INTRODUCTION

Review question / Objective: Evaluate and compare the effectiveness of hypertonic saline and mannitol in patients with traumatic brain injury.

Rationale: Traumatic brain injury is one of the main reasons for death and disability worldwide. Generally, the frequency of traumatic brain injury in Europe is >2,000 per million yearly; guidelines suggest more conservative interventions, e.g., raising of the upper body, cerebrospinal fluid drainage, and the use of hypertonic saline or mannitol before executing decompressive craniectomy. It is still uncertain whether hypertonic saline is better than mannitol in managing pediatric and adult patients with traumatic brain injury. The present systemic review and meta-analysis aimed to evaluate the effect of hypertonic saline compared to mannitol for managing TBI in traumatic brain injury.

Eligibility criteria: Studies were included based on the described eligibility criteria using PICOS: P (Population); I (Intervention); C (Control); O (Outcome); S (Studies); only clinical trials and cohort studies published in English were selected.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 November 2022 and was last updated on 03 November 2022 (registration number INPLASY2022110010).
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**Condition being studied:** Traumatic Brain Injury.

**METHODS**

**Search strategy:** We conducted a systematic search of Embase, PubMed, Cochrane Library, OVID, and Google Scholar till OCT 2022, by using a blend of keywords and related words for the hypertonic saline, mannitol, intracranial pressure, treatment failure, cerebral perfusion pressure, traumatic brain injury.

**Participant or population:** Adult and Pediatric patients.

**Intervention:** Hypertonic saline.

**Comparator:** Mannitol.

**Study designs to be included:** RCT or cohort studies.

**Eligibility criteria:** Studies were included based on the described eligibility criteria using PICO(S): P (Population); I (Intervention); C (Control); O (Outcome); S (Studies); only clinical trials and cohort studies published in English were selected.

**Information sources:** Embase, PubMed, Cochrane Library, OVID, and Google Scholar.

**Main outcome(s):** Four outcomes: treatment failure, mortality, CPP and ICP.

**Quality assessment / Risk of bias analysis:**
1- The Cochrane Collaboration's Tool was employed to assess any risk of bias
2- Newcastle Ottawa Scale (NOS) was employed to evaluate the risk of bias in the included cohorts.

**Strategy of data synthesis:** We performed meta-analysis to pool fatality outcomes of included studies using Rev Man 5.3. We expressed summary estimates for mortality as odds ratio (OR) and 95% confidence limits using a random-effects model analysis. We used I-square (I²) statistics to quantify proportion of statistical heterogeneity. To detect substantial heterogeneity, we considered I² statistics above 50%.

**Subgroup analysis:** No Subgroup analysis.

**Sensitivity analysis:** Reporting of sensitivity analyses in a systematic review was done by producing a summary table.

**Language restriction:** English.

**Country(ies) involved:** Saudi Arabia Kingdom of suadi arabia.


**Contributions of each author:**
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