Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Nov 2026

Comparison of the effects of Mirtazapine and Topiramate on headache severity in patients with migraine

Protocol summary

Study aim
Comparison of the effects of Mirtazapine and Topiramate in treatment of migraine

Design
This study will be a randomized controlled clinical trial with two parallel groups, including an intervention group receiving mirtazapine and a control group receiving topiramate. The study will be a phase II trial conducted on 60 patients with migraine. Eligible patients will be randomly allocated to one of the two study groups in a 1:1 ratio. A computer-generated block randomization method with variable block sizes will be used to generate the randomization sequence using R statistical software.

Settings and conduct
Setting: The Neurology Department of Atieh 2 Hospital in Tehran; Study population: 60 patients with migraine who meet the eligibility criteria; Blinding type: Double-blind; Blinding procedure: Both the patients and the outcome assessors will be blinded to the patients' treatment allocation to either the mirtazapine or topiramate group.

Participants/Inclusion and exclusion criteria
Inclusion criteria: Diagnosis of migraine with at least 4 migraine days per month; history of migraine for more than one year; history of at least two previous preventive migraine treatments with treatment failure. Exclusion criteria: Presence of a serious comorbid disease other than migraine that may affect the study outcomes; concomitant use of medications that may affect the course of migraine or the efficacy of the study medications

Intervention groups
Intervention group: Patients with migraine who will receive mirtazapine at a starting dose of 15 mg once daily, with the dose increased to a target dose of 30 mg once daily as tolerated. Control group: Patients with migraine who will receive topiramate at a starting dose of 25 mg once daily, with the dose gradually increased to a target dose of 50 mg once daily as tolerated.

Main outcome variables
Headache severity score based on MIDAS questionnaire

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20250526065900N1**
Registration date: **2026-08-21, 1405/05/30**
Registration timing: **registered_while_recruiting**

Last update: **2026-08-21, 1405/05/30**
Update count: **0**

Registration date
2026-08-21, 1405/05/30

Registrant information

Name
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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
2026-08-21, 1405/05/30

Expected recruitment end date
2026-09-21, 1405/06/30

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date

empty

Scientific title

Comparison of the effects of Mirtazapine and Topiramate on headache severity in patients with migraine

Public title

Comparison of the effects of Mirtazapine and Topiramate in treatment of Migrane

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Patients experiencing migraine for at least 4 days per month Patients who have undergone at least 2 previous unsuccessful migraine prophylaxis treatments Duration of migraine illness exceeding one year

Exclusion criteria:

Presence of serious diseases other than migraine that might affect the study results Use of other medications that may affect the course of the migraine or the efficacy of the study medications.

Age

From **18 years** old to **70 years** old

Gender

Both

Phase

3

Groups that have been masked

- Investigator
- Data analyser

Sample size

Target sample size: **60**

Randomization (investigator's opinion)

Randomized

Randomization description

Eligible patients, following the verification of inclusion and exclusion criteria and the procurement of informed consent, will be randomized in a 1:1 ratio into one of the two treatment groups: the mirtazapine group or the topiramate group. The unit of randomization will be the individual (patient), with each patient being assigned to only one of the two study groups. To generate the randomization sequence, a computer-based block randomization method with variable block sizes will be employed to minimize the predictability of subsequent allocations. This sequence will be generated using R statistical software by an independent researcher who is not involved in the patient recruitment or assessment process. In this process, the total required sample size will first be determined, followed by the generation of the allocation sequence in a 1:1 ratio, ensuring that within each block, the number of allocations to both groups is equal to maintain a balanced total number of patients in both groups as much as possible. No stratification will be applied in this study, and all eligible patients will be placed within a single randomization sequence. Following the generation of the randomization sequence by the independent researcher, a unique code will be assigned to each patient. Patients will be numbered according to their order of enrollment after eligibility is confirmed, and each patient will be assigned to one of the two treatment groups based on the randomization code corresponding to their number. To ensure allocation concealment and prevent bias by withholding treatment allocation information from the investigator responsible for recruitment, the randomization sequence will be generated and maintained by an independent individual outside of the recruitment and assessment process. Consequently, the investigator responsible for enrolling patients will remain unaware of whether a patient is assigned to the mirtazapine or topiramate group until all inclusion criteria have been fully met, informed consent has been obtained, and the patient is formally registered in the study. Once formal enrollment is complete, allocation will be performed based on the pre-determined sequence, thereby minimizing the possibility of intentional selection or group changes based on prior knowledge.

Blinding (investigator's opinion)

Double blinded

Blinding description

This study is a randomized, single-blind clinical trial. The assessors will be blinded to the type of intervention (i.e., which medication is being administered). Drug coding and labeling will be performed by an independent individual or organization that is not involved in the implementation of the intervention or the assessment of outcomes.

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics Committee of Tehran Azad University of Medical Sciences

Street address

No. 62, Proshat Street, Shekarabi Street, Shariati Street, Sohrevardi Street

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Tehran

Province

Tehran

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1567716193

Approval date

2025-03-16, 1403/12/26

Ethics committee reference number

IR.IAU.TMU.REC.1404.031

Health conditions studied

1

Description of health condition studied
Migraine
ICD-10 code
G43
ICD-10 code description
Migraine

Primary outcomes

1

Description
Headache severity score based on MIDAS questionnaire
Timepoint
4 and 8 weeks after medication use
Method of measurement
By the MIDAS questionare

Secondary outcomes

empty

Intervention groups

1

Description
Intervention group: Patients with migraine who will receive mirtazapine at a starting dose of 15 mg once daily, with a target dose of 30 mg once daily.
Category
Treatment - Drugs

2

Description
Control group: Patients with migraine who will receive mirtazapine at a starting dose of 25 mg once daily, with a target dose of 50 mg once daily.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Ateyeh 2 hospital and clinic
Full name of responsible person
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
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Full name of responsible person
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Vice Presidency for Research and Technology, 3rd Floor, Administrative Building, Islamic Azad University of Medical Sciences, Corner of Gol Yakh Street and Abneh Boulevard, Pabarja Street, Gholhak Junction, Dr. Shariati Street
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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
Islamic Azad University
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
Islamic Azad University
Full name of responsible person
Radnoush Pashmforoush
Position
Professor
Latest degree
Subspecialist
Other areas of specialty/work

Neurology

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

Statistical Analysis Plan
Not applicable

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