

## **Is the use of hypertonic saline effective in reducing intracranial pressure after traumatic brain injury?**

### Clinical bottom line

Hypertonic saline appears to be effective in reducing intracranial pressure after traumatic brain injury in experimental studies.

### Question

Does hypertonic saline reduce intracranial pressure after traumatic brain injury in dogs?

### Clinical scenario

A three year old 15kg male entire Terrier cross is brought in after running into the road and colliding with a car. It is in hypovolaemic shock and after fluid resuscitation (25ml/kg lactated ringer solution in 15 minutes) the only visible injuries found are epistaxis and a fractured jaw. However, the dog is stuporous and consciousness does not seem to improve with stabilising cardiovascular parameters.

Would treatment with hypertonic saline be beneficial for this dog?

### Abbreviations Used

CPP	cerebral perfusion pressure
CVP	central venous pressure
ICP	intracranial pressure
LRS	lactated Ringers solution
MAP	mean arterial pressure

### Summary of the evidence

#### **Prough et al. (1986)**

**Population:** dogs

**Sample size:** 17

**Intervention details:** after 30 minutes of experimentally induced haemorrhagic shock (MAP <50mmHg) dogs were resuscitated with hypertonic saline solution or lactated ringer solution

**Study design:** randomised, experimental study

**Outcome studied:** systolic and diastolic blood pressure, cardiac output, MAP and ICP

**Main Findings (relevant to PICO question):** ICP after resuscitation with hypertonic saline was lower than after LRS while restoring systolic blood pressure and cardiac output to the same level

**Limitations:**

- experimental study
- no brain injury or increased ICP to begin with

#### **Gunnar et al. (1988)**

**Population:** laboratory Beagles

**Sample size:** 22

**Intervention details:** Hypovolaemic shock and closed head injury were simulated via bleeding of 40% of blood volume and epidurally inflated balloon. This was maintained for 1h, after that resuscitation with the shed blood and either 3% hypertonic saline, 0.9% saline or dextran-40 was attempted. A solution of Evans Blue was also injected. After 2h of resuscitation the dogs were euthanased and their brains weighed and checked for Evans Blue staining under microscope. A control group wasn't bled or ballooned but received fluids and Evans Blue solution only.

**Study design:** experimental controlled study

**Outcome Studied:** continuous ICP monitoring, blood brain barrier function assessed by degree of Evans Blue staining and cerebral oedema formation assessed by wet brain weights

**Main Findings (relevant to PICO question):** hypertonic saline causes lower intracranial pressure and less cerebral oedema, but blood brain barrier integrity is not restored

**Limitations:**

- experimental study
- no survivors to assess clinical outcome
- short term study of only 2h duration

### **Gunnar et al. (1989)**

**Population:** Beagles

**Sample size:** 18

**Intervention details:** Hypovolaemic shock and closed head injury were simulated via bleeding of 40% of blood volume and epidurally inflated balloon. This was maintained for 1h, after that resuscitation with the shed blood and either with 3% hypertonic saline, 0.9% saline or dextran-40 was attempted, after this, normal saline was given at a rate to maintain CVP at 10mmHg.

**Study design:** experimental uncontrolled study

**Outcome Studied:** Cerebral blood flow and intracranial pressure were measured at baseline, at the end of the shock period, during resuscitation and two hours after resuscitation

**Main Findings (relevant to PICO question):** Though the intracranial pressure was lower in the hypertonic saline group, cerebral blood flow did not vary

**Limitations:**

- experimental study
- no assessment of clinical outcome
- short term study of only 2h duration

### **Pinto et al. (2006)**

**Population:** crossbreed dogs

**Sample size:** 15

**Intervention details:** 20 minutes after experimentally induced haemorrhagic shock via bleeding to MAP of 40mmHg and simulated traumatic brain injury via fluid percussion and epidural balloon, volume was replaced with 3% hypertonic saline (8ml/kg over 10 min) or lactated ringer solution (16ml/kg over 10 ml). 20 minutes later shed blood and more of the previous fluids were given to a haematocrit of 30% and a MAP of >70mm Hg. A control group received no fluids at either point. After 60 minutes the epidural balloon was deflated in the treatment groups.

**Study design:** experimental, randomised, controlled study

**Outcome Studied:** MAP, cardiac index, ICP, CPP, biochemistry & blood gases

**Main Findings (relevant to PICO question):** Hypertonic saline results in lower ICP than LRS even though CPP remains similar. Hypertonic saline also causes higher serum sodium concentration and osmolarity than LRS.

**Limitations:**

- experimental study
- no clinical outcome described

**Sharma & Holowaychuk (2015)**

**Population:** client-owned dogs with head trauma <5 days before hospital admission

**Sample size:** 72

**Intervention details:** no specific interventions, clinical records were analysed

**Study design:** retrospective descriptive study, based on case records

**Outcome Studied:** the prognostic value of clinical and laboratory variables, scoring systems and treatments (such as hypertonic saline) in dogs with head trauma was calculated

**Main Findings (relevant to PICO question):** hypertonic saline administration was associated with lower likelihood of survival to discharge

**Limitations:**

- retrospective case study
- no control
- multiple parameters observed, prognostic value of individual variables on their own hard to quantify

**Pinto et al. (2015)**

**Population:** crossbreed dogs

**Sample size:** 15

**Intervention details:** 20 minutes after experimentally induced haemorrhagic shock via bleeding to MAP of 40mmHg and simulated traumatic brain injury via fluid percussion and epidural balloon, volume was replaced with 3% hypertonic saline (8ml/kg over 10 min) or lactated ringer solution (16ml/kg over 10 min). 20 minutes later shed blood and more of the previous fluids were given to a haematocrit of 30% and a MAP of >70mm Hg. A control group received no fluids at either point. After 60 minutes the epidural balloon was deflated in the treatment groups. All dogs were euthanized after 180 minutes and the brains removed, visually assessed and further analysed after tissue fixation

**Study design:** experimental controlled study

**Outcome Studied:** MAP and ICP were measured, changes in pupil state were assessed every 10 minutes, macroscopic and microscopic brain pathology and prostaglandoid production were assessed

**Main Findings (relevant to PICO question):** ICP was the lowest in the hypertonic saline cases during the initial 60 minutes. In brains that had received hypertonic saline, no cerebral oedema was identified macroscopically and ischaemic lesions were less evident. In cases with pupil changes, the pupils reversed to normal sooner in the hypertonic saline group.

**Limitations:**

- experimental study
- no survivors to assess clinical outcome
- short term study of only 3h duration
- macroscopic assessment for cerebral oedema only
- small number of cases

The purpose of this knowledge summary was to look at the evidence for the use of hypertonic saline in head trauma patients.

In human literature there has been some interest towards using hypertonic saline instead of mannitol as its effects on ICP appear to be stronger and longer lasting.

The experimental studies available in dogs seem to indicate that hypertonic saline might have a good effect on increased intracranial pressure after traumatic brain injury while achieving desirable haemodynamic parameters.

There are no controlled clinical studies that evaluate the use of hypertonic saline as an independent variable. In the descriptive study from Sharma & Holowaychuck (2015) the decision to use hypertonic saline was the clinician's, and was sometimes combined with mannitol. The choice to use hypertonic saline appears mostly to have been made in very severe cases, which explains the negative predictive value of hypertonic saline use on survival until discharge.

In conclusion, hypertonic saline appears to be effective in reducing intracranial pressure after traumatic brain injury in experimental studies. How effective its use might be in clinical settings cannot be answered.

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## Methodology

### Search Strategy

Databases searched and dates covered:

PubMed database, accessed via the NCBI website (1910-2015) and the CAB abstracts database (1973-2015)

Search terms:

(dog OR dogs OR canine OR puppy OR puppies OR canis) AND (((brain AND (trauma OR injur\*)) OR (head AND (trauma OR injur\*))) AND (hypertonic AND (saline OR sodium)))

Date searches performed:

18.07.16

Exclusion / Inclusion Criteria

Exclusion:

Articles not available in English or German, single case reports, book chapters and conference proceedings, articles which were not relevant to the question.

Inclusion:

Articles available in English or German, which were relevant to the question.

### Search Outcome

Database	Total Number of results	Excluded – language	Excluded – not relevant to question	Total relevant papers
CAB Abstracts	2	0	1	1
PubMed	15	0	9	6

Total relevant papers when duplicates removed:  
6

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## References

- Gunnar, W. et al., 1988. Head injury and hemorrhagic shock: studies of the blood brain barrier and intracranial pressure after resuscitation with normal saline solution, 3% saline solution, and dextran-40. *Surgery*, 103(4), pp.398–407.
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- Sharma, D. & Holowaychuk, M.K., 2015. Retrospective evaluation of prognostic indicators in dogs with head trauma: 72 cases (January-March 2011). *Journal of Veterinary Emergency and Critical Care*, 25(5), pp.631–639.