Clinical Trial Protocol
Iranian Registry of Clinical Trials

11 Sep 2026

Comparison of Efficacy of Venlafaxine and Amitriptyline in Migraine Prophylaxis: A Randomized Controlled Trial

Protocol summary

Study aim

To compare the efficacy and safety of venlafaxine extended-release with amitriptyline for migraine prophylaxis in adults with episodic migraine.

Design

This was a prospective, single-center, open-label, parallel-group randomized controlled trial conducted at the Department of Neurology, Allied Hospital, Faisalabad, Pakistan. Eligible patients were randomized in a 1:1 ratio to receive either venlafaxine extended-release or amitriptyline for 12 weeks. Allocation was concealed using sealed opaque envelopes. Patients and treating physicians were not blinded because of different dosing schedules and expected adverse-effect profiles; however, endpoint assessment was performed by a clinician blinded to treatment allocation.

Settings and conduct

Department of Neurology, Allied Hospital, Faisalabad City: Faisalabad Country: Pakistan

Participants/Inclusion and exclusion criteria

Inclusion criteria: Adults aged 18 to 70 years; diagnosis of migraine according to International Headache Society criteria for at least 2 years; episodic migraine with 3 to 10 migraine attacks per month; ability to provide written informed consent. Exclusion criteria: Secondary headache disorders; major depression or psychiatric illness requiring medication; hypersensitivity to venlafaxine or amitriptyline; hepatic impairment; renal impairment; significant cardiac disease; pregnancy; lactation; concurrent monoamine oxidase inhibitor use; unwillingness to provide informed consent.

Intervention groups

Intervention Group 1 Group name: Venlafaxine group
Intervention Group 2 Group name: Amitriptyline group

Main outcome variables

Efficacy, defined as reduction in migraine severity by at least one grade on a 1 to 3 clinical severity scale compared with baseline.

General information

Reason for update

Acronym

VAM Trial

IRCT registration information

IRCT registration number: **IRCT20260630070026N1**
Registration date: **2026-07-07, 1405/04/16**
Registration timing: **retrospective**

Last update: **2026-07-07, 1405/04/16**
Update count: **0**

Registration date

2026-07-07, 1405/04/16

Registrant information

Name

Aasim Ali

Name of organization / entity

Allied Hospital Faisalabad

Country

Pakistan

Phone

+92 345 1129704

Email address

dr.aasimali1111@gmail.com

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2025-08-01, 1404/05/10

Expected recruitment end date

2026-01-31, 1404/11/11

Actual recruitment start date

2025-08-01, 1404/05/10

Actual recruitment end date

2026-01-31, 1404/11/11

Trial completion date

2026-04-30, 1405/02/10

Scientific title
Comparison of Efficacy of Venlafaxine and Amitriptyline in Migraine Prophylaxis: A Randomized Controlled Trial

Public title
Venlafaxine versus amitriptyline for prevention of migraine

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Adults aged 18 to 70 years; diagnosis of migraine according to International Headache Society criteria for at least 2 years; Episodic migraine with 3 to 10 migraine attacks per month; ability to provide written informed consent.

Exclusion criteria:
Secondary headache disorders; major depression or psychiatric illness requiring medication; hypersensitivity to venlafaxine or amitriptyline; hepatic impairment; renal impairment; significant cardiac disease; pregnancy; lactation; concurrent monoamine oxidase inhibitor use; unwillingness to provide informed consent.

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

Gender
Both

Phase
4

Groups that have been masked

- Outcome assessor

Sample size
Target sample size: **126**
Actual sample size reached: **126**

Randomization (investigator's opinion)
Randomized

Randomization description
Eligible participants were randomized in a 1:1 ratio using a computer-generated random number table. Allocation was concealed in sealed opaque envelopes. Participants were assigned to Group A receiving venlafaxine extended-release or Group B receiving amitriptyline.

Blinding (investigator's opinion)
Single blinded

Blinding description
Blinding of participants and treating physicians was not feasible because venlafaxine and amitriptyline have different dosing schedules and adverse-effect profiles. However, outcome assessment was performed by a clinician who was blinded to treatment allocation.

Placebo
Not used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Faisalabad Medical Univeristy

Street address
Sargodha Road

City
Faisalabad

Postal code
38000

Approval date
2025-07-28, 1404/05/06

Ethics committee reference number
48.ERC/FMU/2025-26/105

Health conditions studied

1

Description of health condition studied
Episodic migraine

ICD-10 code
G43.9

ICD-10 code description
Migraine, unspecified

Primary outcomes

1

Description
Efficacy, defined as reduction in migraine severity by at least one grade on a 1 to 3 clinical severity scale compared with baseline.

Timepoint
Baseline and 12 weeks after start of treatment

Method of measurement
Clinical migraine severity scale: 1 = mild, able to work; 2 = moderate, unable to work; 3 = severe, bedridden.

2

Description
Frequency of treatment-emergent adverse events.

Timepoint
Assessed during follow-up visits at week 4, week 8, and week 12.

Method of measurement
Clinical assessment and adverse-event reporting, graded according to CTCAE version 5.0.

Secondary outcomes

empty

Intervention groups

1

Description
Intervention group:
Category
Treatment - Drugs

2

Description
Intervention group:
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Department of Neurology, Allied Hospital, Faisalabad
Full name of responsible person
Dr. Mansoor Ul Hassan
Street address
Sargodha Road
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Faisalabad
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38000
Phone
+92 345 1129704
Email
dr.aasimali1111@gmail.com

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Faisalabad Medical University
Full name of responsible person
Dr. Aamir Shoukat
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mukeshsharmakumar95@gmail.com
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Faisalabad Medical University
Proportion provided by this source
10
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
Faisalabad Medical University
Full name of responsible person
Aasim Ali
Position
Resident
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Medical doctor
Other areas of specialty/work
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Person responsible for updating data

Contact

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Aasim Ali

Position
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Latest degree
Medical doctor

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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
Deidentified individual participant data will not be publicly shared because of participant confidentiality and because consent was not specifically obtained for public data sharing. Relevant study documents, including the study protocol and informed consent form, may be made available by the principal investigator on reasonable request and subject to institutional approval.

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
No - There is not a plan to make this available

Clinical Study Report
Not applicable

Analytic Code
Not applicable

Data Dictionary
Not applicable