ISRCTN16770388 https://doi.org/10.1186/ISRCTN16770388

Study of beta blockers for salt wasting in patients with brain TB

Submission date
11/09/2025

Recruitment status
No longer recruiting

Registration date
26/09/2025

Overall study status
Completed

Last Edited
12/09/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
Tuberculous meningitis (TBM) is a serious brain infection caused by tuberculosis. TBM can cause serious problems in the brain, including increase volume of cerebrospinal fluid (CSF) leading to enlargement of brain's hollow cavities (ventricles), strokes (especially in younger people), and convulsions. One common complication in TBM is hyponatremia, which means low levels of sodium in the blood. This happens in about one in three TBM patients. There are many reasons why sodium levels can drop, including poor appetite, vomiting, diarrhea, certain medications, and other health issues. In the past, a condition called SIADH (a condition where the body makes too much of a hormone called ADH) was thought to be the main reason for low sodium in TBM patients, but newer studies suggest that cerebral salt wasting (CSW) - a problem where the body loses too much salt due to brain stress - might actually be more common. CSW may be linked to the body's stress response, especially when there is brain pressure, infection, or stroke. One chemical involved in this stress response is called catecholamine. High levels of this chemical can cause the body to lose too much salt and water. Some research has shown that a type of medication called a beta blocker (which lowers stress signals in the body) may help improve outcomes in patients with brain injuries or stroke. Propranolol is one such beta blocker. In this study, we are testing whether propranolol can safely and effectively help to correct the low sodium levels and fluid loss in people with TBM-related CSW. We will compare it to standard care in a group of patients chosen at random.

Who can participate?
Patients aged between 15 to 70 years with TBM admitted during 2022 and 2024 in a tertiary care centre in India were screened for CSW

What does study involve?
The patients were randomly allocated to propranolol or placebo (saccharine). The intervention group received propranolol 10 mg twice daily on day one, which increased to 20 mg from day 2. Propranolol was continued until 1 month irrespective of correction of serum sodium; thereafter, gradually tapered within 2 weeks. Placebo group received a saccharine tablet in the similar manner.

What are possible benefits and risks of participating?
Propranolol is a drug used for reducing stress and to suppress catecholamine induced injury. Low serum sodium and high urinary output due to CSW may have early correction following adjunctive propranolol treatment. Hyponatremia is an independent risk factor of death in intensive care unit. Early correction of sodium and volume loss may reduce death and improve outcome. Propranolol is a drug used in medical practice for long time. It has a side effect profile including slowing of heart rate and reduction in blood pressure. The pulse and blood pressure will be monitored closely and in case of such side effects, the drug will be withdrawn.

Where is the study run from?
Sanjay Gandhi Post Graduate Institute of Medical Sciences (India)

When is the study starting and how long is it expected to run for?
March 2022 to December 2024

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Jayantee Kalita, jkalita@sgpgi.ac.in, jayanteek@yahoo.com

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Prof Jayantee Kalita

ORCID ID
https://orcid.org/0000-0002-6141-3592

Contact details
Department of Neurology, C-block
Sanjay Gandhi Post Graduate Institute of Medical Sciences
Raebareli Road
Lucknow
India
226014
+91 (0)5222494177
jkalita@sgpgi.ac.in

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Role of beta blockers in cerebral salt wasting in the patients with tuberculous meningitis: an open labelled randomized control trial

Acronym
BEST - TBM

Study objectives
Primary objective:
Number of days to normalize serum sodium

Secondary objective:
1. Number of days to achieve positive fluid balance
2. Number of days to have 3 l urinary output
3. Mortality at 1 month
4. Side effects
5. Functional outcome was assessed at 3 and 6 months using a modified Rankin Scale (mRS), and categorized as good (mRS score <3) and poor (mRS score 3 to 6)

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 11/03/2022, Institutional Ethics Committee, Sanjay Gandhi Post Graduate Institute of Medical Sciences (Raebareli Road, Lucknow, 226014, India; +91 (0)522-2494918, +91 (0)522 2668017; iec@sgpgi.ac.in), ref: 2021-225-DM-122

Study design
Investigator-initiated single center open-label randomized placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Cerebral salt wasting syndrome in patients with tuberculous meningitis

Interventions
Once the diagnosis of cerebral salt wasting syndrome was ascertained in the patients with tuberculous meningitis, the patients were randomized to propranolol or placebo (saccharine) using simple randomization with a 1:1 allocation ratio. The intervention group received

propranolol 10 mg twice daily on day one, which increased to 20 mg from day two. Propranolol was continued until 1 month irrespective of correction of serum sodium; thereafter, gradually tapered within 2 weeks. The placebo group received saccharine tablet in the similar manner.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Propranolol

Primary outcome(s)
The number of days for normalization of serum sodium: serum sodium levels were measured every third day for up to 1-month post-randomization, at 1 month, 3 months and 6 months follow-up

Key secondary outcome(s))
1. Number of days to achieve 500 ml positive fluid balance (Intake- output >500 ml). Daily fluid balance (intake and output over 24 hours) was recorded to monitor fluid status.
2. Number of days to have <3 L urinary output. Daily fluid balance (intake and output over 24 hours) was recorded to monitor fluid status.
3. Mortality recorded at 1 month
4. Side effects recorded during hospitalization and at follow-up visits at 1 month, 3 months, and 6 months
5. Functional outcome assessed using a modified Rankin Scale (mRS) and categorized as good (mRS score < 3) and poor (mRS score 3 to 6) at 3 and 6 months

Completion date
15/12/2024

Eligibility

Key inclusion criteria
Patients aged between 15 to 70 years with tuberculous meningitis and having cerebral salt wasting syndrome (CSW)

Diagnostic criteria of tuberculous meningitis

Essential criteria:
The clinical features of meningitis (fever, headache, vomiting) for more than 2 weeks

Supportive criteria:
1. Cranial imaging: CT/MRI evidence of excaudate, hydrocephalous, granulomas in isolation or in combination
2. Cerebrospinal fluid: cells 10-500/mmb, lymphocytic predominance, protein >1 g/liter
3. Evidence of extra CNS active tuberculosis
4. Exclusion of alternative diagnosis of meningitis

The diagnosis of CSW was based on the following essential and supportive criteria

Essential criteria, all are mandatory
1. Polyuria (>3 l/day for two consecutive days)
2. Serum sodium <135 mEq/L in two consecutive tests 24 hours apart
3. Absence of secondary causes of hyponatremia such as renal, hepatic or cardiac failure, endocrinal disorder, natriuretic drugs etc

Supportive criteria: three out of five are needed
1. Clinical incidence of hypovolemia: dry skin, hypotension, tachycardia or postural hypotension
2. Consistent fluid deficit on intake output chart
3. Laboratory evidence of dehydration such as elevated hematocrit, hemoglobin, albumin and blood urea
4. Central venous pressure less than 6 cm of water
5. Urinary sodium more than 40 mEq/L or urine osmolality more than 300 mOsmol/L on two consecutive days

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
15 years

Upper age limit
70 years

Sex
All

Total final enrolment
38

Key exclusion criteria
1. Patients with endocrinal disorder, organ (renal, liver, heart) failure, vasculities, renal tubular acidosis, malignancy, pregnancy, lactation, on chemotherapy, radiotherapy, inotrope, dopaminergic, antidopaminergic, diuretics, carbamazepine, mannitol or aminoglycosides
2. Above 70 years and below 15 years of age
3. Denial of consent
4. Patients requiring mechanical ventilation or cardiopulmonary resuscitation

Date of first enrolment
12/03/2022

Date of final enrolment
15/12/2024

Locations

Countries of recruitment
India

Study participating centre
Sanjay Gandhi Post Graduate Institute of Medical Sciences
Raebareli Road
Lucknow
India
226014

Sponsor information

Organisation
Sanjay Gandhi Post Graduate Institute of Medical Sciences

ROR
https://ror.org/01rsgrz10

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and analysed during the current study will be available upon request from Jayantee Kalita (jkalita@sgpgi.ac.in, jayanteek@yahoo.com)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			12/09/2025	No	Yes

Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan			12/09/2025	No	No