Clinical Trial Protocol
Iranian Registry of Clinical Trials

02 Oct 2026

Investigating the effect of adding subcutaneous ketamine to routine treatment of treatment-resistant depressed patients

Protocol summary

Study aim
1.Determination and Comparison of mean depression scores between intervention and control groups before the intervention, at weeks 2, 4, 6, and one month after the last session. 2.Determination and Comparison of the mean number of adverse events between intervention and control groups at the same time points.

Design
A clinical trial with control group, with the parallel groups, Double-blind, randomized

Settings and conduct
in a double-blind clinical trial at Khorshid Hospital in Isfahan enrolls 52 patients with treatment-resistant major depressive disorder, who are randomly assigned to two parallel groups. Depression severity and adverse effects are evaluated at baseline, during weeks 2, 4, and 6 of treatment, and one month after the final intervention.

Participants/Inclusion and exclusion criteria
Inclusion criteria: 1.Age between 60-18 years 2.Individual who have DSM-V indicators for major depression without psychotic characteristics and mania or hypomania 3.Individual who do not have an adequate response to monotherapy with antidepressants for at least two times (at least 4-6 weeks) 4.Satisfaction with participating in the study Exclusion criteria: 1.Pregnant or breastfeeding women 2.History of substance dependence or abuse in the last 3 months 3.Serious and unstable physical patients 4.Untreated hypothyroidism or hyperthyroidism 5.Current or past history of psychotic symptoms 6.History of mania or hypomania, catatonia, or depression secondary to a medical condition 7.History of hypertension 8.History of seizure disorder 9. renal failure

Intervention groups
In the intervention group, ketamine(0.5 mg/kg) is administered subcutaneously, and in the control group, normal saline is administered subcutaneously, both twice weekly for six weeks

Main outcome variables
severity of depression: side effects

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20090801002266N22**
Registration date: **2026-02-09, 1404/11/20**
Registration timing: **prospective**

Last update: **2026-02-09, 1404/11/20**
Update count: **0**

Registration date
2026-02-09, 1404/11/20

Registrant information

Name
Gholamreza Kheirabadi

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
2026-04-04, 1405/01/15

Expected recruitment end date
2027-04-04, 1406/01/15

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date

empty

Scientific title
Investigating the effect of adding subcutaneous ketamine to routine treatment of treatment-resistant depressed patients

Public title
ketamine injection on improving treatment-resistant depression

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Age between 60-18 years Individuals who have DSM-V indicators for major depression without psychotic characteristics and mania or hypomania individuals who do not have an adequate response to monotherapy with antidepressants for at least two times (at least 4-6 weeks) Satisfaction with participating in the study

Exclusion criteria:
Pregnant or breastfeeding women History of substance dependence or abuse in the last 3 months Serious and unstable physical patients including liver, kidney, gastrointestinal, respiratory, cardiovascular diseases (such as ischemic heart disease), endocrine, neurological, hematological Untreated hypothyroidism or hyperthyroidism Current or past history of psychotic symptoms History of mania or hypomania, catatonia, or depression secondary to a medical condition History of hypertension History of seizure disorder Diagnosis of renal failure

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

Gender
Both

Phase
3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size
Target sample size: **52**

Randomization (investigator's opinion)
Randomized

Randomization description
Eligible participants will be randomized using block randomization with a block size of two. Within each block, participants are ordered by national ID number. A random number table is used to determine the allocation sequence. Two possible sequences exist (A-B,B-A) , and neither participants nor investigators know which label(A orB) corresponds to ketamin or placebo . A third party who is aware of the treatment codes prepares the study medications in sealed opaque envelopes and delivers them to the research team, maintaining double blinding. This process continues until all participants have received their assigned intervention.

Blinding (investigator's opinion)
Double blinded

Blinding description
Both participants and investigators involved in outcome assessment are unaware of the treatment assignments. Study medications, labeled as A and B, are prepared by a third party who is not involved in patient evaluation. The third party is aware of the correspondence between the labels and the actual interventions (drug or placebo). The medications are placed in sealed opaque envelopes and delivered to the research team for administration. Blinding is maintained until all study outcomes have been collected.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Research Ethics Committee of School of Medicine ,Isfahan University of Medical Sciences

Street address
Isfahan University of Medical Sciences, Hezar Jerib street

City
Isfahan

Province
Isfehan

Postal code
8174673461

Approval date
2026-01-27, 1404/11/07

Ethics committee reference number
IR.MUI.MED.REC.1404.436

Health conditions studied

1

Description of health condition studied
Treatment-Resistant Major Depressive Disorder

ICD-10 code
F33.9

ICD-10 code description
Major depressive disorder, recurrent, unspecified

Primary outcomes

1

Description
Depression score (assessed using the HDRS)

Timepoint
Before the intervention, at week 2, week 4, and week 6 during the intervention, and one month after the last intervention session
Method of measurement
Hamilton Depressive Rating Scale (HDRS)

Secondary outcomes

1

Description
Intervension side effects
Timepoint
Before the intervention, at week 2, week 4, and week 6 during the intervention, and one month after the last intervention session
Method of measurement
checklist evaluation

Intervention groups

1

Description
Intervention group: In this group, ketamine at a dose of 0.5 mg/kg is administered subcutaneously twice weekly for six weeks, for a total of 12 injections.
Category
Treatment - Drugs

2

Description
Control group: n this group, Placebo (normal saline) is administered subcutaneously twice weekly for six weeks, for a total of 12 injections.
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Khorshid Hospital
Full name of responsible person
Gholamreza Kheirabadi
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Sponsors / Funding sources

1

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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
Esfahan 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
Esfahan University of Medical Sciences
Full name of responsible person
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Position
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Sharing plan

Deidentified Individual Participant Data Set (IPD)
No - There is not a plan to make this available
Justification/reason for indecision/not sharing IPD
There is no further information
Study Protocol
No - There is not a plan to make this available
Statistical Analysis Plan
No - There is not a plan to make this available
Informed Consent Form
No - There is not a plan to make this available
Clinical Study Report
No - There is not a plan to make this available
Analytic Code
No - There is not a plan to make this available
Data Dictionary
No - There is not a plan to make this available