Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

Comparison of the efficacy of duloxetine and bupropion in reducing neuropathic pain due to diabetic neuropathy: a randomized triple-blind clinical trial

Protocol summary

Study aim
To evaluate the effect of duloxetine and bupropion on neuropathic pain reduction and quality of life improvement in patients with diabetic neuropathy

Design
Randomized triple-blind clinical trial with three parallel groups, total sample 300, allocation concealment using sealed envelopes

Settings and conduct
This study is a triple-blind, randomized clinical trial with three parallel groups conducted at Shahid Beheshti Hospital, Qom, targeting patients with diabetes-related neuropathic pain who visit this center. Eligible patients, after providing written informed consent, are randomly assigned using Random Allocation Software to one of three groups (Bupropion, Duloxetine, or Control/Placebo), and the interventions continue for four weeks. The active drugs and placebos are identical in appearance, color, size, packaging, and administration, allowing participant-level blinding. The study is conducted in a triple-blind manner, meaning that participants, evaluating physicians, clinical care staff, and data analysts are unaware of group assignments, while only the responsible pharmacist has access to the randomization codes. This approach ensures unbiased data collection, outcome assessment, and result analysis.

Participants/Inclusion and exclusion criteria
Inclusion: Patients over 18 years with type 1 or 2 diabetes, symptomatic peripheral neuropathy with pain ≥4/10, stable standard treatment, informed consent
Exclusion: Other causes of neuropathy, drug hypersensitivity, severe hepatic or renal disease, severe psychiatric disorders, pregnancy or breastfeeding

Intervention groups
Group 1: Bupropion 75 mg twice daily + duloxetine placebo Group 2: Duloxetine 60 mg daily + bupropion placebo Group 3: Placebo + matching placebos (control group)

Main outcome variables
Neuropathic pain intensity measured by VAS at baseline, week 4, and three months follow-up

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20260105068551N1**
Registration date: **2026-01-29, 1404/11/09**
Registration timing: **registered_while_recruiting**

Last update: **2026-01-29, 1404/11/09**
Update count: **0**

Registration date
2026-01-29, 1404/11/09

Registrant information

Name
Maryam sadat Mirzaamini

Name of organization / entity

Country
Iran (Islamic Republic of)

Phone
+98 25 3292 4067

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maryamamini9846@gmail.com

Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2026-01-29, 1404/11/09

Expected recruitment end date
2026-03-29, 1405/01/09

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Comparison of the efficacy of duloxetine and bupropion in reducing neuropathic pain due to diabetic neuropathy: a randomized triple-blind clinical trial

Public title

The effect of duloxetine and bupropion on neuropathic pain in diabetic neuropathy

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Age 18 years or older Confirmed diagnosis of type 1 or type 2 diabetes mellitus based on medical records Clinically diagnosed symptomatic diabetic peripheral neuropathy with neuropathic pain confirmed by a specialist physician History of neuropathic pain related to diabetic neuropathy for at least 3 months Neuropathic pain intensity of at least 4 out of 10 based on the VAS scale during the previous week Receiving stable standard treatment for diabetes for at least 4 weeks prior to enrollment Ability to understand the study procedures and provide written informed consent Negative pregnancy test in women of childbearing potential and use of effective contraception

Exclusion criteria:

Presence of known causes of peripheral neuropathy other than diabetes History of hypersensitivity or intolerance to duloxetine or bupropion History of seizure disorders or eating disorders such as anorexia nervosa or bulimia nervosa Severe hepatic disease or severe renal impairment Presence of unstable systemic diseases that may interfere with safe participation in the study Severe and uncontrolled psychiatric disorders Concurrent use of medications specifically indicated for neuropathic pain within the past 14 days Active alcohol or substance abuse Pregnancy or breastfeeding Participation in another clinical trial within the past 30 days Inability or unwillingness to comply with study procedures

Age

From **18 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

Sample size

Target sample size: **300**

Randomization (investigator's opinion)

Randomized

Randomization description

The study is designed as a triple-blind, randomized clinical trial with three parallel groups, and the unit of randomization is individual patients. Eligible participants are randomly assigned to one of the three groups. The random sequence was generated using Random Allocation Software with fixed-size blocks of 6 or 9 patients per block to ensure balanced group sizes. No stratified randomization was used in this study. For allocation concealment, the randomization codes were placed in sealed, numbered envelopes, accessible only to the responsible pharmacist. Patients, evaluating physicians, and data analysts are blinded to group assignments, ensuring that the study is conducted in a triple-blind manner.

Blinding (investigator's opinion)

Triple blinded

Blinding description

In this study, the active drugs and placebos are identical in appearance, color, size, packaging, and administration, allowing for participant-level blinding. The trial is conducted as a triple-blind study, meaning that participants, evaluating physicians and clinical care staff, and data analysts are unaware of the group assignments. The pharmacist responsible for dispensing the medications is the only individual with access to the randomization codes, and no other research team members are informed of patient allocation. This approach ensures unbiased data collection, outcome assessment, and result analysis. The Data Safety and Monitoring Committee and the team preparing manuscripts also have no access to group assignments. It should be noted that participants are not informed of their assigned group, solely to maintain blinding, and this is conducted in full compliance with ethical standards and informed consent requirements.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics Committee of Qom University of Medical Sciences

Street address

Chamran Street, Shahid Beheshti Hospital

City

Qom

Province

Ghoum

Postal code

3714816311

Approval date
2025-08-18, 1404/05/27
Ethics committee reference number
IR.MUQ.REC.1404.132

Health conditions studied

1

Description of health condition studied
neuropathic pain
ICD-10 code
G63.2
ICD-10 code description
Diabetic polyneuropathy is a type of neuropathy that results from chronic diabetes, causing damage to the peripheral nerves. It often affects the feet and legs, but can also impact other body areas.

Primary outcomes

1

Description
Mean score of diabetic neuropathic pain intensity based on the Visual Analogue Scale
Timepoint
Measurement at baseline (before the start of intervention), at the end of week 4 after treatment initiation, and at 3 months (12 weeks) after treatment initiation
Method of measurement
Using the standard 100-mm Visual Analogue Scale. Patients will mark their perceived pain intensity on a 100-mm horizontal line, where the left endpoint (0 mm) is labeled "no pain" and the right endpoint (100 mm) is labeled "the worst pain imaginable." The score is the distance in millimeters from the left endpoint.

2

Description
Mean score of paresthesia severity (tingling/burning sensation) based on the Visual Analogue Scale.
Timepoint
Measurement at baseline (before the start of intervention), at the end of week 4 after treatment initiation, and at 3 months (12 weeks) after treatment initiation.
Method of measurement
Using the standard 100-mm Visual Analogue Scale. Patients will mark the severity of their tingling/burning sensation on a 100-mm horizontal line, where the left endpoint (0 mm) is labeled "no paresthesia" and the right endpoint (100 mm) is labeled "the most severe paresthesia imaginable." The score is the distance in millimeters from the left endpoint.

Secondary outcomes

1

Description
Percentage of medication adherence.
Timepoint
Assessment at the end of week 4 and at 3 months (12 weeks) after treatment initiation.
Method of measurement
Using a combination of pill count and patient self-report via a medication diary. Adherence rate will be calculated using the formula: [(Number of pills dispensed - Number of pills returned) / Number of pills prescribed] × 100. An adherence rate of 80% or higher will be considered acceptable.

2

Description
Mean score of health-related quality of life.
Timepoint
Assessment at baseline (before the start of intervention) and at 3 months (12 weeks) after treatment initiation.
Method of measurement
Using the validated Persian version of the Short Form-36 Health Survey questionnaire. This standard instrument consists of 36 items across eight domains: physical functioning, role limitations due to physical health, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health. Scores for each domain range from 0 to 100, with higher scores indicating better health status.

3

Description
Incidence of treatment-related adverse events.
Timepoint
Monitoring and recording throughout the study period from the start of intervention until the final visit at 3 months (12 weeks). Systematic inquiry will be conducted at each follow-up visit (week 4 and month 3).
Method of measurement
Through direct questioning of participants, open-ended inquiry, and clinical examination at each visit. All reported or observed adverse events will be recorded in a standardized Case Report Form, detailing the event description, time of onset, severity (graded as mild, moderate, or severe), duration, action taken regarding the study drug, and outcome. Causality to the study drug (duloxetine or bupropion) will be assessed by the investigator.

Intervention groups

1

Description
Intervention group: Patients receive standard diabetes treatment plus oral bupropion 75 mg every 12 hours for 4 weeks, along with duloxetine placebo. Medications are obtained from reputable domestic pharmaceutical companies, and the appearance and packaging are identical to placebos. Patients, physicians, and data

analysts are blinded to group allocation

Category

Treatment - Drugs

2

Description

Intervention group: Patients receive standard diabetes treatment plus oral duloxetine 60 mg daily for 4 weeks, along with bupropion placebo. Medications are obtained from reputable domestic pharmaceutical companies, and the appearance and packaging are identical to placebos. Patients, physicians, and data analysts are blinded to group allocation

Category

Treatment - Drugs

3

Description

Control group: Patients receive only standard diabetes treatment and routine care, along with bupropion placebo and duloxetine placebo. Medications and placebos are identical in appearance and packaging, obtained from reputable domestic pharmaceutical companies. Patients, physicians, and data analysts are blinded to group allocation

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Shahid Beheshti Hospital

Full name of responsible person

Dr. Freshte Shahrab

Street address

Chamran Street, Shahid Beheshti Hospital

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Ghoum University of Medical Sciences

Full name of responsible person

Mohammad Aghali

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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

Ghoum 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

Ghoum University of Medical Sciences

Full name of responsible person

Maryam sadat Mirzaamini

Position

Resident

Latest degree

Medical doctor

Other areas of specialty/work

Neurology

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Person responsible for scientific inquiries

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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is a plan to make this available
Study Protocol
Yes - There is a plan to make this available
Statistical Analysis Plan
Yes - There is a plan to make this available
Informed Consent Form
No - There is not a plan to make this available
Clinical Study Report
Yes - There is a plan to make this available
Analytic Code
Yes - There is a plan to make this available
Data Dictionary
Yes - There is a plan to make this available
Title and more details about the data/document
De-identified individual participant data (IPD) related to the primary and secondary outcomes of the clinical trial: "Determining the effect of Duloxetine in reducing neuropathic pain compared to Bupropion".
When the data will become available and for how long
Data will become available 6 months after the publication of the primary results of the trial and will remain accessible for a period of 5 years.
To whom data/document is available
Access will be granted to researchers affiliated with academic or scientific institutions who provide a methodologically sound research proposal. Access for commercial or for-profit entities is not permitted.
Under which criteria data/document could be used
The data can only be used for the purpose of conducting individual participant data meta-analysis, reanalysis for validation, or other scientifically approved questions as outlined in the approved research proposal. All users must sign a Data Use Agreement committing to: 1) Not attempting to re-identify participants, 2) Securely storing the data, 3) Not transferring the data to third parties, 4) Acknowledging the original study in any publications, and 5) Destroying the data after the completion of their analysis.
From where data/document is obtainable
All requests must be sent via email to the principal investigator of the study (drmaryamamini6771@yahoo.com) and should include the research proposal and the requester's institutional affiliation details. The principal investigator and holder of the study is Ms. Maryam Mirzaamini
What processes are involved for a request to access data/document
Submission of a formal request via email. 2. Initial review by the PI for completeness. 3. Evaluation of the scientific merit and objectives by a designated data access committee (DAC) within 4 weeks. 4. If approved, preparation and execution of the Data Use Agreement. 5. Secure transfer of de-identified data in a common format (e.g., .csv, .sav). The entire process is expected to take 6 to 8 weeks from initial request to data transfer.
Comments
The study protocol, statistical analysis plan (SAP), and analytic code will be made publicly available on a recognized repository (e.g., ClinicalTrials.gov or OSF) upon completion of participant enrollment.