

# 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 criteria: Unwillingness to participate in the study, Changes in dosage and type of migraine 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)

###### Phone

+98 21 4489 9564

###### Email address

shiva.gorgani@sbmu.ac.ir

##### 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 migraine 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, 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

**Street address**

Imam Khomeini Street

**City**

Tehran

**Province**

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**Sponsors / Funding sources****1****Sponsor****Name of organization / entity**

Shahid Beheshti University of Medical Sciences

**Full name of responsible person**

Dr Esmat Naseri

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Nasseri\_esm@yahoo.com

**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

**Province**

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4741-19395

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**Person responsible for general inquiries****Contact****Name of organization / entity**

Shahid Beheshti University of Medical Sciences

**Full name of responsible person**

Shiva Nematgorgani

**Position**

Ph.D candidate

**Latest degree**

Master

**Other areas of specialty/work**

Nutrition

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**Other areas of specialty/work**

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**Full name of responsible person**

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**Position**

Assistant professor

**Latest degree**

Ph.D.

**Other areas of specialty/work**

Nutrition

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Qods**City**

Tehran

**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