Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Jul 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

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Email address

khalili_h@sums.ac.ir

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 than120 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
Street address
Shahid Rajaei (Emtiaz) Trauma Hospital, Chamran Blvd, Shiraz, Iran
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7194815711
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+98 71 3624 8980
Email
khalili_h@sums.ac.ir

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Shiraz University of Medical Sciences
Full name of responsible person
Abbas Rezaian zadeh
Street address
Deputy of research and technology, seventh floor, Shiraz University of Medical Sciences, Zand Street, Shiraz, Fars
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Province
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Postal code
7134814336
Phone
+98 71 3212 2430
Email
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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
Neurosurgery
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Person responsible for scientific inquiries

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Hosseinali Khalili
Position
Assistant Professor
Latest degree
Specialist
Other areas of specialty/work
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Person responsible for updating data

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
Neurosurgery
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7194815644
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khalili_h@sums.ac.ir
Web page address

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