Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Nov 2026

Efficacy of Memantine vs Placebo as Adjunctive Therapy on Craving ،Impulsive Behaviors and Treatment Retention in Opioid Use Disorder Following Detoxification : a Randomized Double-blind Clinical Trial

Protocol summary

Study aim
Determining the effectiveness of memantine versus placebo on craving and impulsive behaviors in opioid withdrawal

Design
Clinical trial with intervention and control group (placebo), with parallel groups, double-blind, randomized, phase 2 on 80 patients. The rand function of Excel software was used for randomization.

Settings and conduct
The outcome assessor, psychologist, and researcher are blinded to the type of intervention received by the subjects. The assignment of drug or placebo to each subject is done by the rand command in Excel software and by an independent pharmacist. The shape, smell, and color of the capsules are standardized. Outcomes are assessed every 2 weeks.

Participants/Inclusion and exclusion criteria
People with a history of using opium, syrup, heroin, meeting OUD criteria, who have completed at least 4 weeks and a maximum of 6 weeks of detoxification and have been treated with methadone (MMT) at a fixed dose. • People with a minimum age of 18 and a maximum of 60 years • Meeting OUD criteria according to DSM-5

Intervention groups
After the initial assessments, the volunteers will be randomly assigned to one of two groups - 1. Memantine - 2. Placebo The memantine group will start with a dose of 7 mg for 5 days, then 14 mg for 5 days, and finally reach the target dose of 21 mg daily. The placebo group will also receive placebo capsules according to the drug group's schedule Memantine 21 mg extended-release capsule from Tasnim Company (Alzixa 21 mg ER) Placebo capsules are prepared, packaged, and coded by an independent pharmacist, taking into account the similarity in color and odor

Main outcome variables
Craving intensity Consumption Impulsivity Negative/positive urine test Evaluation of immediate reward value versus delayed reward

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20260713070165N1**
Registration date: **2026-08-01, 1405/05/10**
Registration timing: **prospective**

Last update: **2026-08-01, 1405/05/10**
Update count: **0**

Registration date
2026-08-01, 1405/05/10

Registrant information

Name
Hossein Ghadiry

Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status
recruiting

Funding source

Expected recruitment start date
2026-08-23, 1405/06/01

Expected recruitment end date
2027-01-21, 1405/11/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Efficacy of Memantine vs Placebo as Adjunctive Therapy on Craving ،Impulsive Behaviors and Treatment Retention in Opioid Use Disorder Following Detoxification : a Randomized Double-blind Clinical Trial

Public title

Memantime in Opioid use Disorder

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Individuals with a history of opium, opium extract (shireh), or heroin use who met the diagnostic criteria for opioid use disorder (OUD), had completed detoxification between 4 and 6 weeks prior to enrolment, and were receiving methadone maintenance treatment (MMT) at a stable dose Adults aged 18–60 years. Confirmation of OUD based on a clinical interview and completion of the SCID-II by an experienced psychiatrist, in accordance with the DSM-5 diagnostic criteria, with participants meeting at least 5 of the 11 DSM-5 criteria for OUD. Completion of the Mini International Neuropsychiatric Interview (MINI) by an experienced psychiatrist to assess psychiatric comorbidities, including depression and anxiety, and to confirm the absence of any severe psychiatric disorder. Negative urine drug screening results for amphetamines, methamphetamine, and cannabinoids.

Exclusion criteria:

Severe hepatic, cardiac, or renal insufficiency. Severe neurological disorders, such as advanced dementia or multiple sclerosis (MS). Concomitant use of NMDA receptor antagonists, such as amantadine, ketamine, or high-dose dextromethorphan. Recent traumatic brain injury Pregnancy or breastfeeding.

Age

From **18 years** old to **60 years** old

Gender

Both

Phase

2-3

Groups that have been masked

- Participant
- Investigator
- Outcome assessor

Sample size

Target sample size: **80**

Randomization (investigator's opinion)

Randomized

Randomization description

Following confirmation of eligibility, acquisition of written informed consent, and completion of baseline assessments, participants will be allocated in a 1:1 ratio to receive either memantine or placebo. Individual-level stratified permuted-block randomization will be used. The stratification variables will include participant age, categorized as 18–39 years and 40–60 years, and duration of regular opioid use, categorized as less than 10 years and 10 years or longer. Accordingly, four strata will be formed. Within each stratum, an independent randomization sequence will be generated using randomly varying permuted block sizes of 4 and 6, with a 1:1 allocation ratio. The random allocation sequence will be generated before participant recruitment by an independent statistician using computer-based randomization software. Information regarding block sizes and sequence order will not be disclosed to members of the research team involved in participant recruitment, treatment administration, or outcome assessment. Memantine and placebo will be prepared and packaged in an identical manner by an independent pharmacist and labeled only with sequential numerical codes. Participants, treating physicians, outcome assessors, and investigators will remain blinded to treatment allocation until completion of the initial data analysis.

Blinding (investigator's opinion)

Double blinded

Blinding description

Participants will be informed, before enrollment, about the nature of the trial, the possibility of receiving either memantine or placebo, and the 1:1 allocation ratio, and will provide written informed consent. However, they will remain unaware of their assigned intervention until completion of the initial data analysis. Memantine and placebo will be prepared, packaged, and coded by an independent pharmacist who will have no role in participant recruitment, clinical care, data collection, outcome assessment, or data analysis. The active medication and placebo will be made as similar as possible with respect to appearance, color, size, odor, packaging, and administration schedule. Participants in the placebo group will follow the same dose-escalation schedule as those in the memantine group, with corresponding stages matching the 7-, 14-, and 21-mg doses, to prevent the capsule-administration pattern from revealing treatment allocation. Medication packages will be labeled only with sequential numerical codes and will contain no information indicating the assigned intervention. The following individuals will remain blinded to participants' treatment allocation: Participants; The principal investigator and other academic investigators involved in conducting the study; Outcome assessors, including personnel responsible for administering the Desire for Drug Questionnaire (DDQ), the delay-discounting task, the cue-induced craving task, and recording urine drug-screening results. The random allocation sequence will be generated by an independent statistician. For operational reasons, the statistician responsible for generating the sequence and the pharmacist responsible for coding the study medications will be aware of the correspondence between allocation codes and treatment assignments. However, neither individual will be involved in participant recruitment, treatment delivery, outcome assessment, or the primary data analysis. The code-identification list linking

medication codes to treatment allocation will be stored in an encrypted electronic file or in sealed envelopes and will be accessible only to the independent pharmacist or another designated code custodian. During statistical analysis, the dataset will be provided to the analyst using neutral labels, such as “Group A” and “Group B.” The treatment codes will be revealed only after the database has been locked and the initial analysis of the prespecified outcomes has been finalized. Whenever feasible, the initial draft of the study results will also be prepared using these neutral group labels.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Working Group/Research Ethics Committee, Faculty of Medicine - Shahid Sadoughi University of Medical

Street address
shohadaie gomnam Boulevard - Shahid Sadoughi Medical Sciences Campus, Yazd

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Province
Yazd

Postal code
8915173143

Approval date
2026-07-13, 1405/04/22

Ethics committee reference number
IR.SSU.MEDICINE.REC.1405.140

Health conditions studied

1

Description of health condition studied
Opioid use disorder

ICD-10 code
F11.2

ICD-10 code description
Opioid use disorder

Primary outcomes

1

Description
Craving intensityConsumption

Timepoint
Before the start of the intervention and then every 2 weeks until the end of week 12

Method of measurement
Desires for Drug Questionnaire

2

Description
Positive/negative methadone urine test

Timepoint
Before the start of the intervention and then every 2 weeks until the end of week 12

Method of measurement
Methadone urine test

3

Description
cue induced craving

Timepoint
Before the start of the intervention and then every 2 weeks until the end of week 12

Method of measurement
Visual sequence that stimulates drug use

4

Description
Preference for immediate rewards over delayed rewards

Timepoint
Before the start of the intervention and then every 4 weeks until the end of week 12

Method of measurement
monetary choice questioner(MCQ) Kirby

Secondary outcomes

empty

Intervention groups

1

Description
Intervention group: Memantine 21mg

Category
Treatment - Drugs

2

Description
Control group: placebo

Category
Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center
Taft Psychiatric Hospital - Yazd

Full name of responsible person
hossein ghadiry

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Yazd - Taft - Beginning of Shahid Beheshti Boulevard - Opposite the Courthouse - End of the Alley of the University of Applied Sciences
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Sponsors / Funding sources

1

Sponsor
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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
No
Title of funding source
Student personal expenses
Proportion provided by this source
100
Public or private sector
Private
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Persons

Person responsible for general inquiries

Contact
Name of organization / entity
Yazd University of Medical Sciences
Full name of responsible person
hossein ghadiry
Position
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Latest degree
A Level or less
Other areas of specialty/work
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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
Yes - There is a plan to make this available
Statistical Analysis Plan
No - There is not a plan to make this available
Informed Consent Form
Yes - There is a plan to make this available
Clinical Study Report
No - There is not 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
Title and more details about the data/document
Research implementation protocol
When the data will become available and for how long
After the end of the study
To whom data/document is available
All persons who submit a written request
Under which criteria data/document could be used
Subject to written request and presentation of identity documents
From where data/document is obtainable
Scientific Officer of the Study
What processes are involved for a request to access data/document
Send the request email - Attach the applicant's identity details - If the identity documents are confirmed, send the research protocol file.
Comments