

# Mannitol versus hypertonic saline for brain relaxation in patients undergoing craniotomy

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*The independent commentary was written by Jean Gonçalves de Oliveira*

## ABSTRACT

**BACKGROUND:** Patients with brain tumour usually suffer from increased pressure in the skull due to swelling of brain tissue. A swollen brain renders surgical removal of the brain tumour difficult. To ease surgical tumour removal, measures are taken to reduce brain swelling, often referred to as brain relaxation. Brain relaxation can be achieved with intravenous fluids such as mannitol or hypertonic saline. This review was conducted to find out which of the two fluids may have a greater impact on brain relaxation.

**OBJECTIVES:** To compare the effects of mannitol versus those of hypertonic saline on intraoperative brain relaxation in patients undergoing craniotomy.

### METHODS:

*Search methods:* We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (2013, Issue 10), Medline via Ovid SP (1966 to October 2013) and Embase via Ovid SP (1980 to October 2013). We also searched specific websites, such as [www.indmed.nic.in](http://www.indmed.nic.in), [www.cochrane-sadcct.org](http://www.cochrane-sadcct.org) and [www.Clinicaltrials.gov](http://www.Clinicaltrials.gov).

*Selection criteria:* We included randomized controlled trials (RCTs) that compared the use of hypertonic saline versus mannitol for brain relaxation. We also included studies in which any other method used for intraoperative brain relaxation was compared with mannitol or hypertonic saline. Primary outcomes were longest follow-up mortality, Glasgow Outcome Scale score at three months and any adverse events related to mannitol or hypertonic saline. Secondary outcomes were intraoperative brain relaxation, intensive care unit (ICU) stay, hospital stay and quality of life.

*Data collection and analysis:* We used standardized methods for conducting a systematic review, as described by the Cochrane Handbook for Systematic Reviews of Interventions. Two review authors independently extracted details of trial methodology and outcome data from reports of all trials considered eligible for inclusion. All analyses were made on an intention-to-treat basis. We used a fixed-effect model when no evidence was found of significant heterogeneity between studies, and a random-effects model when heterogeneity was likely.

**MAIN RESULTS:** We included six RCTs with 527 participants. Only one RCT was judged to be at low risk of bias. The remaining five RCTs were at unclear or high risk of bias. No trial mentioned the primary outcomes of longest follow-up mortality, Glasgow Outcome Scale score at three months or any adverse events related to mannitol or hypertonic saline. Three trials mentioned the secondary outcomes of intraoperative brain relaxation, hospital stay and ICU stay; quality of life was not reported in any of the trials. Brain relaxation was inadequate in 42 of 197 participants in the hypertonic saline group and in 68 of 190 participants in the mannitol group. The risk ratio for brain bulge or tense brain in the

hypertonic saline group was 0.60 (95% confidence interval (CI) 0.44 to 0.83, low-quality evidence). One trial reported ICU and hospital stay. The mean (standard deviation (SD)) duration of ICU stay in the mannitol and hypertonic saline groups was 1.28 (0.5) and 1.25 (0.5) days (P value 0.64), respectively; the mean (SD) duration of hospital stay in the mannitol and hypertonic saline groups was 5.7 (0.7) and 5.7 (0.8) days (P value 1.00), respectively.

**AUTHORS' CONCLUSIONS:** From the limited data available on the use of mannitol and hypertonic saline for brain relaxation during craniotomy, it is suggested that hypertonic saline significantly reduces the risk of tense brain during craniotomy. A single trial suggests that ICU stay and hospital stay are comparable with the use of mannitol or hypertonic saline. However, focus on other related important issues such as long-term mortality, long-term outcome, adverse events and quality of life is needed.

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## REFERENCE

1. Prabhakar H, Singh GP, Anand V, Kalaivani M. Mannitol versus hypertonic saline for brain relaxation in patients undergoing craniotomy. Cochrane Database of Systematic Reviews 2014, issue 7. Art. No.: CD010026. DOI: 10.1002/14651858.CD010026.pub2. Available from: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010026.pub2/abstract>. Accessed in 2014 (Dec 29).

## COMMENTS

Hyperosmolar therapy, using mannitol or hypertonic saline solution, is the main medical management method for providing brain relaxation during neurosurgical procedures in which craniotomy and opening of the dura mater are performed, especially in patients with intracranial hypertension. When the blood-brain barrier (BBB) is intact, an increase in serum osmolality produces brain dehydration, thereby reducing the cerebral volume as well as the intracranial pressure. The hydroelectrolytic changes caused by hyperosmolar therapy are a confounding factor in managing neurosurgical patients, who frequently have hydroelectrolytic imbalances, usually attributed to salt wasting syndrome, inadequate antidiuretic hormone secretion and diabetes insipidus. Although mannitol has been used since the 1980s and remains the first choice in many circumstances, use of hypertonic saline solution is becoming much greater, which explains why several studies have compared these two therapies during neurosurgical procedures in which craniotomy is required.

In this manuscript, the authors conducted a systematic review that brought together six randomized controlled trials comparing the use of mannitol versus hypertonic saline for brain relaxation. The primary outcomes were mortality, long-term follow-up, Glasgow Outcome Scale score at three months and any adverse events relating to mannitol or hypertonic saline solution, but none of these were mentioned in the studies included. Regarding the secondary outcomes, brain relaxation was better achieved in the hypertonic saline group, since brain relaxation in the mannitol group was considered inadequate in 35.8% of the cases, versus 21.3% in the hypertonic saline group. Hospital and inten-

sive care unit stay were not significantly different between the groups. Lastly, further studies are required in order to clarify the risks and benefits of these two therapies in specific situations such as brain tumor surgery, traumatic brain injury and aneurysmal subarachnoid hemorrhage, for instance.

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