Supplementary Materials

Table 1. Clinical evidence comparing hypertonic saline and mannitol.

Study	Objective	Study design	Sample	Interventions	Results
Vialet et al. (70)	The study evaluates if increasing hypertonic solution osmotic load treats intracranial hypertension.	Prospective, randomized study	Twenty individuals with head injuries and prolonged coma were studied.	7.5% hypertonic saline solution or 20% mannitol.	The hypertonic saline group experienced significantly lower total and duration of ICP compared to the mannitol group.
Harutjunya et al.(71)	To compare the effectiveness and reliability of hypertonic saline to mannitol in case of elevated intracranial pressure (ICP).	prospective randomized clinical study	Forty neurosurgery patients are at risk of having their ICP rise.	7.2% NaCl/HES 200/0.5 or mannitol – 15%	Hypertonic saline infusion increases arterial pressure, while mannitol has no effect. Mannitol 15% or 7.2% bolus lowers ICP and increases CPP, with hypertonic saline having a greater effect.
Francony et al (72).	To assess the effects of equimolar dosages of 20% mannitol solution and 7.45%	Parallel, randomized, controlled trial.	A total of 20 stable individuals with a sustained ICP of >20 mm Hg	231 mL of 20% mannitol or 100 mL of 7.45% hypertonic saline	When an equal osmotic load is administered to stable individuals, both hypertonic saline and mannitol have equivalent efficiency in

	hypertonic saline solution.				lowering ICP with adequate pressure autoregulation.
Oddo et al (73)	To investigate the effects of mannitol and hypertonic saline (HTS) on brain tissue oxygen tension in patients with serious brain injury	Prospective, nonrandomized, cross-over study	12 individuals with severe TBI who have increased intracranial pressure	25% Mannitol (0.75 g/kg), 412 mOsmol/dose and 7.5% Hypertonic Saline (250 mL), 641 mOsmol/dose	7.5% hypertonic saline delivered as therapy in patients with severe TBI and increased ICP unresponsive to earlier mannitol treatment.
Kerwin et al (74)	To assess the safety and effectiveness of 23.4% HTS vs mannitol for the immediate therapy of high ICP following traumatic brain injury (TBI).	Retrospective analysis	Twenty-two patients have increased intracranial pressure and suffered from blunt brain injury.	The dose of mannitol was determined and hypertonic saline was given at a fixed dose of 30 mL.	The mean ICP drop after HTS treatment was significantly higher than that after mannitol administration, indicating a 50% higher reduction in ICP compared to mannitol.

Mangat et al.(75)	To compare the effects of HTS against mannitol on the combined impact of elevated ICP and low CPP in individuals with severe TBI.	Prospective case-control study	patients included were suffering from TBI who received only either mannitol or hypertonic saline.	Patients received either mannitol 20% or hypertonic saline 3%	HTS bolus treatment reduces the incidence and persistence of elevated ICP and reduces CPP load in individuals with severe head trauma and intracranial hypertension.
Huang et al.(76)	To see how well-repeated bolus doses of HTS and mannitol in identical osmotic loads worked in individuals with severe TBI.	Randomized controlled trial	Eighty-three individuals with severe TBI were involved.	20% mannitol, 2 ml/kg, or 10% HTS, 0.63 ml/kg, delivered as a bolus via the central venous catheter and infused over 15 minutes	The study found that repeated bolus dosages of 10% hypertonic saline and 20% mannitol effectively reduce intracranial pressure and enhance cerebral perfusion pressure, with HTS showing slightly higher efficacy.
Jagannatha et al. (77)	To compare the preliminary intracranial mechanism and long-term prognosis of mannitol with	a prospective randomized controlled study	The research included 38 individuals with serious traumatic brain injuries (TBI).	Refractory ICH was treated with equimolar boluses of 20% mannitol in 20 individuals and 3.0% HTS in 18 cases.	Severe TBI patients experience an ICP reduction equivalent to 20% mannitol within 6 days, but a steeper ICP drop due to HTS does not provide any additional

	hypertonic saline in serious brain injuries.				advantage in general ICP management.

Table 2. Summarising the comparison of safety efficacy profile of mannitol and hypertonic saline.

Parameters assessed	Hypertonic saline	Mannitol
1. Intra cranial pressure	Hypertonic saline had a greater favorable impact on intracranial pressure than mannitol	The mean ICP drop following mannitol treatment was substantially lower than that following mannitol administration.
2. Cerebral Perfusion Pressure	HTS bolus treatment was linked with decreased incidence and persistence of elevated ICP and reduced CPP load. Individuals receiving HTS showed a decreased frequency and duration of low CPP	Mannitol demonstrates significant and comparable effectiveness in reducing intracranial pressure (ICP) and enhancing cerebral perfusion pressure (CPP). However, on the lower end compared to that of hypertonic saline.

3.	Electrolyte imbalance	HTS alone or in combination with dextran restores intravascular volume with less volume, raises CPP, decreases ICP	At first mannitol acts by raising intravascular free water content, which can exacerbate electrolyte imbalances, such as hyponatremia then it excretes surplus free water in the urine during its second phase of action, which may lead to hypernatremia.
4.	Neurological improvement	HTS appears to promote brain tissue oxygenation more than mannitol. Thus improving neurological functioning.	Mannitol is non-inferior in improving neurological functioning compared to that of mannitol.
5.	Mean arterial pressure	Hypertonic saline raised mean arterial pressure whereas mannitol had no effect.	Mannitol had no effect in increasing mean arterial pressure.
6.	Urine production	Urine production was lower with HSS.	Urine production was greater following mannitol infusion, which acts as a diuretic, than after HSS