Original Article

Comparing the Efficacy of Mannitol Versus Hypertonic Saline in Management of Raised Intracranial Pressure Using Ultrasonographic Measurement of the Optic Nerve Sheath Diameter: A Prospective Randomized Study

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ABSTRACT

Background: Increased intracranial pressure (ICP) often occurs due to traumatic brain injury (TBI), necessitating prompt management to prevent adverse outcomes. Osmotic agents like mannitol and hypertonic saline are commonly used, but their comparative efficacy remains uncertain.

This study aimed to compare the efficacy of mannitol 20% and hypertonic saline 3% in reducing intracranial pressure (ICP) and assess their impact on optic nerve sheath diameter (ONSD) measured by ultrasonography.

Methods: This prospective, randomized, double-blinded study compared mannitol 20% and hypertonic saline 3% in reducing ICP using ultrasonographic measurement of the optic nerve sheath diameter (ONSD). Fifty adult TBI patients with elevated ICP were enrolled, and clinical parameters were monitored.

Results: Both mannitol and hypertonic saline effectively reduced ICP, with no significant difference between groups (mean reduction: 15.5% for mannitol, 29.2% for hypertonic saline). hypertonic saline demonstrated a more sustained reduction in ONSD compared to mannitol, showing significant differences at various time points ($p<0.05$). Correlation analysis revealed significant associations between ONSD measurements and MAP ($r= 0.754$, $p= 0.025$), serum osmolarity ($r= 0.721$, $p= 0.029$), serum sodium ($r= 0.778$, $p= 0.021$), and length of ICU stay ($r= 0.598$, $p= 0.069$).

Conclusions: Mannitol and hypertonic saline are both effective in reducing ICP in TBI patients. Hypertonic saline may offer advantages in sustained ICP reduction, especially in severe TBI cases. Ultrasonographic measurement of ONSD proves valuable for monitoring ICP dynamics and predicting clinical outcomes. Further research is needed to optimize treatment strategies for managing elevated ICP in TBI.

Key Words: Hypertonic saline, Intracranial pressure, Mannitol, Optic nerve sheath diameter, Ultrasonographic measurement.

Received: 27 August 2024**, Accepted:** 12 December 2024

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ISSN: 2090-925X, Vol.17, No.1, 2025

INTRODUCTION

Traumatic brain injury (TBI) stands as a significant contributor to both disabilities and fatalities globally. In the United States alone, roughly one-third of injury-related deaths are linked to TBI. Among the severe consequences of TBI is the escalation of intracranial pressure (ICP), often triggered by brain edema[1].

Elevated intracranial pressure can precipitate various complications, including distortion of brain compartments, spatial compression, and diminished cerebral perfusion pressure. If left unaddressed, increased ICP can lead to dire neurological outcomes such as brain herniation, cerebral ischemia, and even death[2].

Osmotic agents, such as mannitol and hypertonic saline, are commonly employed to manage increased ICP following traumatic brain injury, as they enhance cerebral perfusion pressure and cerebral blood flow[3].

While both mannitol and hypertonic saline are acknowledged for their efficacy in reducing intracranial pressure, the clinical superiority of one over the other remains uncertain. Current evidence, including meta-analyses, fails to decisively favor either agent, emphasizing the need for further research in this domain[4,5].

The gold standard method for monitoring and measuring ICP involves invasive direct measurement using intraventricular or intraparenchymal devices[6,7]. However, these invasive modalities are associated with risks such as hemorrhage and infection and require substantial resources and expertise, limiting their accessibility[8,9].

DOI: 10.21608/ASJA.2024.316125.1148

Invasive ICP monitoring is typically reserved for patients with suspected impaired cerebral perfusion, while non-invasive methods, including physical examinations and radiological imaging, are commonly utilized by emergency and ICU physicians[10]. However, the reliability of clinical signs in diagnosing increased ICP has been questioned, prompting the exploration of alternative methods such as measuring the optic nerve sheath diameter (ONSD)[11].

Previous studies have demonstrated the utility of trans-orbital ultrasonography, computed tomography, or magnetic resonance imaging in accurately assessing elevated ICP through ONSD measurements[12,13].

This study aimed to compare the efficacy of intermittent mannitol 20% versus intermittent hypertonic saline 3% in management of post-traumatic raised ICP using ultrasonographic measurements of the optic nerve sheath diameter (USG-ONSD).

METHODS

A prospective, randomized double-blinded study was conducted to investigate the efficacy of intermittent mannitol 20% versus intermittent hypertonic saline 3% in managing raised intracranial pressure (ICP) using ultrasonographic measurement of the optic nerve sheath diameter (USG-ONSD).

Fifty eligible patients (with ICP due to TBI) were randomly assigned to one of two treatment groups (*Group I:* patients received mannitol, *Group II:* patients received hypertonic saline) using a computer-generated random-number table. Allocation concealment was achieved using sequentially numbered opaque envelopes.

The study took place in the Critical Care Unit of Menoufia University hospitals from June to October 2023. The study population included adult patients aged 18-45 years who had suffered severe brain damage (Glasgo%w Coma Score ≤8) due to traumatic brain injury (TBI) with diagnosed elevation of ICP by CT brain.

Patients with significant ocular trauma, elevated ICP due to space-occupying lesions, or those requiring neurosurgical intervention (e.g., bleeding, hydrocephalus, etc.) were excluded. Additionally, patients with contraindications to hypertonic saline or mannitol, such as hypotension, pregnancy, renal impairment, coagulopathy, initial serum sodium >150mmol/L, initial serum osmolarity >320mosm/kg, metabolic disorders, and serum creatinine >2mg/dL were excluded. Patients reaching a sodium level >160mmol/L during hypertonic administration were also excluded and replaced by other patient.

A convenience sample was utilized for the study. Sample size calculation was performed using MedCalc software (version 22; MedCalc Software, Ostend, Belgium). A total sample size of 20 patients was determined, with a power of 90%, an alpha value of 5%, a mean difference of ONSD at 48 hours of 1mm, and standard deviations of 0.4 and 0.8 in the hypertonic and mannitol groups, respectively. Considering a dropout rate of 20%, the sample size was increased to 25 participants.

Ethical approval was obtained from the local research and ethical committee of the Anesthesia Department, Faculty of Medicine, Menoufia University, Egypt (IRB 6/2023 ANET 43). Written informed consent was obtained from the patient's first-degree relative.

The diagnosis of increased intracranial pressure (ICP) was established through the review of CT images by an experienced neuroradiologist. Clinical judgment and specific CT criteria, including mass effect, collapse of the third ventricle, and hydrocephalus, were utilized for diagnosis.

After initial management and checking patients' eligibility, patients were assigned to the mannitol group (Group I) who received an intravenous dose of 0.5gm/kg (2mL/kg) of 20% mannitol every six hours over 20 minutes for 72 hours or assigned to the hypertonic saline group received an intravenous dose of 3mL/kg of 3% hypertonic saline every six hours over 30 minutes for 72 hours (Figure 1).

All patients were intubated and received pressure-controlled mechanical ventilation (Bilevel Positive Airway Pressure (BiPAP), ETCo2 31.5–36mmHg, FiO2 0.3–1.0). Care was taken to keep the arterial partial oxygen pressure above 75mmHg, the hemoglobin concentration above 8. If necessary, blood pressure was supported with vasopressor therapy (low dose norepinephrine, 0.5mcg/min iv infusion) when needed. Blood glucose was adjusted to values between 70–120mg/dl by continuous application of human insulin. Patients' core temperature was measured via the esophagus, with a target temperature of 36.0–37.0˚C. If the core temperature exceeded 37.0˚C, external cooling blankets were used to cool the patient.

Analgosedation (fentanyl at a dose of 100mcg/h, or dexmedetomidine at a dose of 0.5mcg/kg/h) and continuous patient monitoring were managed according to the standards of the Department of Critical Care at Menoufia University. The standard monitoring was applied including electrocardiogram, arterial blood pressure, central venous pressure, and peripheral oxygen saturation.

USG-ONSD measurements were performed in B-mode using an Affiniti 50 ultrasound machine (Philips, Amsterdam, Netherlands). The 4–12 MHz linear probe was applied lightly on the closed upper eyelids of patients lying in the supine position. ONSD was measured 3mm behind the posterior aspect of the globe twice in each eye. The average of all four measurements were calculated to

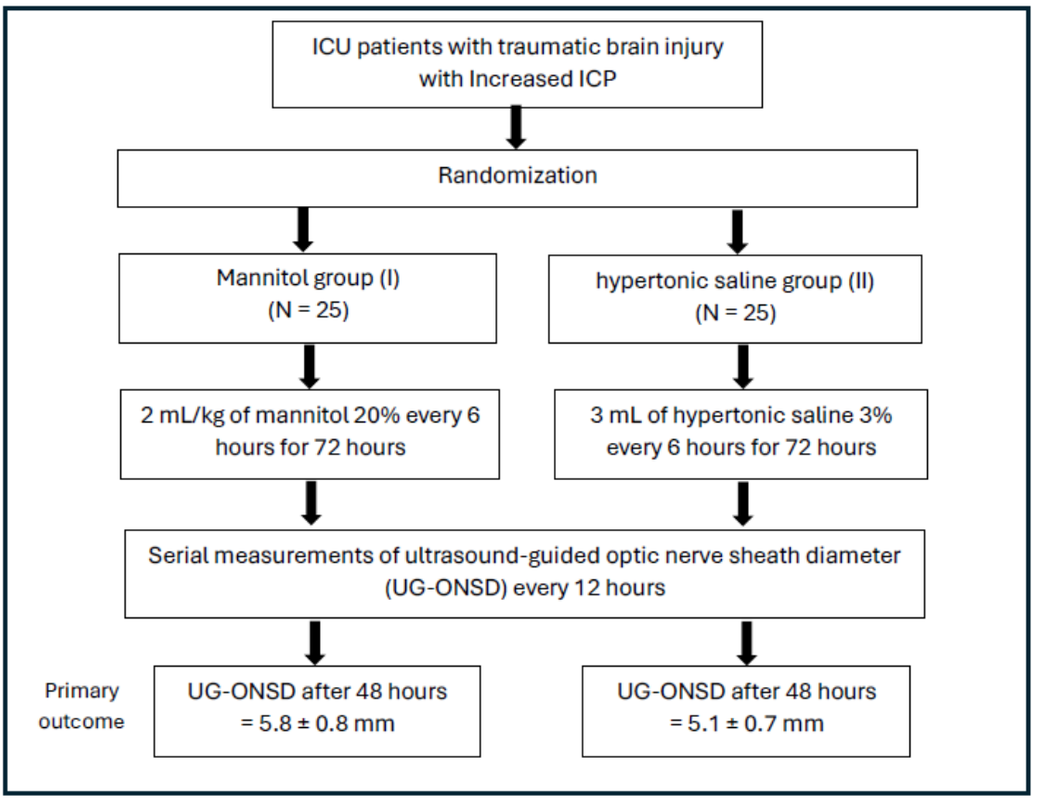

Figure 1: Flow Chart.

yield a mean USG-ONSD. ONSD measurements were recorded on admission and every 12 hours for 72 hours for both groups. We compared measurements of the ONSD on admission before the start of the osmotic agent, and every 12 hours after the start of the osmotic agent. The primary endpoint was ONSD measurements at 48 hours after the start of the osmotic agent.

Additionally, other parameters such as Glasgow Coma Scale (GCS), serum sodium, and serum potassium levels were monitored at regular intervals throughout the study period. Demographic and clinical data, including vital signs, medications, and laboratory findings, were recorded. Length of ICU stay, and mortality rates were also documented.

To mitigate potential bias, blinding procedures were implemented during data collection and analysis. Statistical analyses were conducted using appropriate methods to compare outcomes between the mannitol and hypertonic saline groups. Finally, it's worth noting that the study did not receive specific funding.

RESULTS

This randomized controlled trial comprised 50 patients diagnosed with increased intracranial pressure (ICP) resulting from traumatic brain injury. The patients were evenly divided into two groups: Group I, which received mannitol 20%, and Group II, which received hypertonic saline.

There were no significant differences between mannitol and hypertonic saline groups regarding vital signs. The Glasgow Coma Scale (GCS) scores were similar between the two groups (median 6 [IQR 5–7] for mannitol vs. median 6 [IQR 5–8] for hypertonic saline; *P*= 0.856).

The mean arterial pressure (MAP) was also comparable (81.5±28.3mmHg for mannitol vs. 81.2±26.9mmHg for hypertonic saline; *P*= 0.691). Heart rate did not differ significantly between the groups (81.1±19.6bpm for mannitol vs. 87.2±19.8bpm for hypertonic saline; *P*= 0.424).

Respiratory rate was similar (24±6 breaths/min for both groups; *P*= 0.222). Core body temperature showed no significant difference (37.1±0.2˚C for mannitol vs. 37.2±0.3˚C for hypertonic saline; *P*= 0.881). Urine output was comparable (0.9±0.2ml/kg/hour for mannitol vs. 1±0.1ml/kg/hour for hypertonic saline; *P*= 0.208). Oxygen saturation (SpO2) was also similar (95±2% for both groups; *P*= 0.952).

The mean length of ICU stay was 7.8 days (±5.2), with a mean hospital stay of 9.5 days (±6.9). Eighteen percent of patients required vasopressor support, and mortality within 28 days of admission was 62%. Significant associations

were found between USG-ONSD and hypertension (p= 0.023), vasopressor use (p= 0.013), and mortality (p= 0.004).

Comparing baseline characteristics between the studied groups, there were no significant differences in the mean length of ICU stay (Mannitol: 8.1±5 days, Hypertonic saline: 7.5±5.4 days, p= 0.088) or the mean length of hospital stay (Mannitol: 9.8±6.7 days, Hypertonic saline: 9.2±7.2 days, p= 0.214). The incidence of vasopressor use was similar between the Mannitol (16%) and Hypertonic saline (20%) groups (p= 0.125). Within 28 days of admission, mortality rates were 68% in the Mannitol group and 56% in the Hypertonic saline group (p= 0.101).

Comparison of ultrasonographic optic nerve sheath diameter (USG-ONSD) in both groups on admission and at various time points revealed significant differences. On admission, the mean USG-ONSD was 7.1±0.5mm in the Mannitol group and 7.2±0.6mm in the Hypertonic saline group (p= 0.56). However, significant differences were observed after 24, 36-, 48-, 60-, and 72-hours post-admission (p<0.05).

Serial clinical and laboratory findings in both groups demonstrated significant changes over time. Specifically, serum osmolarity, serum sodium, serum potassium, Glasgow Coma Scale (GCS), and urinary output exhibited significant variations between the Mannitol and Hypertonic saline groups across different time intervals (p<0.05).

Correlations between USG-ONSD measurements and various parameters revealed: Positive correlation with MAP (r= 0.754, p= 0.025), serum osmolarity (r= 0.721, p= 0.029), serum Na+ levels (r= 0.778, p= 0.021), and urinary output (r= 0.532, p= 0.218). Moderate positive correlation with GCS scores (r= 0.641, p= 0.081) and length of ICU stay (r= 0.598, p= 0.069). No significant correlations with age, core temperature, SpO2, random blood glucose levels, or pH (p>0.05).

DISCUSSION

This prospective, randomized double-blinded study was conducted in the Critical Care Unit of Menoufia University hospitals from June to October 2023. Eligible patients, aged 18-45 years, who had experienced severe brain damage (Glasgow Coma Score ≤8) due to traumatic brain injury (TBI) with elevated intracranial pressure (ICP) diagnosed by CT brain, were randomly assigned to one of two treatment groups: Group I (patients received intravenous 20% mannitol every six hours over 20 minutes for 72 hours) or Group II (patients received dose of 3mL/kg of 3% hypertonic saline every six hours over 30 minutes for 72 hours). Random allocation was achieved using computer-generated random-number tables, with allocation concealment ensured through sequentially numbered opaque envelopes.

The main results of this study were as following:

As regard demographic characteristics, Fifty patients were included in the study with a mean age of 32.3 years (SD±4.1) and a range from 19 to 45 years. The majority of patients were male (68%) compared to female (32%). The mean BMI was 24.8kg/m² (SD±4.7), ranging from 16.3 to 39.4kg/m². Smoking was reported in 34% of patients, while 18% had hypertension and 14% had diabetes mellitus.

As regards vital data, the Glasgow Coma Scale (GCS) had a median of 6 (IQR 5–7) with a range from 3 to 8. Mean arterial pressure (MAP) was 82mmHg (SD±21), heart rate was 83bpm (SD±24), respiratory rate was 21 breaths per minute (SD±5), core body temperature was 37.3˚C (SD±0.3), urine output was 0.8ml/kg/hour (SD±0.15), and oxygen saturation (SpO2) was 95% (SD±2).

There was no statistically significant difference in serum osmolarity between the mannitol group (mean= 286.9±6.4 µmol/L) and the hypertonic saline group (mean= 291.5±6.5µmol/L; P= 0.224). Random blood glucose levels were similar (mean= 122.9±40.4mg/dL for mannitol vs. mean= 120.8±40.2mg/dL for hypertonic saline; P= 0.44).

Total leucocytic count showed no significant difference (mean= 9.9±2.6×10^9/L for mannitol vs. mean= 9.8±3.2×10^9/L for hypertonic saline; P= 0.119). Hemoglobin levels were comparable (mean= 11±1.5g/dL for mannitol vs. mean= 10.8±1.8g/dL for hypertonic saline; P= 0.098). Platelet count did not differ significantly (mean= 203±87×10^9/L for mannitol vs. mean= 214±99×10^9/L for hypertonic saline; P= 0.105).

Serum urea levels were similar (mean= 24.3±24.7mg/dL for mannitol vs. mean= 15.5±8.2mg/dL for hypertonic saline; P= 0.304). Serum creatinine levels showed no significant difference (mean= 0.8±0.3mg/dL for mannitol vs. mean= 0.9±0.3mg/dL for hypertonic saline; P= 0.654).

Serum sodium levels were comparable (mean= 136.9±4.9mmol/L for mannitol vs. mean= 137.6±5.1mmol/L for hypertonic saline; P= 0.568). Serum potassium levels were also similar (mean= 4.4±0.7mmol/L for mannitol vs. mean= 4.1±0.5mmol/L for hypertonic saline; P= 0.327).

There was no significant difference in the mean pH levels between the mannitol group (mean= 7.4±0.1) and the hypertonic saline group (mean= 7.4±0.1; P= 0.654). Similarly, there were no significant differences between both groups regarding other arterial blood gas (ABG) values.

The partial pressure of carbon dioxide (PCO2) was comparable (mean= 38.9±3.6mmHg for mannitol vs. mean= 38.5±7mmHg for hypertonic saline; P= 0.277). The partial pressure of oxygen (PO2) showed no significant

difference (mean= 77±12mmHg for mannitol vs. mean= 81±15mmHg.

The clinical outcomes in both groups were compared. The length of ICU stay was similar between the mannitol group (mean= 9.4±6 days) and the hypertonic saline group (mean= 9.2±6.2 days; *P*= 0.307).

The length of hospital stay was also comparable (mean= 16.7±7.5 days for mannitol vs. mean= 16.6±6.7 days for hypertonic saline; *P*= 0.214). The use of vasopressors was not significantly different between the groups (16% in the mannitol group vs. 20% in the hypertonic saline group; *P*= 0.125).

The mortality rate within 28 days of admission was higher in the mannitol group (68%) compared to the hypertonic saline group (56%), but this difference was not statistically significant (*P*= 0.101).

Our results were supported by study of Kochanek *et al.,*[14] aimed to characterize the current use of hyperosmolar agents in pediatric severe traumatic brain injury (TBI) and assess whether hypertonic saline (HTS) or mannitol is associated with greater decreases in intracranial pressure (ICP) and/or increases in cerebral perfusion pressure (CPP). A total of 518 children across 44 clinical sites in 8 countries were included in the analysis. Bolus administration of HTS was observed to decrease ICP and increase CPP, while mannitol was associated with increased CPP. However, after adjustments for confounding variables, neither therapy showed a significant association with ICP or CPP. Notably, during ICP crises, HTS outperformed mannitol in reducing ICP. These findings correspond with our results and suggest that while both therapies may have benefits in managing pediatric severe TBI, HTS may be more effective during critical ICP elevations.

Similarly, Shi *et al.,*[15] conducted a recent meta-analysis and found hypertonic saline to be superior to mannitol in reducing ICP among patients with severe TBI with a statistically significant disparity was found between the hypertonic saline and mannitol groups in terms of the duration of effect in reducing intracranial pressure (95% confidence interval: 0.64–1.05, *Z*= 8.09, *P*<.00001) and cerebral perfusion pressure after intervention (95% confidence interval: 0.15–0.92, *Z*= 2.72, *P*= .007).

In addition, Han *et al.,*[16] evaluated the effect of hypertonic saline compared to mannitol for the management of elevated intracranial pressure in traumatic brain injury. They reported that hypertonic saline exhibited significantly lower treatment failure (OR, 0.38; 95% CI, 0.15–0.98, *p*= 0.04), along with lower intracranial pressure 30–60mins after infusion termination (MD, −1.12; 95% CI, −2.11 to −0.12, *p*= 0.03), and higher cerebral perfusion pressure 30–60mins after infusion termination (MD, 5.25; 95% CI, 3.59–6.91, *p*<0.001) compared to mannitol in subjects with traumatic brain injury (TBI). However, hypertonic saline did not demonstrate a significant effect on favorable outcome (OR, 1.61; 95% CI, 1.01–2.58, *p*= 0.05), mortality (OR, 0.59; 95% CI, 0.34–1.02, *p*= 0.06), intracranial pressure 90–120mins after infusion termination (MD, −0.90; 95% CI, −3.21–1.41, *p*= 0.45), cerebral perfusion pressure 90–120mins after infusion termination (MD, 4.28; 95% CI, −0.16–8.72, *p*= 0.06), and duration of elevated intracranial pressure per day (MD, 2.20; 95% CI, −5.44–1.05, *p*= 0.18) compared to mannitol in subjects with TBI.

The present study showed that as regard association between USG-ONSD measurements and different grouping variables, the mean optic nerve sheath diameter (ONSD) was 7.3mm (SD±0.6) in males and 7mm (SD±0.5) in females (*p*= 0.207). Significant associations were found between ONSD and hypertension (*p*= 0.023), vasopressor use (*p*= 0.013), and mortality (*p*= 0.004), with higher ONSD observed in patients with hypertension, vasopressor use, and those who died within 28 days of admission. However, no significant association was found between ONSD and diabetes mellitus (*p*= 0.197).

As regards ultrasonographic optic nerve sheath diameter (USG ONSD) in both groups, A comparison of USG-ONSD between the Mannitol and Hypertonic Saline groups on admission and at various time points thereafter revealed significant differences. On admission, the mean USG-ONSD was 7.1mm (SD±0.5) in the Mannitol group and 7.2mm (SD±0.6) in the Hypertonic Saline group (*p*= 0.56). However, as time progressed, significant reductions were observed in USG-ONSD in both groups. At 72 hours post-admission, the Mannitol group exhibited a mean USG-ONSD of 6mm (SD±0.5), whereas the Hypertonic Saline group had a mean of 5.1mm (SD±0.5) (*p*<0.001).

Our results were supported by study of Kshirsagar *et al.,*[17] that investigated the utility of bedside ultrasonography (USG)-guided optic nerve sheath diameter (ONSD) measurement as a potential predictor of increased intracranial pressure (ICP) in traumatic brain injury (TBI) patients. Brain computed tomography (CT) scans and Glasgow Coma Scale (GCS) scores were assessed upon admission. The mean ONSD was measured using bedside USG guidance, revealing that patients with lower GCS scores exhibited higher mean ONSD values (6.4±1.0mm). A significant association was observed among GCS scores, CT results, and ONSD measurements (*P*<0.001). In comparison to CT scans, bedside USG ONSD demonstrated 86.42% sensitivity and 64.29% specificity for detecting elevated ICP. The positive predictive value of ONSD for identifying elevated ICP was 93.33%, with a negative predictive value of 45.00%. The overall accuracy of ONSD measurement was 83.16%.

Also, Kim *et al.,*[18] prospective observational study where optic nerve sheath diameter (ONSD) was measured using ultrasonography (USG) and computed tomography (CT) at 3mm behind the posterior aspect of the globe. A total of 199 patients were enrolled, and the median USG-ONSD and CT-ONSD were found to be significantly higher in patients with elevated intracranial pressure compared to those with normal intracranial pressure. The interclass correlation coefficient between USG-ONSD and CT-ONSD was calculated as 0.785 (95% CI 0.715–0.837), indicating substantial agreement between the two modalities. Further analysis using a Bland–Altman plot demonstrated significant agreement between USG and CT measurements. The study determined an optimal cutoff for detecting elevated intracranial pressure as >5.3mm for USG (with a sensitivity of 75.4% and specificity of 90.8%) and >5.0mm for CT (with a sensitivity of 68.4% and specificity of 85.2%).

The same findings are supported by previous literature suggesting the superiority of hypertonic saline in maintaining ICP within the desired range[5,19].

Our results showed that as regards comparison between the two groups. baseline characteristics between the Mannitol and Hypertonic Saline groups revealed no significant differences in age, sex distribution, BMI, smoking status, hypertension, or diabetes mellitus prevalence (all $p>0.05$). No significant differences were observed in vital data including Glasgow Coma Scale (GCS), mean arterial pressure (MAP), heart rate, respiratory rate, core body temperature, urine output, and oxygen saturation between the Mannitol and Hypertonic Saline groups on admission (all $p>0.05$). Laboratory findings on admission, including serum osmolarity, random blood glucose, total leucocytic count, hemoglobin, platelet count, serum urea, serum creatinine, serum Na+, and serum K+, did not significantly differ between the Mannitol and Hypertonic Saline groups (all $p>0.05$). Similarly, no significant differences were found in arterial blood gas (ABG) parameters including pH, PCO2, PO2, and HCO3 between the Mannitol and Hypertonic Saline groups on admission (all $p>0.05$). Comparing clinical outcomes, including length of ICU stay, length of hospital stay, vasopressor use, and mortality within 28 days of admission, revealed no statistically significant differences between the Mannitol and Hypertonic Saline groups (all $p>0.05$).

As regards, comparison of serial clinical and laboratory findings between the Mannitol and Hypertonic Saline groups revealed significant differences in serum osmolarity, serum Na+, and urinary output over time. Specifically, serum osmolarity significantly increased over the first 48 hours in the Hypertonic Saline group compared to the Mannitol group ($p<0.001$). Similarly, serum Na+ levels showed a significant increase in the Hypertonic Saline group over time compared to the Mannitol group ($p<0.001$). Conversely, urinary output significantly decreased over time in both groups, with a more pronounced decrease observed in the Hypertonic Saline group compared to the Mannitol group ($p= 0.03$). No significant differences were observed in serum K+ levels or GCS scores over time between the two groups (all $p>0.05$).

As regards, correlation between USG-ONSD measurements and different parameters, the correlation analysis assessed the relationship between USG-ONSD measurements and various parameters. Significant positive correlations were found between USG-ONSD and MAP ($r= 0.754$, $p= 0.025$), serum osmolarity ($r= 0.721$, $p= 0.029$), and serum Na+ ($r= 0.778$, $p= 0.021$). A trend towards a positive correlation was observed between USG-ONSD and GCS ($r= 0.641$, $p= 0.081$) and length of ICU stay ($r= 0.598$, $p= 0.069$), although these did not reach statistical significance. No significant correlations were found between USG-ONSD and age, core temperature, SpO2, urinary output, random blood glucose, or pH (all $p>0.05$).

Our results were supported by meta-analysis of Hourmant *et al.,*[20] that assessed the effects of continuous infusion of hypertonic saline solutions on outcomes of patients with brain injury. A total of 1883 patients were included, with in-hospital mortality data available. The odds ratio (OR) for in-hospital death with the intervention was 0.68 (95% confidence interval (CI), 0.54−0.85, I2= 0%). Subgroup analysis of traumatic brain-injured patients (7 studies, $n= 1521$ patients) showed an OR of 0.74 (95%CI 0.57−0.95) for the primary outcome. Additionally, the OR for intracranial hypertension and unfavorable neurological outcome at day 90 were 0.66(95%CI 0.49−0.88, I2= 42%, $n= 787$ patients) and 0.61(95%CI 0.46−0.81, I2= 15%, $n= 956$ patients), respectively. Regarding safety, the OR of acute kidney injury and severe hypernatremia were 0.82(95%CI 0.47–1.44, I2= 0%) and 3.38(95%CI 2.16–5.27, I2= 24%).

Also, Roquilly *et al.,*[21] conducted a multicenter randomized clinical trial investigated whether continuous infusion of hypertonic saline solution improves neurological outcome at 6 months in patients with traumatic brain injury. Adult patients were randomly assigned to receive continuous infusion of 20% hypertonic saline solution plus standard care ($n= 185$) or standard care alone (controls; $n= 185$), with the hypertonic saline solution administered for 48 hours or longer if patients remained at risk of intracranial hypertension. The primary outcome assessed was the Extended Glasgow Outcome Scale (GOS-E) score at 6 months, obtained centrally by blinded assessors and analyzed with ordinal logistic regression adjusted for prespecified prognostic factors. Among the 370 randomized patients, 359(97%) completed the trial, with the adjusted common odds ratio (OR) for the GOS-E score at 6 months being 1.02(95% CI, 0.71-1.47; $P= .92$). Additionally, there were no significant differences

in 10 of the 12 secondary outcomes measured at multiple time points, including the development of intracranial hypertension and 6-month mortality.

CONCLUSION

Mannitol and hypertonic saline are both effective in reducing ICP in TBI patients. Hypertonic saline may offer advantages in sustained ICP reduction, especially in severe TBI cases. Ultrasonographic measurement of ONSD proves valuable for monitoring ICP dynamics and predicting clinical outcomes. Further research is needed to optimize treatment strategies for managing elevated ICP in TBI.

ABBREVIATIONS

TBI: Traumatic Brain Injury; **ICP:** Intracranial Cranial Pressure; **ONSD:** Optic Nerve Sheath Diameter; **MAP:** Mean Arterial Pressure; **BiPAP:** Bilevel Positive Airway Pressure; **CT:** Computerized Topography; **GCS:** Glasgow Coma Scale; **ICU:** Intensive Care Unit; **CPP:** Cerebral Perfusion Pressure; **USG:** Ultrasound Guided.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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