Clinical Trial Protocol
Iranian Registry of Clinical Trials

31 Jul 2026

Evaluating the effects of vitamin B1, B6, B12 and folic acid supplementation versus placebo on serum levels of CGRP, endothelial nitric oxide synthase, homocysteine and headache characteristics in women with episodic migraine

Protocol summary

Study aim

The aim of this double-blind randomized clinical trial is to determine the effects of vitamin B1, B6, B12 and folic acid supplementation versus placebo on serum levels of CGRP, endothelial nitric oxide synthase, homocysteine and headache characteristics in women with episodic migraine

Design

This study is a double-blind, randomized controlled clinical trial with 5 parallel groups. 100 patients will be randomly assigned into B1, B6, B12, folic acid and control group.

Settings and conduct

The study will perform at the tertiary headache clinic of Sina University Hospital. Information on demographic data and headache characteristics will be collected. After assessing the entrance criteria, 10 cc blood samples are taken. The food recall and physical activity questionnaire is completed. Anthropometric measurements and blood pressure are taken. Supplements are given to patients for a month. For double-blind implementation(patients and investigators), all boxes of supplements by a third party is coded as A, B, C, D, E.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Body mass index 18.5-30, Aged 18-50 years old, Episodic migraine with 3 attacks or more per month Exclusion critera: Unwillingness to participate in the study, Changes in dosage and type of migrane prophylactic drugs during intervention

Intervention groups

Intervention groups: B1, B6, B12, folic acid tablet; Control group: placebo tablet. Patients in the B1, B6, B12, folic acid group will receive 1 tablet per day, each containing 300mg, 80mg, 500mcg and 2mg ,respectively for 12 weeks. Patients in the control group will receive 1 tablets of placebo containing Methylcellulose per day.

The study period is 16 weeks, including 4 weeks of baseline study and 12 weeks for intervention.

Main outcome variables

headache attack frequency per month; headache severity (VAS); attack duration (min per month)

General information

Reason for update

Changing in one of the variables under study

Acronym

IRCT registration information

IRCT registration number: **IRCT20190921044828N1**
Registration date: **2019-09-26, 1398/07/04**
Registration timing: **prospective**

Last update: **2019-12-16, 1398/09/25**
Update count: **1**

Registration date

2019-09-26, 1398/07/04

Registrant information

Name

Shiva Nematgorgani

Name of organization / entity

Country

Iran (Islamic Republic of)

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+98 21 4489 9564

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2019-10-23, 1398/08/01

Expected recruitment end date

2021-10-23, 1400/08/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Evaluating the effects of vitamin B1, B6, B12 and folic acid supplementation versus placebo on serum levels of CGRP, endothelial nitric oxide synthase, homocysteine and headache characteristics in women with episodic migraine

Public title

Evaluating the effects of vitamin B1, B6, B12 and folic acid supplementation in women with episodic migraine

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Body mass index 18.5-30 Aged 18-50 years old Migraine diagnosis according to The Classification Committee of the International Headache Society (IHS) 3rd edition (beta version) Episodic migraine with 3 attacks or more per month Suffering from migraine for at least 6 months prior to study

Exclusion criteria:

Unwillingness to participate in the study Taking vitamin B group supplements in 3 months prior to study Pregnancy and lactation Taking anti-psychotic drugs Suffering from gastrointestinal disorders (malabsorption,IBD,...),diabetes, liver disorders(Cirrhosis, Hepatitis), kidney disorders(Kidney Failure), congestive heart failure, hypertension,cancer Smoking Changes in dosage and type of migrane prophylactic drugs during intervention Not taking more than 10% of supplements

Age

From **18 years** old to **50 years** old

Gender

Female

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size

Target sample size: **100**

Randomization (investigator's opinion)

Randomized

Randomization description

Patients on the basis of random allocation rule method are randomly assigned to the 5 groups; B1, B6, B12, folic acid and placebo. In this study, In this study, 20 codes for each group is placed in a drawing container and then the codes are randomly ejected from the container without replacement and the created sequences are recorded.

Blinding (investigator's opinion)

Double blinded

Blinding description

This study is a double-blind (investigators and patients) trial. For double-blind implementation, at the beginning of the study, all boxes containing B1, B6, B12, folic acid or placebo by a third party (someone other than the researchers) is coded as A, B, C, D and E.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Shahid Beheshti medical university

Street address

No. 46, West Arghavan St., Farahzadi Blv., Shahrak Qods,

City

Tehran

Province

Tehran

Postal code

1981619573

Approval date

2019-09-08, 1398/06/17

Ethics committee reference number

IR.SBMU.nnftri.Rec.1398.031

Health conditions studied

1

Description of health condition studied

migraine headache

ICD-10 code

G43

ICD-10 code description

Migraine

Primary outcomes

1

Description

migraine attack frequency per month

Timepoint

baseline-end of study

Method of measurement
headache diary

2

Description
attack severity
Timepoint
baseline-end of study
Method of measurement
headache diary-visual analogue scale

3

Description
headache attack duration (min per month)
Timepoint
baseline-end of study
Method of measurement
headache diary

Secondary outcomes

1

Description
serum homocysteine
Timepoint
baseline- end of study
Method of measurement
ELISA KIT

2

Description
serum endothelial nitric oxide synthase
Timepoint
baseline- end of study
Method of measurement
ELISA KIT

3

Description
serum Calcitonin gene-related peptide (CGRP)
Timepoint
baseline- end of study
Method of measurement
ELISA KIT

Intervention groups

1

Description
Intervention group: 1. B1(300 mg), 2. B6 (80 mg), 3. B12 (500mcg), 4. folic acid (2mg)
Category
Treatment - Drugs

2

Description
Control group: placebo
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Sina Hospital
Full name of responsible person
Dr Mansoureh Togha
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Sponsors / Funding sources

1

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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
Shahid Beheshti 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
Shahid Beheshti University of Medical Sciences
Full name of responsible person
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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
Not applicable
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
Not applicable
Data Dictionary
Not applicable