Effects of mannitol and hypertonic saline on cerebral oxygenation and metabolism in patients with posttraumatic intracranial hypertension.

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Aim of this study is to compare the effects of mannitol and HS in equimolar concentrations on cerebral blood flow, cerebral oxygenation, metabolism and inflammation in patients with severe TBI.

Ethical review	Approved WMO
Status	Pending
Health condition type	Increased intracranial pressure and hydrocephalus
Study type	Interventional

Summary

ID

NL-OMON30018

Source
ToetsingOnline

Brief title
mannitol and hypertonic saline in patients after traumatic brain injury.

Condition

- Increased intracranial pressure and hydrocephalus

Synonym
brain swelling, intracranial hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Hypertonic saline, Intensive Care, Mannitol, Traumatic brain injury

Outcome measures

Primary outcome

The primary endpoint of the study will be cerebral oxygenation as measured by intracerebral PO2 (expressed as mmHg).

Secondary outcome

Secondary endpoints will be cerebral blood flow, metabolism and inflammation. Cerebral blood flow will be measured by transcranial Doppler and expressed as flow in cm/sec. The balance between aerobic and anaerobic metabolism will be determined by measuring intraparenchymal lactate/pyruvate ratio using cerebral microdialysis. Components of the inflammatory response such as the pro- and anti-inflammatory cytokines IL-6, TNF-a and IL-10 will be measured in blood from the jugular bulb.

Study description

Background summary

Traumatic brain injury (TBI) is the leading cause of death in patients under the age of 45. The prognosis of the TBI is determined by the primary insult to the brain and by a cascade of events leading to secondary brain injury. Cerebral swelling is a key mechanism associated with this secondary brain injury and contributes to intracranial hypertension, secondary ischemia and, if uncontrolled, to brain herniation. Hyperosmolar therapy is one of the main treatments for cerebral edema following TBI. Mannitol and hypertonic saline (HS) are hyperosmolar agents that are routinely used in patients with cerebral swelling. On theoretical grounds, HS is likely to have more favourable effects on cerebral oxygenation, cerebral blood flow and metabolism compared to

mannitol. So far, a direct comparison between these agents has not been made.

Study objective

Aim of this study is to compare the effects of mannitol and HS in equimolar concentrations on cerebral blood flow, cerebral oxygenation, metabolism and inflammation in patients with severe TBI.

Study design

Randomized single blind prospective intervention study

Intervention

Patients are randomized to treatment with 250 mOsm HS or mannitol via a central venous catheter over 5 minutes. The treatment will be administered if the intracranial pressure is > 25 mm Hg for at least 5 minutes and not related to a transient external noxious stimulus or systemic derangement. In this trial patients will be randomized to receive either mannitol or HS. If necessary, additional boluses of the same drug may be administered to the patient in case of persistent intracranial hypertension. If the patient fails to respond to the study drug, the other drug may be used to lower intracranial pressure. In all cases analysis of the results will be performed on an *intention-to treat* basis.

Study burden and risks

Both mannitol and HS are routinely used in the treatment of cerebral swelling, randomisation for one of these drugs is therefore without additional risk for the patients. Intensive monitoring of these patients is part of routine neurological intensive care. This includes monitoring of intracranial pressure, jugular bulb oxygen saturation, and transcranial doppler. Extra procedures related to the study include the following:
For the measurement of components of the inflammatory response and for the measurement of jugular bulb oxygen saturation blood samples will be drawn from the arterial and jugular bulb catheter Total amount of blood drawn from the patients will be approximately 100 ml over a period of 2 days.
Instead of a single lumen transcranial bolt a 3 lumen transcranial bolt will be threaded and tapped into the cranium under local anaesthesia. Introduction of a bolt into the cranium is part of standard care of these patients and serves to hold a catheter measuring intracranial pressure. The bolt will also be used to grip and immobilize a microdialysis catheter (CMA Microdialysis, Sweden). After insertion of the microdialysis catheter, dialysis is a semi-automatic process, with no adverse events reported in the literature (29). Brain oxygen tension will be measured continuously, through the 3th lumen of the bolt.
Measurement of cerebral blood flow with transcranial doppler is a noninvasive

procedure with no risks and minimal burden to the patient.
The risks of this study are negligible and the burden minimal, mostly because treatment and monitoring are to a large extent part of routine care. The study can only be carried out in incapacitated patients since it concerns comatose patients in the acute phase after TBI injury.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Adult patients
Severe traumatic brain injury (Glasgow Coma Scale at first presentation < 9)
Intracranial hypertension (intracranial pressure > 20 mm Hg)

Exclusion criteria

No informed consent from the patient*s legal representative.
Expected survival < 2 days

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2007
Enrollment:	32
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	mannitol
Generic name:	mannitol
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2006-005173-22-NL
CCMO	NL13009.091.06