Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Investigating the effect of adding N-acetylcysteine to treatment compared to placebo on improving depressive symptoms in patients with bipolar disorder: a clinical trial

Protocol summary

Study aim
Determining the effect of adding N-acetylcysteine to treatment on depressive symptoms in bipolar patients.

Design
A Phase 2, double-blind, placebo-controlled, parallel-group clinical trial will be conducted on 60 patients. A block randomization method will be used.

Settings and conduct
This study will be conducted on bipolar inpatients at Golstan Hospital in Ahvaz. Neither the patients nor the outcome assessors will know which type of medication is being administered.

Participants/Inclusion and exclusion criteria
Inclusion Criteria: Diagnosis of bipolar depression based on DSM-5 criteria; Hamilton Depression Rating Scale (HAM-D) score > 8; Hospitalization in the Psychiatry Ward of Golestan Hospital; Age between 18 and 65 years. Exclusion Criteria: Concomitant use of any other medications with antidepressant properties (outside of the standard therapy); Co-existing psychiatric disorders, such as psychotic disorders; Acute substance abuse or substance abuse within the past 12 months (excluding nicotine); Pregnancy; Intellectual disability or other cognitive disorders

Intervention groups
Intervention group: In addition to standard treatment, this group will receive N-acetylcysteine (NAC) tablets. Control group: In addition to standard pharmacological treatment, this group will receive placebo tablets identical in appearance to the NAC tablets.

Main outcome variables
Depressive symptoms

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20251011067589N1**
Registration date: **2025-11-09, 1404/08/18**
Registration timing: **prospective**

Last update: **2025-11-09, 1404/08/18**
Update count: **0**

Registration date
2025-11-09, 1404/08/18

Registrant information

Name
Ehsan Goshtasbi Zadeh

Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2025-12-22, 1404/10/01

Expected recruitment end date
2026-04-21, 1405/02/01

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
Investigating the effect of adding N-acetylcysteine to treatment compared to placebo on improving depressive

symptoms in patients with bipolar disorder: a clinical trial

Public title
Investigating the Effect of Adding N-acetylcysteine to Treatment in Bipolar Depression

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Patients diagnosed with bipolar depression according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition criteria. A score greater than 8 on the Hamilton Depression Rating Scale. Patients hospitalized in the Psychiatry Ward of Golestan Hospital Patients in the age range of 18-65 years

Exclusion criteria:
The use of any other medication that has antidepressant effects, except for the study drug, or mood stabilizers or antipsychotics that have been initiated for the patient. The presence of comorbid psychiatric disorders such as schizoaffective disorder or other psychotic disorders like schizophrenia Acute substance, sedative, or alcohol dependence or abuse within the past 12 months (excluding nicotine), as defined by the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition criteria for substance dependence, or a positive urine drug test at the start of the study Sensitivity to N-acetylcysteine or to any of the components present in the placebo. Diagnosis of major depressive disorder (unipolar depression) based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Diagnosis of a manic episode based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Individuals with intellectual disabilities or other cognitive disorders Neurological disorders such as dementia, delirium, head trauma, or seizure disorders Pregnant women

Age
From **18 years** old to **65 years** old

Gender
Both

Phase
2-3

Groups that have been masked

- Participant
- Investigator

Sample size
Target sample size: **50**

Randomization (investigator's opinion)
Randomized

Randomization description
The method of assigning the intervention to individuals is randomly divided into two groups of intervention and control by the method of random permutation blocks with a size of 4 random blocks (using the table related to random permutations). The randomization list is prepared by a statistician. In this method, group A is related to the intervention and group B is considered as the control and is classified into 4 blocks including AABB, ABAB, ABBA, BBAA, BABA, BAAB.T o hide the assignment of individuals in the intervention and control groups, 20 even four-digit numbers will be selected as the codes of the participants in the control group and 20 four-digit individuals as the codes of the participants in the intervention group will be selected from a random number table. Then, the numbers of intervention and control groups are placed in sealed envelopes, respectively, and are randomly delivered by one of the personnel to the eligible individuals participating in the study. Random allocation software is also used for randomization. The site https://www.randomizer.org/ is used for randomization. In the empty fields, the total number of random numbers and the number of random numbers in each group, the range of numbers are entered and the output is received as an excel.

Blinding (investigator's opinion)
Double blinded

Blinding description
In this study, both the investigator and the patient are unaware of which participants in each group are receiving the drug or the placebo. The drug and the placebo will be identical in appearance, color, smell, and taste.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics Committee of Ahvaz Jundishapur University of Medical Sciences

Street address
Jundishapur University of Ahvaz, Golestan Highway

City
Ahvaz

Province
Khouzestan

Postal code
15794-61357

Approval date
2025-09-17, 1404/06/26

Ethics committee reference number
IR.AJUMS.REC.1404.211

Health conditions studied

1

Description of health condition studied
Depression in Bipolar patients

ICD-10 code
F31.4

ICD-10 code description

Bipolar disorder, current episode depressed, severe, without psychotic features

Primary outcomes

1

Description
Depressive symptoms
Timepoint
At the beginning of study and 4th and 8th week of study.
Method of measurement
Hamilton Depression Rating Scale

Secondary outcomes

1

Description
Cognitive function
Timepoint
At the beginning of study and 4th and 8th week of study.
Method of measurement
Montreal Cognitive Assessment

Intervention groups

1

Description
Intervention Group: Patients in the intervention group will receive, in addition to the standard pharmacological treatment they have been already receiving, a daily dose of 1800 mg to 2000 mg of N-acetylcysteine tablets for a duration of 8 weeks.
Category
Treatment - Drugs

2

Description
Control group: Patients in the control group will receive, in addition to the standard pharmacological treatment they have been already receiving, a placebo identical to the N-acetylcysteine tablet (in shape, smell, taste, size, and color) for a duration of 8 weeks.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Golestan hospital
Full name of responsible person
Ehsan Goshtasbi Zadeh
Street address
Golestan Hospital of Ahvaz, Golestan Boulevard
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Ahvaz University of Medical Sciences
Full name of responsible person
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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
Ahvaz 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
Ahvaz University of Medical Sciences
Full name of responsible person
Shahin Norouzi
Position
Associate professor
Latest degree
Specialist
Other areas of specialty/work

Psychiatrics

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Position
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Person responsible for updating data

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Position
Resident

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Medical doctor

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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