Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

Evaluation of the effect of non-organic nitrate supplementation on macro- and micro-vascular changes in active and inactive men with metabolic syndrome

Protocol summary

Study aim
Evaluating the effect of inorganic nitrate supplementation with or without physical activity on micro- and macro-vascular status of men with metabolic syndrome

Design
A single center, concealed, randomised, non-blinded, no placebo, controlled trial will be conducted based on parallel group design of 60 participants (15 in each group).

Settings and conduct
Fasting blood sugar, lipid profile, CRP, blood pressure, physical fitness test, pulse wave velocity (PWV) and capilaroscopy will be performed at baseline and at the end of study. IPAQ, Vo2Max and 24-hour urine nitrate will be evaluated at baseline. Height, weight, waist circumference, bioelectric impedance analysis, serum nitrate, 3-day diet recall, step test, and blood pressure will be evaluated weekly.

Participants/Inclusion and exclusion criteria
Inclusion criteria: Willingness to participate in the study, male gender, age >18 till 40 years old, metabolic syndrome diagnosis based on IDF criteria, light to moderate physical activity level based on IPAQ Non-inclusion criteria: Chronic diseases (Diabetes, heart failure), rheumatologic or articular disorders that prevent exercise performance, underlying diseases (Cushing's syndrome, Addison's disease), hypertension, diabetes, and dyslipidemia exclusion criteria: Consuming medications that affect metabolic syndrome (chemotherapy, corticosteroids), cancer, physical disability, mental or psychological disorders that prevent exercise performance

Intervention groups
Intervention groups will receive either beetroot extract (30% ADI divided dose twice/week), exercise intervention (high intensity interval training), or combined beetroot extract and exercise and the control group will receive general instruction on healthy lifestyle for 4 weeks. All participants will be instructed to limit the intake of dietary sources of inorganic nitrate.

Main outcome variables
PWV, nail fold capillaroscopy

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20220101053579N1**
Registration date: **2022-01-12, 1400/10/22**
Registration timing: **prospective**

Last update: **2022-01-12, 1400/10/22**
Update count: **0**

Registration date
2022-01-12, 1400/10/22

Registrant information

Name
Ali Jafarzadeh Esfehani

Name of organization / entity

Country
Iran (Islamic Republic of)

Phone
+98 915 316 8951

Email address
jafarzadehea982@mums.ac.ir

Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2022-05-22, 1401/03/01

Expected recruitment end date

2022-12-21, 1401/09/30

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Evaluation of the effect of non-organic nitrate supplementation on macro-and micro-vascular changes in active and inactive men with metabolic syndrome

Public title

Effect of beetroot extract on cardiovascular factors in men with metabolic syndrome

Purpose

Supportive

Inclusion/Exclusion criteria

Inclusion criteria:

Willingness to participate in the study by signing an informed consent Age between 18 and 40 years old Diagnosis of metabolic syndrome based on the International Diabetes Federation (IDF) criteria Low to moderate level of physical activity based on the International Physical Activity Questionnaire (IPAQ) No history for chronic diseases (Diabetes Mellitus, heart failure) No history for Rheumatologic or joint disorders that impair the ability of performing exercises No history for underlying diseases that may affect metabolic syndrome (Cushing syndrome, Addison's disease) No history for hypertension, diabetes and dyslipidemia Male gender

Exclusion criteria:

Using medications that affect metabolic syndrome (chemotherapy, corticosteroids) Cancer Physical disability that prevents performing the exrcises Mental or psychological disorders that prevent performing the study protocol

Age

From **18 years** old to **40 years** old

Gender

Male

Phase

3

Groups that have been masked

No information

Sample size

Target sample size: **60**

Randomization (investigator's opinion)

Randomized

Randomization description

Randomization will be performed based on stratified block randomization. Block size would be 8 and participants will be randomized into each block based on age (below 30, 30 or above), BMI (below 30 kg/m2, 30 kg/m2 or over), and presence of elevated blood pressure (below 130/85 mmHg, 130/85 mmHg or over). Randomization concealment will be performed using sealed envelops. One of the research team members will perform the concealment based on the randomization list. Envelops will be opaque and sealed so that other researchers and the participants will not be aware of their group allocation.

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics Committee of the Mashhad University of Medical Scineces

Street address

School of Medicine, East door of Ferdowsi University, Azadi Sq.

City

Mashhad

Province

Razavi Khorasan

Postal code

9177948564

Approval date

2021-12-11, 1400/09/20

Ethics committee reference number

IR.MUMS.REC.1400.282

Health conditions studied

1

Description of health condition studied

Metabolic syndrome

ICD-10 code

E88.81

ICD-10 code description

Metabolic syndrome

Primary outcomes

1

Description

mean pulse wave velocity

Timepoint

Baseline and the end of study (4th week)

Method of measurement

PWV at the bifurcation of carotid artery using Doppler ultrasound

2

Description
Augmentation index (AI)
Timepoint
Baseline and the end of study (4th week)
Method of measurement
PWV using Doppler ultrasound

3

Description
Avascular area
Timepoint
Baseline and the end of study (4th week)
Method of measurement
Nail fold capillaroscopy

4

Description
Increase in the diameter of the capillaries
Timepoint
Baseline and the end of study (4th week)
Method of measurement
Nail fold capillaroscopy

5

Description
Microhaemorrhage
Timepoint
Baseline and the end of study (4th week)
Method of measurement
Nail fold capillaroscopy

6

Description
Hairpin structures
Timepoint
Baseline and the end of study (4th week)
Method of measurement
Nail fold capillaroscopy

7

Description
Tortuous structures
Timepoint
Baseline and the end of study (4th week)
Method of measurement
Nail fold capillaroscopy

8

Description
Crossing structures
Timepoint
Baseline and the end of study (4th week)
Method of measurement
Nail fold capillaroscopy

Secondary outcomes

1

Description
Fasting blood sugar
Timepoint
Baseline and at the end of the study
Method of measurement
Biochemical analysis of blood sample

2

Description
Total cholesterol
Timepoint
Baseline and at the end of the study
Method of measurement
Biochemical analysis of blood sample

3

Description
Serum triglyceride
Timepoint
Baseline and at the end of the study
Method of measurement
Biochemical analysis of blood sample

4

Description
Low-density lipoprotein (LDL)
Timepoint
Baseline and at the end of the study
Method of measurement
Biochemical analysis of blood sample

5

Description
High density lipoprotein (HDL)
Timepoint
Baseline and at the end of the study
Method of measurement
Biochemical analysis of blood sample

6

Description
Serum nitrate
Timepoint
Weekly from the beginning of the study
Method of measurement
Measuring serum nitrate using nitrate kit

7

Description
Step test
Timepoint
Baseline and at the end of the study
Method of measurement

Measured using a standard step

8

Description
Systolic blood pressure
Timepoint
Weekly from the beginning of the study
Method of measurement
Measured using sphygmomanometer

9

Description
Diastolic blood pressure
Timepoint
Weekly from the beginning of the study
Method of measurement
Measured using sphygmomanometer

10

Description
VO2Max
Timepoint
Baseline, second week, and at the end of the study
Method of measurement
Measured on treadmill using CPET device

11

Description
Dietary intake
Timepoint
Weekly from the beginning of the study
Method of measurement
3-day 24-hour recall

Intervention groups

1

Description
Intervention group 1: Physical activity intervention will be conducted using low volume high intensity interval training method. Due to the COVID-19 pandemic, instructions will be provided to the participants and the participants will perform the exercises at home after ensuring their mastery on the methods. Intensity of the exercises will be defined based on primary evaluations of perceived exertion, heart rate at 65% and 85% of VO2 Max. Exercises will be conducted in the form of two repetitions of four sets of high intensity intermittent exercises, which are composed of a training phase and a rest phase. Training phase will last for 2 minutes. Participants should keep their heart rate above 85% of VO2Max during the training phase. Then, participants will continue the training phase exercise at a lower intensity (65% of VO2Max). Active rest can be conducted in the form of walking or jogging in place. Duration of the physical activity intervention will be 66 minutes per week. In order to ensure that the participants perform exercises in the correct way, a software that includes video and textual instructions on each exercise is designed and provided to the participants. The software sends twice weekly messages to the participants based on their progress. Participants will receive general dietary advice (300 Cal deficit per day) and limit dietary nitrate intake.
Category
Lifestyle

2

Description
Intervention group 2: Beetroot extract will be administered at 30% ADI equal to 3.7 mg/kg/d as two divided doses consumed twice weekly for 4 weeks. Participants will receive general dietary advice (300 Cal deficit per day) and limit dietary nitrate intake.
Category
Other

3

Description
Intervention group 3: This group will receive both the mentioned physical activity and beetroot extract interventions all together. The intervention duration will be 4 weeks. Participants will receive general dietary advice (300 Cal deficit per day) and limit dietary nitrate intake.
Category
Lifestyle

4

Description
Control group: The control group will receive general dietary advice (300 Cal deficit per day) and limit dietary nitrate and following an active lifestyle. The control group will not receive placebo.
Category
N/A

Recruitment centers

1

Recruitment center
Name of recruitment center
Mashhad Cohort center
Full name of responsible person
Mohsen Nemati
Street address
Emam Reza Hospital, Emam Reza Sq.
City
Mashhad
Province
Razavi Khorasan
Postal code
9137913316
Phone
+98 51 3180 6802
Email
cohort@mums.ac.ir

Web page address
https://v-research.mums.ac.ir/index.php/component/content/article/43-persian-category/1319-mums-persian-cohort/#visited

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Mashhad University of Medical Sciences
Full name of responsible person
Mohsen Nemati
Street address
Azadi Sq. Eastern door of Ferdowsi University, School of Medicine, Nutrition Department
City
Mashhad
Province
Razavi Khorasan
Postal code
9177948564
Phone
+98 51 3882 7034
Email
mds.nutrition@mums.ac.ir
Web page address
https://nutdept.mums.ac.ir/
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Mashhad 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
Mashhad University of Medical Sciences
Full name of responsible person
Ali Jafarzadeh Esfehani
Position
PhD Candidate
Latest degree
Master
Other areas of specialty/work
Nutrition
Street address
East door of Ferdowsi University, Azadi Sq.
City
Mashhad
Province
Razavi Khorasan
Postal code
9177948564
Phone
+98 51 3882 7034
Fax
Email
JafarzadehEA982@mums.ac.ir

Person responsible for scientific inquiries

Contact
Name of organization / entity
Mashhad University of Medical Sciences
Full name of responsible person
Mohsen Nemati
Position
Professor
Latest degree
Ph.D.
Other areas of specialty/work
metabolic syndrome
Street address
School of Medicine, East door of Ferdowsi University, Azadi Sq.
City
Mashhad
Province
Razavi Khorasan
Postal code
9177948564
Phone
+98 51 3882 7034
Email
NematyM@mums.ac.ir

Person responsible for updating data

Contact
Name of organization / entity
Mashhad University of Medical Sciences
Full name of responsible person
Ali Jafarzadeh Esfehani
Position
PhD Candidate
Latest degree
Master
Other areas of specialty/work
Nutrition
Street address
East door of Ferdowsi University, Azadi Sq.
City
Mashhad
Province
Razavi Khorasan
Postal code
9177948564

Phone
+98 51 3882 7034
Fax
Email
JafarzadehEA982@mums.ac.ir

Sharing plan

Deidentified Individual Participant Data Set (IPD)
No - There is not a plan to make this available
Justification/reason for indecision/not sharing IPD
Persian cohort center will provide the data to researchers in a case-by-case basis and the center has the complete ownership of the data.
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
No - There is not a plan to make this available
Data Dictionary
No - There is not a plan to make this available
Title and more details about the data/document
Some collected data including the results of primary outcome measures will be presented.
When the data will become available and for how long
Access to data will be granted 6 months after publication
To whom data/document is available
Data will be accessible for people working in academic institutions and people working in businesses upon request.
Under which criteria data/document could be used
Criteria for sharing deidentified data or other products will be evaluated based on case-by-case approach by the Mashhad University of Medical Sciences.
From where data/document is obtainable
Contact info: Dr. Mohsen Nemati, Department of Nutrition, Mashhad University of Medical Sciences, East door of Ferdowsi University, Azadi Sq., Mashhad, Iran Post code: 9177948564 email: NematyM@mums.ac.ir Phone number: 0098 51 38827034
What processes are involved for a request to access data/document
Applicants should submit their detailed request through email. Their request will be evaluated by the researchers and the Mashhad University of Medical Sciences and will be available to the applicant if approved by the organization.
Comments