n=30): treated with 3% HTS, and group B (n=30): treated with 20% MTL.

Inclusion criteria

Study participants older than 18 years of age, severe TBI (GCS score ≤8 in emergency), hospital stays of length ≥24 hours, and patients with ICP >20 mm of Hg were included

Exclusion criteria

Patients with severe multiple comorbidities and systemic abnormalities, patients who were transferred to another acute care hospital within 24 hours of hospital stay, patients who leave against medical advice, patients with penetrating injury or other chest and abdominal blunt injury, and operated cases were excluded.

Data collection and pre-operative evaluation

The prospectively collected data (epidemiological details, detailed history; proforma) in the brain and spine database of Rajendra Institute of Medical Sciences, Ranchi was utilized for the study. Data on patient age, sex, date and time of presentation of trauma and that of a confirmed diagnosis, clinical features at the time of presentation (especially headache, vomiting, eye, nose, and throat seizure attacks), status of systemic disease burden and co-morbidities (namely-diabetes, hypertension, and morbid obesity) immediately before surgery were noted. Pre-operative imaging included plain computed tomography of the brain. Pre-anesthetic check-up and surgical profile investigations consisted of electrocardiography, echocardiography, chest radiographs (plain; postero-anterior view), evaluating the blood for complete blood count, fasting and post-prandial blood glucose levels, blood urea and serum creatinine levels, serum electrolytes, coagulation profile.

Size, location, and radiological appearance of the lesion, size of the ventricles, midline shift (if any), depth of the hematoma from the cortical surface, and associated radiological findings like extension of bleed into the ventricles were noted. Clot volume (A×B×C)/2, where A, B, and C are the three diameters of the clot. Note was made of any subarachnoid hemorrhage, hydrocephalus. If an external ventricular drain was applied, details regarding the same were also taken.

Intervention

20% MTL and 3% HTS was administered in their respective groups as a loading dose (5 ml/kg) followed by a maintenance dose (2 ml/kg) every 6 hours for 6 days.

Measurements taken

ICP monitoring was done by ICP monitor (CODMAN MODEL MONITOR); blood pressure by NIBP, at admission and every 6 hours, both pre and post-drug (30 min of 3% HTS or MTL therapy); serum creatinine: before starting treatment and after 48 hours; blood urea nitrogen: before starting treatment and after 48 hours; serum electrolytes: before starting treatment and then in every 12 hours; ABG: before starting treatment, and after 12, 24, 36 and 48 hours; computed tomography (CT) scan or magnetic resonance imaging (MRI) when needed of the head; GOS: at the time of discharge; and GCS.

Surgical procedure for ICP probe insertion

The ICP monitoring procedure occurred under general anesthesia, sedation, or with local anesthetic with a small amount of hair shaved off.

For insertion of the ICP catheter first it is ensured that the patient is properly sedated (or under general anesthetic) then the scalp is made numb by applying local anesthetic and a fine burr hole is made in the skull just behind the hairline in Kocher point through which the catheter is placed.

The catheter is then kept in place with a locking mechanism (bolt) or the wire coiled and stitched to the scalp to stop it from being pulled out. The patient is then shifted to the ward.

Data analysis

All the findings were noted on Microsoft excel sheet and data were analyzed using the statistical package for the social sciences (SPSS) 21.0 package (SPSS Inc., Chicago, USA). Quantitative data were analyzed using Student's t-test (paired and unpaired) and categorical data were analyzed by the test of proportion, Chi-square, Fisher's exact test. Results of the analysis were evaluated under a 95% confidence interval and mean values as mean±standard error of the mean. The value p less than equal to 0.05 was considered statistically significant.

RESULTS

The descriptive statistics of age show that the mean age of the subjects with TBI included in the study was 43.3 with a standard deviation of 15.8. There was statistically no difference in the age of the patients included in both the study groups. The study included 47 males and 13 females. Group A included 27 males and 3 females while group B included 20 males and 10 females.

RTA was the highest among the modes of injuries followed by falls. In the 3% HTS group, the highest mode of injury was fall followed by RTA while in the mannitol group, RTA was the highest mode of injury followed by falls. When a two-sample t-test with equal variances was applied, the combined mean GCS was 5.45±1.29. This table shows that GCS on admission did not differ significantly between 3% HTS (5.53±1.22) and MTL group (5.36±1.37) with p value=0.62.

With a two-sample t-test with equal variances, the combined mean blood volume was 36.53±9.33. This shows that blood volume at first CT did not differ significantly between 3% HTS (35.9±9.2) and MTL group (37.1±9.56) with p value=0.62.

With a two-sample t-test with equal variances, the combined mean ICP was 25±4.51. We observed slightly low ICP in the 3% HTS group (24.1±4.7) compared to the MTL group (25.8±4.1), statistically, this difference was not significant (p value=0.13).

With a two-sample t-test with equal variances, the combined mean ICP was 22.06±4.70. Here we observed low ICP in the 3% HTS group (21.6±4.5) compared to the MTL group (22.5±4.8). However, statistically, this difference was not significant (p value=0.44).

With a two-sample t-test with equal variances, the combined mean ICP was 21.53±5.41. We observed low ICP in the 3% HTS group (20.7±4.9) compared to the MTL group (22.3±5.8). However, statistically, this difference was not significant (p=0.23).

With a two-sample t-test with equal variances, the combined mean of total hospital stay was 29.45±11.82. We did not observe a statistically significant difference in duration of hospital stay between the 3% HTS group (29.1±11.3) compared to the MTL group (29.7±12.4), p value=0.83. When a two-sample t-test with equal variances was applied, the combined mean GCS was 9.28±4.58. We did not observe a statistically significant difference in the duration of GCS at discharge between the 3% saline group (9.4±4.4) compared to the MTL group (9.1±4.8), p value=0.75.

In group A, the mortality was 12 whereas in group B it was 11. We did not observe a statistically significant difference in the mortality between the 3% HTS and MTL group (p value=0.79).

DISCUSSION

TBI has been termed a silent epidemic. With the spread of motorized transport, its prevalence is growing and it has the unfortunate predilection for targeting young adults resulting in devastating health, economic, and societal effects.[6] The management of severe TBI requires detailed knowledge of complex intracranial systemic physiology. Intracranial monitoring offers the possibility for early detection and therefore amelioration of physiological insults.

ICP monitoring is currently considered the standard of care for patients with severe TBI which provides the ability to monitor ICP, CPP, or tissue-perfusion modification. The threshold for ICP in patients with severe TBI is currently 20 mmHg.[7] Cerebral edema occurs due to the leakage of large molecules such as albumins from blood vessels through the damaged blood-brain barrier. Water flows into the brain after the albumins by osmosis. This vasogenic edema causes compression of and damage to brain tissue. An increase in ICP results in decreased cerebral perfusion pressure (CPP) and cerebral blood flow (CBF). This ultimately contributes to cerebral hypoxia, ischemia, herniation, and death.[8]

To combat the deleterious effects of progressive cerebral edema in moderate/severe TBI, various guideline-based therapeutics have been developed.[9,10] One such cornerstone of TBI therapeutics is the use of hyperosmolar/hypertonic agents. Examples of hyperosmolar therapy include solutions such as mannitol and HTS. HTS is an osmotherapeutic agent that is being used in practice as an alternative to mannitol in the treatment of cerebral edema, typically guided by continuous invasive ICP monitoring.

In recent years, the use of HS has increased as an osmotic agent for hyperosmolar therapy. Similar to mannitol, its principal mechanism of action is the creation of an osmolar gradient across the blood-brain barrier (BBB) leading to cerebral parenchymal fluid shift thus reducing cerebral edema and ICP. Compared to mannitol, the reflection coefficient of HS, which denotes its impermeability to BBB, is higher so the incidence of rebound rise in ICP after its withdrawal is less.

Our study compared the effects of equiosmolar doses of 3% HTS (group A) and 20% MTL (group B) in lowering the ICP in subjects with traumatic brain injury. Sixty patients (30 in each group) were randomly allocated to receive either mannitol or HS. We also compared the GCS at admission, ICP at 6, 24, and 48 hours, duration of ICU and hospital stay, GCS at the time of discharge, and the mortality rate.

A prospective, randomized controlled trial (RCT) study was done by Cottenceau et al that evaluated the effect of HTS and MTL on ICP, CBF and neurologic outcomes. Forty-seven patients with severe TBI and ICP >15 mmHg was randomized to receive equiosmolar doses of either MTL or HTS. Infusions were administered in <20 min. The baseline characteristics between groups were similar. MTL and HTS were equally effective in reducing ICP. However, while both osmolar agents increased CBF, the magnitude of augmentation was greater in the HTS group. There was no difference in neurologic outcome between groups at 6 months using the Glasgow outcome score.[11]

Similar observation was observed in a study done by Kerwin et al, Vialet et al, Sakellaridis et al, and Mangat et al.[12-15]

Limitations

The subject inclusion criteria vary between studies, clinical outcomes are inconsistently reported across studies, and more data on long-term clinical outcomes are needed. Reducing ICP alone is a practical goal, but may be a point of controversy if not accompanied by improved patient functional outcomes. Evaluation of the prognosis of children after treatment with HTS and MTL requires a randomized study with adequate power and a reasonable follow-up period to confirm that HTS is superior to MTL in patient-centered outcomes.

CONCLUSION

Both 3% HTS and MTL can effectively reduce ICP, but 3% HTS has a more sustained effect on ICP and can effectively increase cerebral perfusion pressure.

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