Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

Effect of Folic Acid and Vitamin B12 Supplementation on Cognitive Function in Patients with Type 2 Diabetes

Protocol summary

Study aim

Assessment of the effect of Vitamin B12 and folic acid on cognitive function in patients with type 2 diabetes

Design

A clinical ، three-blind, randomized, two-arm parallel-group, placebo-controlled trial on 76 people with type 2 diabetes. Randomization is done by software available on the Internet.

Settings and conduct

This study is a randomized, Three -blind, placebo-controlled trial. 76 people from the patients of Imam Khomeini Hospital in Tehran (40-65 years old) with a history of type 2 diabetes for at least 10 years were randomly assigned to receive either 400 microgram/day of folic acid and 1000 microgram/day of vitamin B12 (group 1; n = 38) and/or placebo (group 2; n = 38) for 12 weeks. HCY, cognition, and CRP are measured at the study baseline and after 12 weeks of intervention. In this study, the researcher, the patients, and the analyzer are blinded.

Participants/Inclusion and exclusion criteria

At least ten years of history of diabetes HbA1C< 8.5% Metformin prescription Age between 40 to 65 years old Not receiving CNS-related medications or other interfering supplements Not undergoing any change in the types or doses of medications in the last 3 months before the trial

Intervention groups

Intervention group: In this group, 38 people with a history of type 2 diabetes for over ten years take 1000 microgram/day B12 and 400 microgram/day folic acid for 12 weeks. Control group: In this group, there are 38 people receiving placebo who take starch-based capsules completely similar to the original supplements for 12 weeks.

Main outcome variables

CRP, HCY, cognition

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20090901002394N48**
Registration date: **2023-07-03, 1402/04/12**
Registration timing: **prospective**

Last update: **2023-07-03, 1402/04/12**
Update count: **0**

Registration date

2023-07-03, 1402/04/12

Registrant information

Name

Shima Jazayeri

Name of organization / entity

Iran University of Medical Sciences

Country

Iran (Islamic Republic of)

Phone

+98 21 8670 4805

Email address

sjazayeri@razi.tums.ac.ir

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-07-25, 1402/05/03

Expected recruitment end date

2024-07-24, 1403/05/03

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title
Effect of Folic Acid and Vitamin B12 Supplementation on Cognitive Function in Patients with Type 2 Diabetes

Public title
Folic Acid and Vitamin B12 in Diabetes

Purpose
Supportive

Inclusion/Exclusion criteria

Inclusion criteria:
Diagnosis of diabetes by a specialist and based on the laboratory results for HA1C and 2HPG At least ten years of history of diabetes Stable blood glucose level defined by HbA1C< 8.5% Taking Metformin Age between 40 to 65 years old Willing and able to participate in the study until the end Educated enough to answer the tests

Exclusion criteria:
Visual and hearing problems Taking medications effective on CNS Any uncontrolled disease based on the participant's biography including malabsorption, stroke, TIA, psychoses, peripheral neuropathy, losing consciousness, high anxiety, clinical depression, mania, dementia, Parkinson, Huntington, schizophrenia, or other chronic illnesses such as liver failure, thyroid diseases, advanced kidney complications, cancer, etc. Smoking cigarettes and taking other abusive drugs Any change in the patient's medicine or its dosage during the last 3 months before the trial Taking folate or other supplementations that interfere with the intervention since the last 2 months before the start of trial Pregnancy or breastfeeding or the intention to get pregnant Any acute illnesses a month prior to the trial

Age
From **40 years** old to **65 years** old

Gender
Both

Phase
3

Groups that have been masked

- Participant
- Investigator
- Data analyser

Sample size
Target sample size: **76**

Randomization (investigator's opinion)
Randomized

Randomization description
In order to randomize the samples, first, a list of 78 items is generated by the software available on the internet into two groups of 38 items labeled as A or B. This list is provided to the researcher, and the eligible participants are allocated to either group A or B. The manufacturer of the placebo is asked to put one of the labels A or B on the drug and the other on the placebo by throwing a coin and keep this confidential until the end of the data analysis. Therefore the drugs are indicated with one of the letters A or B, and the placebos by the other letter. According to the randomization table, the researcher will distribute the drug and placebo according to the order of reference of the samples from packages A or B. So this study will be a three-blind study in which the patient, the researcher, and the analyst will not be aware of the type of packages received by the samples until the end of the data analysis.

Blinding (investigator's opinion)
Triple blinded

Blinding description
This research is a triple-blind clinical trial study in which participants, researchers, and data analysts will not know the type of intervention (placebo and synbiotic) received by the participants during the study.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics committee, Iran University of Medical Sciences

Street address
Iran University of Medical Sciences, near Milad Hospital, between the intersection of Sheikh Fazlollah Nouri and Shahid Chamran, Shahid Hemmat Highway

City
Tehran

Province
Tehran

Postal code
1449614535

Approval date
2023-06-18, 1402/03/28

Ethics committee reference number
IR.IUMS.REC.1402.26

Health conditions studied

1

Description of health condition studied
Type 2 diabetes

ICD-10 code
E11.4

ICD-10 code description
Type 2 diabetes mellitus with neurological complications

Primary outcomes

1

Description
Serum HCY

Timepoint
At the beginning of the study (before intervention), after 12 weeks of taking folate and B12 supplements

Method of measurement
Laboratory test

2

Description
Cognition
Timepoint
At the beginning of the study (before intervention), after 12 weeks of taking folate and B12 supplements
Method of measurement
MoCA test

3

Description
CRP
Timepoint
At the beginning of the study (before intervention), after 12 weeks of taking folate and B12 supplements
Method of measurement
Laboratory test

Secondary outcomes

1

Description
Depression
Timepoint
Beginning and end of intervention
Method of measurement
Beck questionnaire

Intervention groups

1

Description
Intervention group: In this group, 38 people with a history of type 2 diabetes for over ten years take 1000 microgram/day B12 and 400 microgram/day folic acid for 12 weeks.
Category
Treatment - Other

2

Description
Control group: In this group, there are 38 people receiving placebos who take capsules completely similar to the original supplements for 12 weeks. The manufactured placebo for B12 and folic acid includes starch, which is completely similar to vitamin tablets in terms of appearance, color, smell, size, and packaging.
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Imam Khomeini Hospital
Full name of responsible person
Dr. Alireza Esteghamati
Street address
Imam Khomeini Hospital Complex, Tohid Square, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1419733141
Phone
+98 21 6119 0000
Email
Imamhospital@tums.ac.ir
Web page address

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Iran University of Medical Sciences
Full name of responsible person
Reza Falak
Street address
Iran University of Medical Sciences, 5th floor of the central headquarters, Hemat Highway, next to Milad Tower, Tehran
City
Tehran
Province
Tehran
Postal code
1449614535
Phone
+98 21 8670 5533
Email
falak.r@iums.ac.ir
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Iran 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
Iran University of Medical Sciences

Full name of responsible person
Fatemeh Mehdipoor

Position
Master student in nutrition sciences

Latest degree
Bachelor

Other areas of specialty/work
Nutrition

Street address
Iran University of Medical Sciences, Faculty of Health, Hemat Highway, next to Milad Tower, Tehran

City
Tehran

Province
Tehran

Postal code
1449614535

Phone
+98 21 8670 4805

Email
fm.mhdp@gmail.com

Person responsible for scientific inquiries

Contact

Name of organization / entity
Iran University of Medical Sciences

Full name of responsible person
Shima Jazayeri

Position
Associate Professor

Latest degree
Ph.D.

Other areas of specialty/work
Nutrition

Street address
Iran University of Medical Sciences, Faculty of Health, Hemat Highway, next to Milad Tower, Tehran

City
Tehran

Province
Tehran

Postal code
1449614535

Phone
+98 21 8670 4805

Email
sh_jazayeri@tums.ac.ir

Person responsible for updating data

Contact

Name of organization / entity
Iran University of Medical Sciences

Full name of responsible person
Fatemeh Mehdipoor

Position
Master student in nutrition sciences

Latest degree
Bachelor

Other areas of specialty/work
Nutrition

Street address
Iran University of Medical Sciences, Faculty of Health, Hemat Highway, next to Milad Tower, Tehran

City
Tehran

Province
Tehran

Postal code
1449614535

Phone
+98 21 8670 4805

Email
fm.mhdp@gmail.com

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