

Clinical Trial Protocol

Iranian Registry of Clinical Trials

21 Jul 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, aminosalicilic 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)

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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 ($EDSS \leq 6$) 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, aminosalicic 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

AgeFrom **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 sizeTarget 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.

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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.

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Province

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Postal code

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Phone

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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

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

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Person responsible for scientific inquiries

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Name of organization / entity

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Latest degree

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Other areas of specialty/work

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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

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

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

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