Clinical Trial Protocol
Iranian Registry of Clinical Trials

16 Sep 2026

The effect of black grape seed extract supplementation on inflammatory biomarkers, oxidative stress, clinical symptoms, and quality of life in patients with migraine

Protocol summary

Study aim

The effect of black grape seed extract supplementation on inflammatory biomarkers, oxidative stress, clinical symptoms, and quality of life in patients with migraine

Design

A randomized controlled clinical trial with parallel groups, double-blind, on 50 patients. Stratified randomization based on migraine type and body mass index

Settings and conduct

Migraine patients will be selected from the patients referred to the neurology clinic of Khorshid Hospital in Isfahan City. Then the patients will be divided into two intervention (black grape seed extract) and control (placebo) groups. The duration of the intervention will be eight weeks. Anthropometric measures and biochemical factors will be assessed at the baseline and end of the intervention.

Participants/Inclusion and exclusion criteria

Inclusion criteria: willingness to participate in the study, diagnosed with migraine by a neurologist and according to the criteria of the International Classification of Headache Disorders-3 (ICHD-3), age 18 to 60 years, having at least one migraine attack per month, body mass index between 18.5 to 30. Non-inclusion criteria: suffering from tension-type headaches, chronic kidney diseases, cancer, and other neurological disorders, change in type and dosage of medications in the past month, taking supplements containing antioxidants and black grape seed extract in the past 3 months, following a special diet, pregnancy, and lactation.

Intervention groups

Intervention group: Daily two capsules containing black grape seed extract for eight weeks. Control group: Two placebo capsules per day for eight weeks.

Main outcome variables

Migraine symptoms, migraine disability, calcitonin gene-related peptide, vascular cell adhesion molecule-1, total antioxidant capacity, and malondialdehyde

General information

Reason for update

Correction of main outcome variables in the protocol abstract.

Acronym

IRCT registration information

IRCT registration number: **IRCT20121216011763N56**
Registration date: **2023-03-26, 1402/01/06**
Registration timing: **prospective**

Last update: **2024-01-02, 1402/10/12**
Update count: **2**

Registration date

2023-03-26, 1402/01/06

Registrant information

Name
Gholamreza Askari
Name of organization / entity
Isfahan University of Medical Sciences
Country
Iran (Islamic Republic of)
Phone
+98 31 1792 2110
Email address
askari@mui.ac.ir

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-06-22, 1402/04/01

Expected recruitment end date

2023-09-23, 1402/07/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

The effect of black grape seed extract supplementation on inflammatory biomarkers, oxidative stress, clinical symptoms, and quality of life in patients with migraine

Public title

The effect of black grape seed extract supplement in patients with migraine

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Patients who are willing to participate in the study Migraine diagnosis by a neurologist based on the International Classification of Headache Disorders-3 (ICHD-3) Age 18 to 60 years Having at least one migraine attack per month Body mass index between 18.5 to 30

Exclusion criteria:

Suffering from chronic kidney diseases, cancer, and other neurological disorders Suffering from tension-type headaches Change in the type of medicine used and its dosage during the last month Pregnancy and lactation Taking supplements containing antioxidants and black grape seed extract in the last 3 months Following a special diet

Age

From **18 years** old to **60 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Outcome assessor

Sample size

Target sample size: **50**

Randomization (investigator's opinion)

Randomized

Randomization description

Randomization was done based on the stratified randomization method. To distribute patients into intervention and control groups, first, persons are classified into four states according to the type of migraine (with aura/without aura) and body mass index (18.5 to 24.9 and 25 to 30). Then, persons with the same conditions will be randomly assigned to two intervention and control groups. For this purpose, the first person who referred will be in the intervention group and the other person with the same conditions will be in the control group.

Blinding (investigator's opinion)

Double blinded

Blinding description

This study is a double-blind clinical trial study (participant, outcome assessor). The black grape seed extract supplement and its placebo (identical in terms of color, shape, and taste) will be packaged in similar boxes, and the participants and the outcome assessor will not be informed of the contents of the packages until the end of the study.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics Committee of Isfahan University of Medical Sciences

Street address

Isfahan University of Medical Sciences, Hezar Jerib street, Isfahan, Iran

City

Isfahan

Province

Isfehan

Postal code

8174673461

Approval date

2023-03-07, 1401/12/16

Ethics committee reference number

IR.MUI.RESEARCH.REC.1401.405

Health conditions studied

1

Description of health condition studied

Migraine

ICD-10 code

G43

ICD-10 code description

Migraine

Primary outcomes

1

Description

Severity of migraine attacks

Timepoint

Before the start of the intervention and 60 days after the start of the intervention

Method of measurement

Visual Analogue Scale (VAS)

2

Description
Migraine disability
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Headache Impact Test-6 questionnaire (HIT-6)

3

Description
Calcitonin gene-related peptide (CGRP) serum level
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Blood test (ELISA)

4

Description
Vascular cell adhesion molecule-1 (VCAM-1) serum level
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Blood test (ELISA)

5

Description
Malondialdehyde (MDA) serum level
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Blood test (colorimetric method)

6

Description
Serum level of total antioxidant capacity (TAC)
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Blood test (colorimetric method)

7

Description
Migraine frequency
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Question / Number of attacks per month

8

Description
Duration of migraine headache
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Question/ average duration of migraine attacks per headache (hours)

Secondary outcomes

1

Description
Quality of life in migraine patients
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Migraine-Specific Quality of Life (MSQ)

2

Description
Depression
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Depression Anxiety and Stress Scale-21 questionnaire (DASS-21)

3

Description
Anxiety
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Depression Anxiety and Stress Scale-21 questionnaire (DASS-21)

4

Description
Stress
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Depression Anxiety and Stress Scale-21 questionnaire (DASS-21)

5

Description
Blood pressure
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
Mercury barometer

6

Description
Anthropometric indices
Timepoint
Before the start of the intervention and 60 days after the start of the intervention
Method of measurement
A digital scale and standard stadiometer

Intervention groups

1

Description
Intervention group: Two capsules of black grape seed extract daily (containing 100 mg of black grape seed extract, Daru Pajhuh-e-Jaber company) for eight weeks
Category
Treatment - Drugs

2

Description
Control group: Two placebo capsules daily (containing calcium phosphate, Avicel, and gelatin, Daru Pajhuh-e-Jaber company) for eight weeks.
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Neurology clinic of Khorshid hospital
Full name of responsible person
Dr. Gholamreza Askari
Street address
khorshid medical educational research complex, Ostandari Street, Isfahan
City
Isfahan
Province
Isfehan
Postal code
8145833117
Phone
+98 31 3222 2127
Email
Askari@mui.ac.ir

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Esfahan University of Medical Sciences
Full name of responsible person
Dr. Gholamreza Askari
Street address
Deputy of Research & Technology of Isfahan University of Medical Sciences, Hezar Jarib Street, Isfahan
City
Isfahan
Province
Isfehan
Postal code
8174673461
Phone
+98 31 3792 3060
Email
askari@mui.ac.ir
Web page address
https://research.mui.ac.ir
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Esfahan 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
Esfahan University of Medical Sciences
Full name of responsible person
Dr. Gholamreza Askari
Position
Professor
Latest degree
Ph.D.
Other areas of specialty/work
Nutrition
Street address
Deputy of Research & Technology of Isfahan University of Medical Sciences, Hezar Jarib Street, Isfahan
City
Isfahan
Province
Isfehan
Postal code
8174673461
Phone
+98 31 3792 3060
Email
askari@mui.ac.ir

Web page address
https://research.mui.ac.ir

Person responsible for scientific inquiries

Contact

Name of organization / entity
Esfahan University of Medical Sciences
Full name of responsible person
Dr. Gholamreza Askari
Position
Professor
Latest degree
Ph.D.
Other areas of specialty/work
Nutrition
Street address
Deputy of Research & Technology of Isfahan University of Medical Sciences, Hezar Jarib Street, Isfahan
City
Isfahan
Province
Isfehan
Postal code
8174673461
Phone
+98 31 3792 3060
Email
askari@mui.ac.ir
Web page address
https://research.mui.ac.ir

Person responsible for updating data

Contact

Name of organization / entity
Esfahan University of Medical Sciences
Full name of responsible person
Dr. Gholamreza Askari
Position
Professor
Latest degree
Ph.D.
Other areas of specialty/work
Nutrition
Street address
Deputy of Research & Technology of Isfahan University of Medical Sciences, Hezar Jarib Street, Isfahan
City
Isfahan
Province
Isfehan
Postal code
8174673461
Phone
+98 31 3792 3060
Email
askari@mui.ac.ir

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