Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Evaluation of the effect of coincident supplementation of vitamin B12, folic acid, and vitamin E on improvement of clinical signs and serum inflammatory markers in patients with Multiple sclerosis

Protocol summary

Study aim
Determining the role of vitamins B12, folic acid and vitamin E in improving MS disease

Design
A clinical trial with a control group, parallel groups, double-blind, randomized by blocking, phase 3, on 60 patients, intervention length of 4 months.

Settings and conduct
The participants will be selected among MS patients who will come to the neurology clinic of Imam Khomeini Hospital in Urmia. Then, in one meeting, they fill three questionnaires (demographic and disease characteristics, Chalder fatigue (CFQ), quality of life of MS patients (MSQoL-54)) and the neurologist evaluates their EDSS score. Then, in another meeting A blood sample (5 ml) will be taken from each of participant and supplements and placebos will be distributed among them randomly and in a double-blind manner (researcher and participants). After 4 months of taking the pills daily, in the third session, each patient will fill again the mentioned questionnaires and another blood sample will be taken from them. At the end, the data will be analyzed by SPSS 21 software.

Participants/Inclusion and exclusion criteria
Inclusion criteria: Relapsing-remitting Multiple Sclerosis (RRMS) according to McDonald's diagnostic criteria. EDSS ≤ 6. Body mass index (BMI) above 17 and below 30. Age between 18 and 65 years. Informed consent. Exclusion criteria: Atrophy of the optic nerve (Leber's disease). Consumption of aminoglycosides, chloramphenicol, colchicine, continuous potassium release products, aminosalicylic acid and its solutions, anticonvulsant drugs and alcohol. Taking folate, vitamin B12 and vitamin E supplements up to one year before the start of the study. Thyroid disorders. IBD. IBS.

Intervention groups
Intervention group: supplement group, Control group: placebo group

Main outcome variables
Severity of disability; Fatigue rate; Quality of Life; Interleukin 17 serum level; Interferon gamma serum level

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20230913059422N1**
Registration date: **2023-11-02, 1402/08/11**
Registration timing: **registered_while_recruiting**

Last update: **2023-11-02, 1402/08/11**
Update count: **0**

Registration date
2023-11-02, 1402/08/11

Registrant information

Name
Mahsa Esfandiary

Name of organization / entity

Country
Iran (Islamic Republic of)

Phone
+98 21 4423 5833

Email address
mahsa.esfandiary.aref@gmail.com

Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2023-11-01, 1402/08/10

Expected recruitment end date
2024-01-30, 1402/11/10

Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Evaluation of the effect of coincident supplementation of vitamin B12, folic acid, and vitamin E on improvement of clinical signs and serum inflammatory markers in patients with Multiple sclerosis

Public title
Evaluation of the effect of vitamin B12, folic acid, and vitamin E on Multiple sclerosis amelioration
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Relapsing-remitting Multiple Sclerosis (RRMS) according to McDonald's diagnostic criteria EDSS score equal to 6 or less (EDSS ≤ 6) Body mass index (BMI) above 17 and below 30 Age between 18 and 65 years Informed consent
Exclusion criteria:
Atrophy of the optic nerve (Leber's disease) Consumption of aminoglycosides, chloramphenicol, colchicine, continuous potassium release products, aminosalicylic acid and its solutions, anticonvulsant drugs and alcohol Taking folate, vitamin B12 and vitamin E supplements up to one year before the start of the study Thyroid disorders IBD IBS
Age
From **18 years** old to **65 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: **60**
Randomization (investigator's opinion)
Randomized
Randomization description
In the current study, we will use the blocked randomization method so that the number of samples allocated to each of the studied groups will be equal, and in such a way that it is not clear before the start of the intervention which patient will be in the intervention group and which patient will be in the control group. For this purpose, based on the sample size (60), we will have 6 blocks (including 3 participants in the intervention group and 3 participants in the control group). Then all possibilities of AAABBB will be considered. The number of blocks will be 10, which will be listed randomly by balloting. For concealment, a code will be randomly allocated to each patient and it will remain hidden that which code is allocated to each patient.The generated codes will be randomly listed, then based on the list of codes, they will be assigned to the intervention group (A) or control group (B) through the mentioned blocking. All the steps of randomization will be done under the supervision of an epidemiologist consultant. Random Allocation version 1.0.0 software will be used for randomization, which is capable of both simple randomization and generating a random sequence using the blocking method.
Blinding (investigator's opinion)
Double blinded
Blinding description
In this study, in order to blind the participants, in coordination with pharmaceutical company, a placebo similar to the supplement under the study will be prepared which will be completely identical in shape and will be used with the same usage method and will be released to the individuals based on the code. The researcher also will not know which code is dedicated to each group until the last stage. In the stage of statistical analysis, people will be entered based on the code, and finally, the codes will be revealed at the end.
Placebo
Used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Ethics committee of Urmia University of Medical Sciences
Street address
Urmia University of Medical Sciences, 11th Km of Nazloo Rd.
City
Urmia
Province
West Azarbaijan
Postal code
5714783734
Approval date
2023-06-24, 1402/04/03
Ethics committee reference number
IR.UMSU.REC.1402.080

Health conditions studied

1

Description of health condition studied

multiple sclerosis

ICD-10 code

G35

ICD-10 code description

Multiple sclerosis

Primary outcomes

1

Description

Severity of disability (Expanded Disability Status Scale)

Timepoint

At the beginning of the study (before the start of the intervention) and 4 months after the start of taking the supplements

Method of measurement

Examination of a neurologist

2

Description

Fatigue rate

Timepoint

At the beginning of the study (before the start of the intervention) and 4 months after the start of taking the supplements

Method of measurement

Chalder fatigue questionnaire

3

Description

Quality of life

Timepoint

At the beginning of the study (before the start of the intervention) and 4 months after the start of taking the supplements

Method of measurement

Multiple Sclerosis Quality of Life-54 questionnaire

4

Description

Interleukin 17 serum level

Timepoint

At the beginning of the study (before the start of the intervention) and 4 months after the start of taking the supplements

Method of measurement

Blood sampling

5

Description

Serum level of interferon gamma

Timepoint

At the beginning of the study (before the start of the intervention) and 4 months after the start of taking the supplements

Method of measurement

Blood sampling

Secondary outcomes

1

Description

Calorie intake in the diet

Timepoint

Before the start of the intervention, after the end of the intervention

Method of measurement

24-hour food reminder

2

Description

Intake of macronutrients in the diet

Timepoint

Before the start of the intervention, after the end of the intervention

Method of measurement

24-hour food reminder

3

Description

vitamin B12 intake in the diet

Timepoint

Before the start of the intervention, after the end of the intervention

Method of measurement

24-hour food reminder

4

Description

Folic acid intake in the diet

Timepoint

Before the start of the intervention, after the end of the intervention

Method of measurement

24-hour food reminder

5

Description

Vitamin E intake in the diet

Timepoint

Before the start of the intervention, after the end of the intervention

Method of measurement

24-hour food reminder

Intervention groups

1

Description

Intervention group: Vitamin B12 (1000 micrograms), sublingual tablet, daily intake for 4 months, produced by Amin Pharmaceutical Company / Folic acid (1000 micrograms), oral tablet, daily intake for 4 months, with food, produced by Iran Daru Pharmaceutical Company / Vitamin E (200 IU), softgel, daily intake for 4 months,

produced by Amin Pharmaceutical Company

Category

Treatment - Drugs

2

Description

Control group: vitamin B12 (1000 micrograms) placebo, sublingual tablet, daily intake for 4 months, produced by Amin Pharmaceutical Company/folic acid (1000 micrograms) placebo, oral tablet, daily intake for 4 months, consumption with food, produced by Pharmaceutical Company Iran Daru/Vitamin E (200 IU) placebo, softgel, daily intake for 4 months, consumption with food, produced by Amin Pharmaceutical Company

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center
Imam Khomeini University Hospital

Full name of responsible person
Ali Akbar Nasiri

Street address
Ershad Ave., Modarres Blvd.

City
Urmia

Province
West Azarbaijan

Postal code
5714783734

Phone
+98 44 3345 9538

Email
imam_h_urm@umsu.ac.ir

Sponsors / Funding sources

1

Sponsor

Name of organization / entity
Oroumia University of Medical Sciences

Full name of responsible person
Mohammad Amin Valizad Hasanlui

Street address
Urmia University of Medical Sciences, Resalat Blvd., Emergency st.

City
Urmia

Province
West Azarbaijan

Postal code
5714783734

Phone
+98 44 3193 7154

Email
mohammad.majidi57@yahoo.com

Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source
Oroumia University of Medical Sciences

Proportion provided by this source
26

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
Oroumia University of Medical Sciences

Full name of responsible person
Mahsa Esfandiary

Position
Student

Latest degree
Bachelor

Other areas of specialty/work
Nutrition

Street address
1st Floor, No. 9, Sajjadi Alley, 1st Aramkan St., Jalal Al Ahmad Hwy.

City
Tehran

Province
Tehran

Postal code
1463634881

Phone
+98 21 4423 5833

Email
mahsa.esfandiary.aref@gmail.com

Person responsible for scientific inquiries

Contact

Name of organization / entity
Oroumia University of Medical Sciences

Full name of responsible person
Mahsa Esfandiary

Position
Student

Latest degree
Bachelor

Other areas of specialty/work
Nutrition

Street address
1st Foor, No. 9, Sajjady Alley, 1st Armakan St., Jalal Al

Ahmad HWY., Tehran City

City
Tehran

Province
Tehran

Postal code
1463634881

Phone
+98 21 4423 5833

Fax

Email
mahsa.esfandiary.aref@gmail.com

Person responsible for updating data

Contact

Name of organization / entity
Oroumia University of Medical Sciences

Full name of responsible person
Mahsa Esfandiary

Position
Student

Latest degree
Bachelor

Other areas of specialty/work
Nutrition

Street address
1st Foor, No. 9, Sajjady Alley, 1st Armakan St., Jalal Al Ahmad HWY., Tehran City

City
Tehran

Province
Tehran

Postal code
1463634881

Phone
+98 21 4423 5833

Fax

Email
mahsa.esfandiary.aref@gmail.com

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
Yes - There is 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
All data is potentially shareable after de-identifying individuals

When the data will become available and for how long
The access round starts from March 2025

To whom data/document is available
Researchers working in academic and scientific institutions and also people who are engaged in industry

Under which criteria data/document could be used
For therapeutic and research purposes, it will be accessible to the therapists and researchers of creditable and legal centers

From where data/document is obtainable
Send request to mahsa.esfandiary.aref@gmail.com

What processes are involved for a request to access data/document
After sending request to mahsa.esfandiary.aref@gmail.com, the answer will be given within one month.

Comments