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Sugar or Salt (SOS) Trial: comparing two current treatments for patients with a brain injury

Submission date
09/04/2019

Recruitment status
No longer recruiting

Registration date
16/04/2019

Overall study status
Ongoing

Last Edited
13/12/2024

Condition category
Injury, Occupational Diseases, Poisoning

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Over one million people a year suffer injuries to their heads which require them to go to hospital. The most severe injuries often result in significant brain swelling. If left untreated, this swelling causes the pressure inside the head to increase, compressing the brain and causing further brain damage. The main treatments used for severe brain swelling involve placing the patient into an artificial coma (to rest the brain), giving drugs (to reduce brain swelling) or brain surgery (to release the pressure). Even with current treatments delivered in intensive care, over half of people with severe brain injury die or are left with severe brain damage. To improve outcomes for patients, doctors need to know the best treatments for severe brain swelling after head injuries. The two main drugs that are currently used to treat brain swelling are hypertonic saline (a strong salt solution) and mannitol (a sugary solution). Both of these drugs work by reducing brain swelling which helps to reduce pressure on the brain. Currently, it is not known which drug is the most effective treatment. Both drugs have undesirable side effects (hypertonic saline causes an imbalance of salts in the blood and mannitol can cause kidney failure). To deliver the best treatment doctors need to know which is most the safest and most effective. This study aims to work out which is the safest and most effective drug to treat the swelling of the brain that occurs after severe trauma to the head.

Who can participate?
Patients aged 16 or over admitted to an intensive care unit with a traumatic brain injury (an injury to the brain which occurs after trauma to the head)

What does the study involve?
Participants are randomly allocated to receive either the salty solution (hypertonic saline) or the sugary solution (mannitol). The study compares how effective the different drugs are at reducing the pressure on the brain. It also assesses which was better at helping the patient to recovery and what the side effects of treatment were. The study team keeps in contact with patients for 12 months after the study to check on how well they have recovered over time. Researchers also calculate how much each treatment costs and compare this to how beneficial they were.

What are the possible benefits and risks of participating?
Doctors do not know which of the two treatments is best, and that is why we are conducting this research. The researchers therefore cannot promise any direct benefits as a result of taking part in this study. However, it is hoped that the research will provide benefit to future patients who have a severe brain injury, as it will help doctors to know which is the best treatment to give. The risk of physical harm from taking part in the study is not considered to be any higher than the risks of standard clinical care, because the study is testing two existing treatments rather than a new treatment. Because the study involves completing questionnaires, there is a risk that participants may find it upsetting to answer some questions about their recovery. Trained research staff are available to talk to participants about any such feelings and can offer to put them in contact with professional services if this would be helpful.

Where is the study being run from?
Queen Elizabeth Hospital - University Hospitals Birmingham NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
June 2019 to February 2026

Who is funding the study?
National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (UK)

Who is the main contact?
University of Warwick study team
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2019-001688-66

IRAS number
260350

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
17/120/01, IRAS 260350

Study information

Scientific Title
Sugar or Salt (SOS) Trial: hyperosmolar therapy in traumatic brain injury

Acronym
SOS

Study objectives
The primary hypothesis is that hypertonic saline is more effective than mannitol in the management of raised ICP after severe TBI through improving clinical outcomes and cost-effectiveness.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 09/09/2019, East of England – Essex Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8115; essex.rec@hra.nhs.uk), ref: 19/EE/0228

Study design
Multicentre open-label randomized controlled clinical and cost-effectiveness trial with an internal pilot

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Traumatic brain injury

Interventions
Current interventions as of 10/06/2019:
A simple and secure, web-based and allocation concealed randomisation system will be used. Randomisation will be stratified by site and predicted probability of 6-month unfavourable outcome. This predicted probability will be calculated using age, pupillary response and documented Glasgow Coma Scale (GCS) motor score at intubation using the IMPACT calculator (Steyerberg et al, 2008).

Patients will be randomized in a 1:1 ratio to receive intravenous boluses of either 2 ml/kg 20% mannitol or 2 ml/kg hypertonic saline (or equivalent osmolar dose using concentration used locally by participating study centres).

If intracranial pressure (ICP) remains higher than 20mmHg, boluses of each treatment can be repeated until serum sodium is >155 mmol/L. If there is a second spike in ICP over 20 mmHg then the allocated IMP should continue to be used.

Trial treatment will continue until therapeutic targets have been met. The total duration of follow-up for both treatment arms will be 12 months.

Previous interventions:
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Patients will be randomized in a 1:1 ratio to receive intravenous boluses of either 2 ml/kg 20% mannitol or 2 ml/kg hypertonic saline (or equivalent osmolar dose using concentration used locally by participating study centres).

If intracranial pressure (ICP) remains high, boluses of each treatment can be repeated until either ICP is less than 20 mmHg or serum sodium is >155 mmol/L or osmolarity is >320 mosmol /L. If there is a second spike in ICP over 20 mmHg then the allocated IMP should continue to be used.

Trial treatment will continue until therapeutic targets have been met. The total duration of follow-up for both treatment arms will be 12 months.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Mannitol, hypertonic saline

Primary outcome measure
Neurological outcome measured by patient/relative/clinician completion of the Extended Glasgow Outcome Scale (GOS-E) questionnaire at 6 months

Secondary outcome measures
1. Intracranial pressure (ICP) control recorded continuously or at regular intervals from ICP bolt readings during the period of monitoring on ICU
2. Progression to stage 3 therapies (i.e. any use of additional treatments e.g. barbiturate coma, decompressive craniectomy, hypothermia, CSF drainage) recorded from the patient's medical records during their ICU stay
3. Which stage 3 therapies were required, recorded from the patient's medical notes during their ICU stay
4. Organ support requirements during ICU recorded from the patient's medical records, or through data linkage, according to the Critical Care Minimum Data Set definitions
5. ICU length of stay obtained from hospital records and through data linkage
6. Hospital length of stay obtained from hospital records and through data linkage
7. Discharge location obtained from hospital records and through data linkage
8. Longer term neurological outcomes measured using the modified Oxford Handicap Score (mOHS) completed by the research or clinical team at hospital discharge, and the Extended Glasgow Outcome Scale (GOS-E) completed by the patient/relative/clinician at 12 months
9. Survival measured from the patient's medical records at hospital discharge, 3 months, 6 months and 12 months
10. Health-related quality of life measured using the EQ-5D-5L at hospital discharge, 3 months, 6 months and 12 months post-TBI, completed by the patient/relative/clinician
11. Resource use collected from hospital records and through data linkage for the patient's duration of hospital stay and up to 12 months post-TBI
12. Serious adverse events recorded from the time that the patient is randomised through and including 28 calendar days after the last administration of IMP

Overall study start date
01/06/2019

Completion date
28/02/2026

Eligibility

Key inclusion criteria

1. Age 16 years or over
2. Admission to ICU following traumatic brain injury
3. ICP > 20mmHg for more than 5 minutes despite stage 1 procedures
4. <10 days from initial head injury
5. Abnormal CT scan consistent with traumatic brain injury

Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Both

Target number of participants
468

Key exclusion criteria
Current participant exclusion criteria as of 21/12/2023:
1. Devastating brain injury with withdrawal of treatment anticipated in the next 24 hours
2. Pregnancy
3. Severe hypernatraemia (Na > 155 mmol/L)
4. 2 or more prior doses of hyperosmolar therapy given on ICU

Previous participant exclusion criteria as of 06/08/2020:
1. Devastating brain injury with withdrawal of treatment anticipated in the next 24 hours
2. Pregnancy
3. Severe hypernatraemia (Na > 155 mmol/L)

Previous participant exclusion criteria from 10/06/2019 to 06/08/2020:
1. Devastating brain injury with withdrawal of treatment anticipated in the next 24 hours
2. Pregnancy
3. Severe hypernatraemia (Na > 160 mmol/L)

Original participant exclusion criteria:
1. Unsurvivable injuries
2. Pregnancy
3. Severe hypernatraemia (Na > 160 mmol/L)

Date of first enrolment
01/12/2019

Date of final enrolment
28/02/2025

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Queen Elizabeth Hospital - University Hospitals Birmingham NHS Foundation Trust
Heritage Building
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2TH

Study participating centre
John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Salford Royal Hospital
Salford Royal NHS Foundation Trust
Stott Lane
Salford
United Kingdom
M6 8HD

Study participating centre
Derriford Hospital
University Hospitals Plymouth NHS Foundation Trust
Derriford Rd
Plymouth
United Kingdom
PL6 8DH

Study participating centre
The Walton Centre NHS Foundation Trust
Lower Lane
Fazakerley
Liverpool
United Kingdom
L9 7LJ

Study participating centre
Southampton General Hospital
University Hospital Southampton NHS Foundation Trust
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Royal Victoria Hospital
Belfast Health & Social Care Trust
Grosvenor Road
Belfast
United Kingdom
BT12 6BA

Study participating centre
King's College Hospital
King's College Hospital NHS Foundation Trust
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre
Royal Infirmary of Edinburgh
NHS Lothian
Little France Cres
Edinburgh
United Kingdom
EH16 4SA

Study participating centre
Addenbrookes Hospital
Cambridge University Hospitals NHS Foundation Trust
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Lancashire Teaching Hospitals NHS Foundation Trust
Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
University Hospital of Wales
Heath Park
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CF14 4XW

Study participating centre
The Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
TS1 4LP

Study participating centre
South Tees Hospitals NHS Foundation Trust
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Royal Hallamshire Hospital
Glossop Road
Sheffield
United Kingdom
S10 2JF

Study participating centre
Nottingham University Hospitals NHS Trust - City Campus
Nottingham City Hospital
Hucknall Road
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NG5 1PB

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
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AB25 2ZN

Study participating centre
Queen Elizabeth University Hospital
1345 Govan Road
Glasgow
United Kingdom
G51 4TF

Study participating centre
University Hospital of North Staffordshire
Princes Road
Stoke-on-trent
United Kingdom
ST4 7LN

Study participating centre
Leeds General Infirmary
Great George Street

Leeds
United Kingdom
LS1 3EX

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
United Kingdom
W2 1BL

Study participating centre
St George's University Hospitals NHS Foundation Trust
St George's Hospital
Blackshaw Road
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London
United Kingdom
SW17 0QT

Study participating centre
Barts Health NHS Trust
The Royal London Hospital
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Sponsor information

Organisation
University Hospitals Birmingham NHS Foundation Trust

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Sponsor type
Hospital/treatment centre

Website
http://www.uhb.nhs.uk/

ROR
https://ror.org/014ja3n03

Organisation
University of Warwick

Sponsor details
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Sponsor type
University/education

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, HTA

Funding Body Type

Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The trial protocol and statistical analysis plan will be available once finalised.

The results of the trial will be reported first to trial collaborators. The main report will be drafted by the trial co-ordinating team, and the final version will be agreed by the Trial Steering Committee before submission for publication, on behalf of the collaboration.

The success of the trial depends on the collaboration of doctors, nurses and researchers from across the UK. Equal credit will be given to those who have wholeheartedly collaborated in the trial. The trial will be reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines (http://www.consort-statement.org).

The researchers will continue to build links with key stakeholder groups (e.g. UK Intensive Care Society, Society of British Neurological Surgeons, Neuroanaesthesia and Critical Care Society of Great Britain and Ireland, Patient/Public Involvement Groups etc). They will continue to publish editorials and review articles related to hyperosmolar therapy use in TBI. The purpose of these activities is to highlight the uncertainty of current treatment with hyperosmolar therapy and to generate and sustain interest from the clinical community so that the trial results will be eagerly anticipated. The researchers will publish the trial protocol and final trial results in high impact, open access peer-reviewed journals. The results of the trial will be reported first to trial collaborators. The main report will be drafted by the WCTU team, and the final version will be agreed by the TSC before submission for publication, on behalf of the collaboration. The trial will be reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The main publications will be the report to the funding body (HTA Monograph) and a journal publication. In addition, the results will be presented at national and international medical conferences as well as disseminated via social media (Twitter/Facebook) and blog postings. This will ensure that the results are communicated rapidly to clinicians who will then be able to put them into practice.

The researchers will aim to incorporate the results into national and international TBI guidelines via existing guideline development groups, which include several of the applicants (Hutchinson /Kolias/Andrews). They will incorporate the findings of the trial into relevant review articles and ensure the findings of the trial are available through NHS Evidence. They will work with our Marketing and Communication team to develop a strategy for communication with the media (television, radio, newspaper etc) to enhance communication of the trial results to patients and participants. They will produce a lay summary of the trial results with their public and patient involvement partners. This will be disseminated through our press officer, user groups, websites and INVOLVE database to participants of the trial who indicated they wanted to know the results.

The researchers expect the output from this trial will impact international TBI practice and they will ensure that the results of this trial are fed into the Brain Trauma Foundation and European Society of Intensive Care Medicine evidence assessment and guideline process. Finally, a policy for authorship of trial publications will be drafted and agreed by the investigators early in the trial, in accordance with the WCTU Standard Operating Procedures.

Intention to publish date
28/02/2026

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	25/02/2020	06/08/2020	Yes	No
HRA research summary			28/06/2023	No	No