Clinical Trial Protocol
Iranian Registry of Clinical Trials

18 Sep 2026

Efficacy and safety of the daily oral supplementation of fish oil with high-dose docosahexaenoic acid content and cobalamin in patients with painful diabetic neuropathy

Protocol summary

Study aim

Determining the efficacy and safety of oral high-dose docosahexaenoic acid fish oil and cobalamin supplementation in patients with diabetic neuropathy accompanied by pain

Design

Clinical trial with a control group, with parallel groups, triple blind, randomized, phase 3 on 86 patients. Random Allocation Software (RAS) was used for randomization.

Settings and conduct

Patients attending outpatient clinics at the Emam Reza Hospital of Tabriz University of Medical Sciences who have been diagnosed with diabetic neuropathy will be invited to an initial assessment to determine if they meet the inclusion and exclusion criteria. Then the patients will be randomly assigned to receive either the doxahexanoic acid and vitamin B12 or the placebo for 12 weeks.

Participants/Inclusion and exclusion criteria

Entry conditions: age 45 years and older, suffering from diabetes according to WHO criteria, regular attendance at the hospital's outpatient clinic, documented clinical diagnosis of distal neuropathic pain, experience of neuropathic pain based on the neuropathic pain diagnosis questionnaire ; Conditions of non-entry: clinical evidence of cardiovascular disease (cardiac arrhythmias, stroke, etc.), Renal disease, cerebrovascular disease, allergy to omega-3 supplements or fish

Intervention groups

Intervention group 1: Doxahexaenoic acid oral supplement containing 1000 mg of fish oil (500 mg of docosahexaenoic acid and 150 mg of eicosapentaenoic acid) + oral vitamin B12 2500 micrograms for 12 weeks Intervention group 2: Doxahexanoic acid oral supplement placebo + vitamin B12 placebo for 12 weeks Active and placebo supplements will be prepared in exactly the same way in terms of shape, color and odor.

Main outcome variables

Pain intensity, functional status, and serum levels of nerve growth factor, uric acid, interleukin 6 and 10

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20161022030424N9**
Registration date: **2023-10-15, 1402/07/23**
Registration timing: **prospective**

Last update: **2023-10-15, 1402/07/23**
Update count: **0**

Registration date

2023-10-15, 1402/07/23

Registrant information

Name

Neda Dolatkhah

Name of organization / entity

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-11-22, 1402/09/01

Expected recruitment end date

2025-03-19, 1403/12/29

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Efficacy and safety of the daily oral supplementation of fish oil with high-dose docosahexaenoic acid content and cobalamin in patients with painful diabetic neuropathy

Public title

Docosahexaenoic acid and cobalamin in diabetic neuropathy

Purpose

Supportive

Inclusion/Exclusion criteria

Inclusion criteria:

Age of 45 and above Having diabetes based on WHO criteria (random plasma glucose ≥11·1 mmol/L, fasting plasma glucose ≥7·0 mmol/L, or 2-hour plasma glucose ≥11·1 mmol/L with oral glucose tolerance test) and based on the patient's record that has been in STABLE condition for at least three months (STABLE hypoglycemic drugs without insulin change +_20% and glycosylated hemoglobin [HbA1c] <9% at screening) Regular attendance at the hospital's outpatient clinic to ensure monitoring of blood sugar control and diabetes complications Documented clinical diagnosis of distal neuropathic pain based on pre-established criteria for peripheral neuropathy, neurological examination and EMG/NCV confirmed Experiencing neuropathic pain by scoring more than four in the Pain Diagnostic Questionnaire (DN4) or scoring more than 12 in the Self-reported Leeds Assessment of Neuropathic Symptoms and Signs (S -LANSS) for at least three months

Exclusion criteria:

Clinical evidence of severe or acute cardiovascular disease (heart attack or stroke in the past year) Atrial fibrillation or other cardiac arrhythmias Renal disease Cerebrovascular disease and any other systemic disease Allergy to omega-3 supplements or fish

Age

From **45 years** old

Gender

Both

Phase

3

Groups that have been masked

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

Sample size

Target sample size: **86**

Randomization (investigator's opinion)

Randomized

Randomization description

86 people were divided into two groups in a simple random manner and after matching based on age with random block method using 2 blocks and random array subset selection (RASS) software 1) Doxahexaenoic acid oral supplement containing 1000 mg fish oil (500 mg docosahexaenoic acid and 150 mg of eicosapentaenoic acid) + oral vitamin B12 1000 micrograms 2) placebo are assigned.

Blinding (investigator's opinion)

Double blinded

Blinding description

Active and placebo supplements will be prepared in exactly the same way in terms of shape, color and odor, and will be placed in a small envelope containing 28 capsules for each participant for 4-week consumption. The envelopes will be opened in the order in which the participants enter this stage from number 1, and an envelope containing the supplement will be provided to the participant for one month. Outcome assessors, the person responsible for statistical analysis of the data, and the respondents will be blinded to the type of supplement received until the end of the study..

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Tabriz University of Medical Sciences

Street address

Research Vice Chancellor, Tabriz University of Medical Sciences, Daneshgah Ave.

City

Tabriz

Province

East Azarbaijan

Postal code

3692588521

Approval date

2023-09-04, 1402/06/13

Ethics committee reference number

IR.TBZMED.REC.1402.445

Health conditions studied

1

Description of health condition studied

Diabetic Neuropathy

ICD-10 code

G63.2

ICD-10 code description

Polyneuropathy in diseases classified elsewhere

Primary outcomes

1

Description
Pain intensity
Timepoint
Pain intensity measurement at baseline (before intervention) and 12 weeks after intervention
Method of measurement
Visual Analogue Scale

2

Description
Functional status
Timepoint
Functional status measurement at baseline (before intervention) and 12 weeks after intervention
Method of measurement
Sheehan Disability Scale

3

Description
Serum nerve growth factor
Timepoint
Serum nerve growth factor measurement at baseline (before intervention) and 12 weeks after intervention
Method of measurement
Biochemical methods

4

Description
Serum uric Acid
Timepoint
Serum uric acid measurement at baseline (before intervention) and 12 weeks after intervention
Method of measurement
Biochemical methods

5

Description
Serum interleukin 6
Timepoint
Serum interleukin 6 measurement at baseline (before intervention) and 12 weeks after intervention
Method of measurement
Biochemical methods

6

Description
Serum interleukin 10
Timepoint
Serum interleukin 10 measurement at baseline (before intervention) and 12 weeks after intervention
Method of measurement
Biochemical methods

Secondary outcomes

1

Description
Quality of life
Timepoint
Quality of life measurement at the beginning of the study (before the start of the intervention) and 12 weeks after the start of the intervention
Method of measurement
36-item quality of life short form (sf-36)

Intervention groups

1

Description
Intervention group: Doxahexaenoic acid oral supplement containing 1000 mg of fish oil (500 mg of docosahexaenoic acid and 150 mg of eicosapentaenoic acid) manufactured by Karen Pharmaceutical Company one tablet per day + oral vitamin B12 2500 micrograms manufactured by Hakim Pharmaceutical Company, one tablet per day for 12 week
Category
Treatment - Drugs

2

Description
Control group: Doxahexanoic acid oral supplement placebo manufactured by Karen Pharmaceutical Company one tablet per day + oral vitamin B12 placebo manufactured by Hakim Pharmaceutical Company one tablet per day for 12 weeks
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Emam Reza Hospital
Full name of responsible person
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Sponsors / Funding sources

1

Sponsor

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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
Tabriz 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
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Full name of responsible person
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Person responsible for updating data

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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