RESEARCH PAPER

Study of the Effect of Osmotherapy in the Treatment of Raised Intracranial Pressure in the Paediatric Intensive Care Unit in a Tertiary Care Teaching Hospital in Rural India

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ABSTRACT

Background: Raised intracranial pressure (ICP) is a life-threatening emergency in the paediatric population. Osmotherapy using 20% Mannitol or 3% Hypertonic Saline (HTS) remains the cornerstone of management. Evidence on comparative efficacy in children, particularly from resource-limited settings, remains sparse.

Objective: To assess the clinical effect of osmotherapy (Mannitol vs. 3% HTS) in reducing raised ICP in children admitted to a Paediatric Intensive Care Unit (PICU) in rural India.

Methods: A prospective observational study was conducted in the PICU of Acharya Vinoba Bhave Rural Hospital, Wardha, Maharashtra, from December 2020 to November 2022. Ninety-six children aged 1 month to 16 years with clinical features of raised ICP were enrolled. ICP was estimated non-invasively as: ICP = MAP − CPP (CPP assumed at 60 mmHg). Participants received either 20% Mannitol (n=48) or 3% HTS (n=48). Outcomes included ICP reduction, haemodynamic parameters, GCS improvement, morbidity, and mortality.

Results: Both agents significantly reduced ICP: mean ICP fell from 22.49 mmHg at admission to 18.27 mmHg after the first dose (p=0.01) and 16.07 mmHg by Day 2 (p=0.01). No statistically significant between-group difference in ICP reduction was observed on Day 2 (Mannitol: 15.19 mmHg; HTS: 14.63 mmHg; p=0.59). Mortality was significantly higher in the HTS group (35.4% vs. 16.7%; p=0.036), attributed to more haemodynamically unstable admissions in that group. PRISM III score significantly predicted mortality (Discharged: 15; Death: 33; p=0.01).

Conclusion: Both Mannitol and 3% HTS are equally efficacious in reducing raised ICP in children. Haemodynamic instability and illness severity should guide the choice of osmotherapy. PRISM III score is a strong predictor of mortality in this cohort.

Keywords: Intracranial pressure; Osmotherapy; Hypertonic saline; Mannitol; Paediatric intensive care; Cerebral perfusion pressure; ICP reduction

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INTRODUCTION

Many medical and surgical central nervous system (CNS) conditions, when severe, lead to cerebral oedema and, consequently, raised intracranial pressure (ICP) — also termed intracranial tension (ICT). These two terms are used interchangeably in clinical practice. Prompt diagnosis and treatment of raised ICP is critical, as it may result in life-threatening cerebral herniation.

Diagnosis of raised ICP can be established through clinical examination, fundoscopy, and invasive monitoring techniques in a well-equipped ICU setup. [1,2] The second essential parameter in this context is Cerebral Perfusion Pressure (CPP), defined as the net pressure gradient driving oxygen delivery to cerebral tissue. CPP is calculated as the difference between Mean Arterial Pressure (MAP) and ICP (CPP = MAP − ICP). Maintaining CPP ≥60 mmHg is imperative to prevent cerebral ischaemia.[3]

Osmotherapy constitutes the primary pharmacological approach to ICP reduction. The two most widely employed hyperosmolar agents are 20% Mannitol and 3% Hypertonic Saline (HTS).[4] Hypertonic saline is particularly favoured in cases of trauma, intracranial haemorrhage, burns, and stroke,[5] and has demonstrated utility when Mannitol has failed, in

addition to possessing a potentially longer duration of ICP-lowering effect.[6] Serum sodium should be monitored at minimum every 6 hours; a value of 155 mEq/L is the recommended upper limit for continuation of HTS therapy.[7]

Mannitol is a naturally occurring sugar alcohol that exerts its ICP-lowering effect through two distinct mechanisms: an immediate plasma volume-expanding effect and a delayed osmotic diuretic effect.[8] Since mannitol cannot cross an intact blood-brain barrier (BBB), its intravenous administration increases plasma tonicity, thereby drawing water from brain parenchyma into the intravascular compartment, which is subsequently excreted renally.[9]

Despite a century of clinical use of osmotherapy, robust evidence — particularly in the paediatric population — remains limited. The objective of this study was therefore to assess the effect of osmotherapy on raised ICP in children admitted to a PICU in rural India, and to compare the clinical efficacy and outcomes between Mannitol and 3% HTS.

MATERIALS AND METHODS

Study Design and Setting

Prospective observational study conducted in the Paediatric Intensive Care Unit (PICU) of Acharya Vinoba Bhave Rural Hospital, associated with Jawaharlal Nehru Medical College, a tertiary care centre in Wardha, Maharashtra, India between December 2020 and November 2022.The data analysis, draft preparation, review and critical inputs were done by Dr Anupam Bahe Bapan, Associate Professor, Indira Medical College and Hospital, Pandur, Tamil Nadu and Dr Swarna Latha J, Team Lead, PICU and Paediatric Emergencies, Tx Children's Hospital, Banjara Hills, Hyderabad.

Study Population

Inclusion criteria: All children aged 1 month to 16 years admitted to the PICU with a clinical diagnosis of raised ICP.

Exclusion criteria: (i) Children with serum sodium >155 mEq/L;

(ii) patients who had received osmotherapy before PICU admission.

Sample Size

Sample size was calculated for a two-sample comparison of means (alpha=0.05, power=0.90, m1=7, m2=8.2, SD1=1.88, SD2=1.74), yielding n1=n2=48 per group, for a final sample size of 96 participants. Group M (n=48) received Mannitol and Group HTS (n=48) received 3% Hypertonic Saline.

Intervention

Group M: 20% Mannitol 5 mL/kg intravenous bolus followed by 2.5 mL/kg maintenance for a minimum of 2 days.

Group HTS: 3% HTS 5 mL/kg bolus followed by continuous infusion of 0.1–1 mL/kg/hour titrated to maintain serum sodium 150–155 mEq/L for a minimum of 2 days.

The choice of osmotherapeutic agent was at the discretion of the treating paediatric physician, guided by clinical status and haemodynamic parameters.

ICP Estimation

ICP was estimated non-invasively using the formula: ICP = MAP − CPP, with CPP assumed constant at 60 mmHg in the absence of invasive monitoring capability. This formula was applied at admission, after the first loading dose, and on Day 2 of osmotherapy.

Outcome Measures

Primary outcomes: Change in ICP at baseline, after first dose, and on Day 2. Secondary outcomes included changes in heart rate, respiratory rate, MAP, GCS score, need for inotropes, need for mechanical ventilation, serum sodium, serum osmolality, PRISM III score, neuro-morbidity at discharge, mortality, and duration of hospital stay.

Ethical Clearance

Institutional Ethics Committee approval was obtained before commencement of data collection (IEC No.: DMIMS(DU)/IEC/2023/543). Written informed consent was obtained from parents/guardians of all participants.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using STATA 10 software. Categorical data were compared using Chi-square or Fischer's exact test; continuous data with

normal distributions were compared using the independent samples t-test. A p-value <0.05 was considered statistically significant.

RESULTS

Demographic and Baseline Characteristics

A total of 96 children were enrolled. The majority (61.5%) were aged >5 years. Male patients predominated (n=61; 63.54%). Figure 1 illustrates the demographic distribution across age groups and gender.

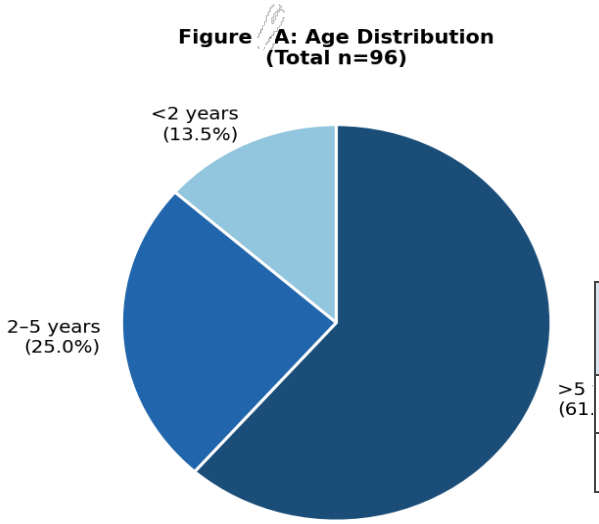

Figure 1. Demographic distribution of the study population by age and gender (n=*96).*

Heart Rate Variability and ICP at Admission

Heart Rate	Mean ICP at Admission (mmHg)	SD	n
Normal	20.38	10.661	72
Bradycardia	23.50	2.121	2
Tachycardia	22.14	9.321	22

Table 1. Heart rate variability and estimated ICP at admission (p=0.308).

Heart rate variability was not significantly associated with the degree of ICP elevation at admission (p=0.308). Patients with normal heart rate had a mean ICP of 20.38 mmHg, those with bradycardia 23.50 mmHg, and those with tachycardia 22.14 mmHg.

Respiratory Rate Variability and ICP at Admission

Respiratory Rate	Mean ICP at Admission (mmHg)	SD	n
Normal	18.81	8.830	64
Bradypnoea	19.63	10.309	8
Tachypnoea	26.71	11.808	24

Table 2. Respiratory rate variability and estimated ICP at admission (p=0.219).

Similarly, respiratory rate variability did not demonstrate statistical significance with calculated ICP at admission (p=0.219).

Mean Arterial Pressure with Osmotherapy

Osmotherapy	n	Mean MAP (mmHg)	SD
Mannitol	48	81.89	12.08
3% HTS	48	78.87	10.65

Table 3. Mean arterial pressure at admission by osmotherapy group (p=0.1971).

Mean MAP was slightly higher in the Mannitol group (81.89 mmHg) compared with the HTS group (78.87 mmHg), consistent with the preferential use of HTS in more haemodynamically compromised patients. The difference was not statistically significant (p=0.1971).

ICP Reduction with Osmotherapy

A significant reduction in estimated ICP was observed following the initiation of osmotherapy. Mean ICP at admission was 22.49 mmHg, which fell to 18.27 mmHg after the first dose (p=0
.01) and further to 16.08 mmHg by Day 2 (p=0.01). Figure 2 presents the trajectory of ICP reduction across both treatment groups.

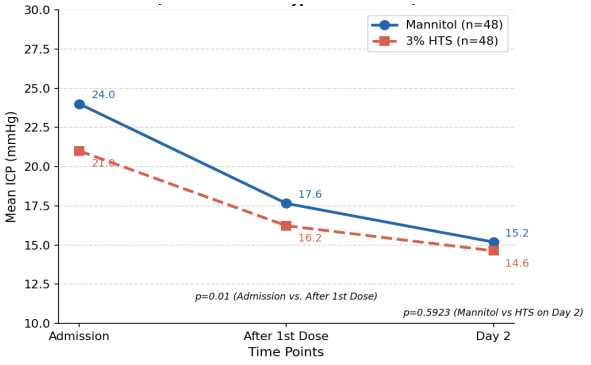

Figure 2. Mean ICP values at admission, after first dose, and on Day 2 of osmotherapy (Mannitol vs. 3% HTS). Error bars indicate standard deviation.

Osmotherapy	n	ICP Admission (mmHg)	ICP After 1st Dose (mmH	ICP Day 2 (mmHg)	SD (Day 2)

			g)		
Mannitol	48	24.00	17.65	15.19	4.88
3% HTS	48	21.00	16.23	14.63	5.36

Table 4. ICP values by osmotherapy group (between-group p=0.5923 on Day 2).

Although ICP reduction was slightly greater with HTS (6.37 mmHg reduction) compared with Mannitol (8.81 mmHg reduction from baseline to Day 2), the between-group comparison did not reach statistical significance (p=0.5923), indicating equivalence of the two agents in ICP reduction.

Clinical Outcomes

Figure 3 provides a comparative overview of clinical outcomes across both osmotherapy groups. Statistically significant differences were observed in the need for inotropic support (p=0.003), requirement for mechanical ventilation (p=0.007), and final mortality (p=0.036). These findings reflect the greater clinical severity of patients enrolled in the HTS cohort.

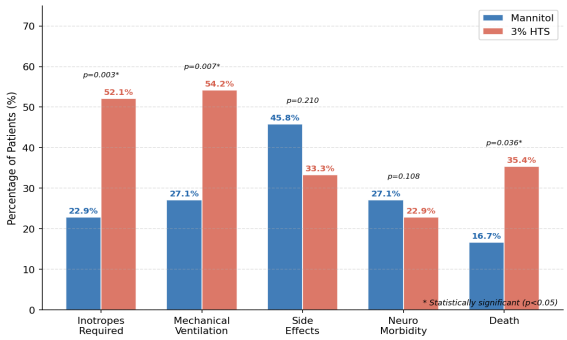

Figure 3. *Comparison of clinical outcomes between Mannitol and 3% HTS groups. Asterisks (*) denote statistically significant differences (p<0.05).*

PRISM III Score and Mortality

Patients who were successfully discharged had a significantly lower mean PRISM III score (15) compared with those who died (33), underscoring the predictive value of this score for mortality (p=0.01). Figure 4 illustrates this association.

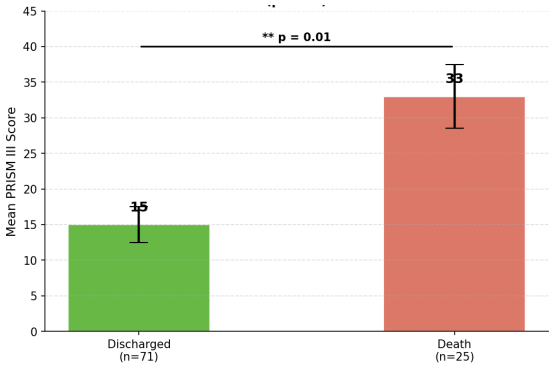

Figure 4. *Mean PRISM III score stratified by final outcome (Discharge vs. Death). Error bars represent standard error (p=0.01).*

Mortality and Neuro-morbidity

Outcome	Mannitol n (%)	HTS n (%)	Total n (%)
Discharge	40 (83.33)	31 (64.58)	71 (73.96)
Death	8 (16.67)	17 (35.42)	25 (26.04)
Total	48 (100)	48 (100)	96 (100)

Table 5. Final outcome by osmotherapy group (p=0.036).

Overall mortality was 26.04% (n=25). Mortality was significantly higher in the HTS group (35.42%) compared with the Mannitol group (16.67%; p=0.036). Neuro-morbidity at discharge was present in 13 (27.1%) Mannitol patients and 11 (22.9%) HTS patients (p=0.108), indicating no significant between-group difference.

Discussion

This prospective observational study evaluated the role of Mannitol and 3% HTS in children admitted with raised ICP to a PICU in rural India. A unique contribution of this study lies in its demonstration that clinical diagnosis and non-invasive ICP estimation are feasible in resource-constrained settings, enabling timely osmotherapy administration.

Both agents produced a significant reduction in estimated ICP: from 22.49 mmHg at admission to 16.08 mmHg by Day 2. This is consistent with findings reported by Cottenceau et al.,[19] who found equiosmolar doses of Mannitol and HTS equally effective in ICP reduction in traumatic brain injury. Similarly, Francony et al.[10] demonstrated comparable time-courses of ICP reduction between

the two agents. Rameshkumar et al.[11] reported an admission ICP of 28±13 mmHg (HTS) and 27±13 mmHg (Mannitol; p=0.82) in children with acute CNS infections, concordant with our findings. Huang et al.[20] likewise reported that equimolar doses of hypertonic saline and mannitol produced equivalent reductions in intracranial hypertension after severe traumatic brain injury, further reinforcing the equivalence observed in the present cohort.

Haemodynamic parameters were comparable between groups. The mean MAP was slightly higher in the Mannitol group (81.89 mmHg) than the HTS group (78.87 mmHg; p=0.197), consistent with the clinical decision to preferentially use HTS in haemodynamically unstable patients — a practice supported by Diringer et al.[12] and Scalfani et al.[13]

The significantly higher requirement for inotropic support (p=0.003) and mechanical ventilation (p=0.007) in the HTS group confirms greater baseline severity in this cohort. This pattern is echoed in the study by Jagannatha et al.,[14] where patients treated with Mannitol required more prolonged inotropic support (mean 95±47 hours) compared to HTS (78±58 hours).

Serum sodium and osmolality were comparable between groups at baseline, consistent with multiple comparative studies.[15,16,17,23,24,25,26] Upadhyay et al.[17] reported serum osmolality of 310±4.3 mOsm/kg (Mannitol) and 308±5.6 mOsm/kg (HTS) with no significant difference — an observation mirrored in the present cohort. Singla et al.[23] and Hernández-Palazón et al.[24] both reported no significant difference in intraoperative serum electrolyte profiles between equiosmolar HTS and mannitol during supratentorial craniotomy. Similarly, Wu et al.[25] and Sokhal et al.[26] found that both agents produced equivalent systemic osmolality changes while achieving comparable degrees of brain relaxation and ICP reduction, consistent with the findings of the present study.

PRISM III score was a robust predictor of mortality in this study (discharged: mean 15; died: mean 33; p=0.01). Rameshkumar et al.[11] reported comparable PRISM III scores of 21 and 22 between HTS and Mannitol groups, supporting its use as a severity and prognostic tool independent of osmotherapy choice.

Overall mortality in this study was 26.04%. The higher mortality in the HTS group (35.4% vs. 16.7%; p=0.036) is attributable to the enrolment of more critically ill, haemodynamically unstable patients in that arm. This selection bias should be interpreted with caution. Comparatively, Rameshkumar et al.[11] reported mortality of 21% (HTS) vs. 35.7% (Mannitol), and Jagannatha et al.[14] reported a significantly higher in-hospital mortality with Mannitol (50%) compared to HTS (16%; p<0.05). Kumar et al.[22] similarly observed comparable mortality outcomes between equiosmolar hyperosmolar agents in paediatric traumatic brain injury, noting that illness severity rather than agent choice was the dominant predictor of outcome. The discrepancy across studies likely reflects heterogeneity in patient selection and disease aetiology.

Side effects requiring osmotherapy discontinuation were more common with Mannitol (22/48, 45.8%) than HTS (16/48, 33.3%), though the difference was not statistically significant (p=0.210). Vialet et al.[18] similarly demonstrated that treatment failure was significantly lower with HTS than Mannitol. Patil and Gupta[21] compared bolus-dose HTS, Mannitol, and a Mannitol-glycerol combination in severe traumatic brain injury and found that while all three regimens effectively reduced ICP, the HTS arm was associated with fewer electrolyte disturbances and rebound ICP elevation, consistent with the tolerability profile observed in the present study. Mangat et al.[27] reported that hypertonic saline significantly reduced cumulative and daily ICP burdens after severe traumatic brain injury compared with mannitol, supporting the clinical preference for HTS in haemodynamically compromised patients observed in this cohort.

Conclusion

Both 20% Mannitol and 3% Hypertonic Saline are effective osmotherapeutic agents for the management of raised intracranial pressure in children. Neither agent demonstrated a statistically significant advantage over the other in ICP reduction. The choice between agents should be guided by haemodynamic status: HTS is preferred in hypotensive or haemodynamically unstable patients, while Mannitol may be used when blood pressure is normal or elevated. PRISM III score is a strong and significant predictor of mortality in this paediatric cohort. Non-invasive ICP estimation using the MAP-CPP formula is a practical approach in resource-limited settings.

Limitations

The primary limitation of this study is the indirect estimation of ICP using the formula ICP = MAP − CPP, as direct invasive ICP monitoring was not available. The fixed assumption of CPP = 60 mmHg may introduce bias. Additionally, as an observational study, the non-randomised allocation of osmotherapy may have introduced selection bias. A larger

randomised controlled trial with invasive ICP monitoring would provide more definitive evidence.

Recommendations

This study provides clinically actionable evidence for the assessment and management of raised ICP in paediatric patients in resource-limited environments. Non-invasive clinical assessment and indirect ICP estimation are feasible alternatives to invasive monitoring in such settings. Future multi-centre randomised trials in the paediatric population are warranted to establish definitive management guidelines.

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