

Clinical Trial Protocol

Iranian Registry of Clinical Trials

17 Sep 2026

Evaluating the Effect of the Concomitant Administration of Methylphenidate and Amantadine on the TBI-related Outcomes: A Randomized, Double-blind, Placebo-controlled, Parallel trial

Protocol summary

Study aim

To evaluate the effect of concomitant administration of Amantadine and methylphenidates on the patients' early consciousness recovery and the short- and long-term outcomes.

Design

Two arm parallel group Double-blind, Placebo-controlled phase 3 randomized trial.

Settings and conduct

The study will be conducted in the ICU of Shahid Rajaei Trauma hospital, Shiraz. Patients are randomly assigned to the intervention or control group using the block randomization method. Patients and clinical providers and the outcomes assessor are blind to the administered drugs/placebo.

Participants/Inclusion and exclusion criteria

Inclusion Criteria: Adults, pure traumatic brain injury (TBI) (head AIS>3 and other AIS ≤3), motor component of Glasgow coma score 4 or 5, Parenchymal damage≤10 cc, Heart rate<100 beats/min Exclusion Criteria: Multiple Trauma, Penetrating TBI, High Cervical Cord Injuries, having neurosurgery interventions, Severe Agitation, Hospital admission due to psychiatric problem, Known case of ADHD, HR > 120 without any systemic diseases, Active cancer or chemoradiotherapy, Ischemic Heart Diseases, Glomerular Filtration Rate< 60 ccs/min, Pregnant women, Cerebral Palsy, Mental Retardation, taking Neuroleptics or SSRI or MAO inhibitors or Lithium salts, Propofol or Thiopental, Involved in other trials during the last three months, Decline to participate.

Intervention groups

Intervention Group: will receive Amantadine 100mg and methylphenidates 20mg two times/day (7 AM and 2 PM). Control group: will receive Placebo two times/day (7 AM and 2 PM). The experiment in both groups will last till two weeks or hospital discharge, or the patients become fully conscious

Main outcome variables

ICU length of stay, the average length of hospital stay, Glasgow outcome score at the beginning, after the end of treatment, and after six months, antipsychotic or antidepressant use at 6-month follow up.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20130310012776N7**

Registration date: **2021-11-23, 1400/09/02**

Registration timing: **prospective**

Last update: **2021-11-23, 1400/09/02**

Update count: **0**

Registration date

2021-11-23, 1400/09/02

Registrant information

Name

Hosseinali Khalili

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone

+98 71 3625 4206

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2022-01-01, 1400/10/11

Expected recruitment end date

2022-12-30, 1401/10/09

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Evaluating the Effect of the Concomitant Administration of Methylphenidate and Amantadine on the TBI-related Outcomes: A Randomized, Double-blind, Placebo-controlled, Parallel trial

Public title

Concomitant Administration of the Methylphenidate and Amantadine

Purpose

Supportive

Inclusion/Exclusion criteria**Inclusion criteria:**

Pure Blunt Traumatic Brain injury The motor component of Glasgow coma score 4 or 5 Parenchymal damage less than or equal to 10 cc Heart rate less than 100 beats/min on the recruitment time intensive care unit staying for at least 5 days

Exclusion criteria:

Having Multiple Trauma Penetrating Traumatic Brain Injuries High Cervical Cord Injuries(C1-C4) Need for neurosurgery intervention for any causes Severe Agitation Previous history of Hospital admission due to psychiatric problem Known case of Attention Deficit Hyperactivity Disorder Heart Rate more than 120 beats/min without any systemic diseases Active cancer or chemoradiotherapy Ischemic Heart Diseases Glomerular Filtration Rate less than 60 ccs/min Pregnant women Cerebral Palsy Mental Retardation Positive Drug history of Taking Neuroleptics, or Selective Serotonin Reuptake Inhibitors, or Monoamine Oxidase Inhibitor, or Lithium salts, or Propofol, or Thiopental Involved in other clinical trials during the last three months Decline to participate

Age

From **18 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Care provider
- Outcome assessor

Sample size

Target sample size: **200**

Randomization (investigator's opinion)

Randomized

Randomization description

Included patients will be allocated randomly into the experiment and placebo groups via the blocked randomization method. A trained research assistant will use blocked randomization with block sizes of 4 with an equal probability to enroll the eligible patients to the

experiment group (group A) and placebo (group B).

Regarding the size of block 4, we have six possible combinations of group assignments, including AABB, ABAB, BAAB, BABA, BBAA, and ABBA. At first, the assistant will select one of these arrangements randomly, and the four eligible admitted patients would be assigned accordingly in each block. We will repeat this process many times to include the eligible patients.

Blinding (investigator's opinion)

Double blinded

Blinding description

Although the patients will be informed of our primary objectives, they won't know which drugs/ placebo they will receive. Well-trained nurses who are unaware of the study's objectives and the drugs containing bottles will be recruited to give the medication/placebo to the patients. As the placebo's color, shape, and size were identical to our medications, their differentiations were only possible via a specific code imprinted on the bottles. The main researchers only know to which category the drugs (codes) belong.

Placebo

Used

Assignment

Parallel

Other design features**Secondary Ids**

empty

Ethics committees**1****Ethics committee****Name of ethics committee**

Ethic Committee of Shiraz University of Medical Sciences

Street address

Shiraz University of Medical Sciences, Zand Street, Shiraz Town

City

Shiraz

Province

Fars

Postal code

32122430

Approval date

2021-10-18, 1400/07/26

Ethics committee reference number

IR.SUMS.REC.1400.558

Health conditions studied**1****Description of health condition studied**

moderate to severe Traumatic Brain Injury

ICD-10 code**ICD-10 code description**

Primary outcomes

1

Description

Intensive Care Unit Length of Stay

Timepoint

At the time of Discharge from intensive care unite

Method of measurement

Counting the days when the patients were admitted in the intensive care unit

2

Description

Hospital Length of Stay

Timepoint

At the time of Discharge from Hospital

Method of measurement

Counting the days when the patients were admitted in the Hospital

3

Description

Glasgow outcome scale

Timepoint

At the beginning of the Experiment, two weeks after starting the experiment (just after the end of the drug administration), 6 months after starting the experiment.

Method of measurement

According to the Glasgow outcome scale

4

Description

Taking the antipsychotic or antidepressant drugs

Timepoint

6 months after starting the experiment

Method of measurement

Taking or not taking the drugs as well as the dosage will be reported

Secondary outcomes

empty

Intervention groups

1

Description

Intervention group: Methylphenidate and Amantadine (AMH) will be given to our intervention group. Dosage of Methylphenidate and AMH will be 20mg and 100mg, respectively, and be given at 7 AM and 2 PM. The treatment will be continued till two weeks or hospital discharge, or the patients become fully conscious. The participants will be evaluated on the first day (before starting the treatment), immediately after the end of the treatment, and six months after starting the experiment

Category

Rehabilitation

2

Description

Control group: Only Placebo with the same color, size, and shape will be given to our Control Group. The Placebo interval was similar to that of the intervention group. The treatment will be continued till two weeks or hospital discharge, or the patients become fully conscious. The participants will be evaluated on the first day (before starting the treatment), immediately after the end of the treatment, and six months after starting the experiment

Category

Rehabilitation

Recruitment centers

1

Recruitment center

Name of recruitment center

Shahid Rajaei (emtiaz) Trauma Hospital, Shiraz
University of Medical Sciences

Full name of responsible person

Hosseinali Khalili

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

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Full name of responsible person

Abbas Rezaian zadeh

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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Shiraz University of Medical Sciences
Proportion provided by this source
100
Public or private sector
Public
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Academic

Person responsible for general inquiries

Contact

Name of organization / entity
Shiraz University of Medical Sciences
Full name of responsible person
Hosseinali Khalili
Position
Assistant Professor
Latest degree
Specialist
Other areas of specialty/work
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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Undecided - It is not yet known if there will be a plan to make this available

Study Protocol

Undecided - It is not yet known if there will be a plan to make this available

Statistical Analysis Plan

Undecided - It is not yet known if there will be a plan to make this available

Informed Consent Form

Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report

Undecided - It is not yet known if there will be a plan to make this available

Analytic Code

Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary

Undecided - It is not yet known if there will be a plan to make this available