Clinical Trial Protocol
Iranian Registry of Clinical Trials

17 Jul 2026

The effect of L-citrulline supplementation on nutrirtional, metabolic, oxidative and inflammatory status and serum levels of L-citrulline and NOx in type 2 diabetes patients: A randomized controlled clinical trial

Protocol summary

Study aim

The aim of the present study is to investigate the effect of L-citrulline supplementation on nutrirtional, metabolic, oxidative and inflammatory status and serum levels of L-citrulline and NOx in type 2 diabetes patients.

Design

Randomized double blind clinical trial with two arm parallel groups

Settings and conduct

Patients volunteering from Tabriz Diabetes Control Center under an endocrinologist with diagnosis of type 2 diabetes will be randomly assigned to one of the two supplement or placebo groups.The duration of the study will be 8 weeks. L-citrulline and placebo sachets will be coded by the person responsible for preparing them, and the main investigators and the patients will be blinded to the type of supplement each group receives.

Participants/Inclusion and exclusion criteria

46 patients with type 2 diabetes and BMI of 25-35 kg / m2 who have been diagnosed with a disease for at least 6 months will be included in the study. Pregnancy, lactation and menopause in women, taking insulin and developing cardiovascular, renal and hepatic diseases are among the exclusion criteria.

Intervention groups

Patients in the L-Citrulline group will use a 3 gram L-Citrulline sachet before their breakfast, daily. In the placebo group, the sachet will contain 3 grams of microcrystalline cellulose.

Main outcome variables

Nutritional status (anthropometric indices , and calorie and macronutrients intake), metabolic status (fasting blood glucose، insulin, HbA1c, Insulin resistance index (HOMA-IR) and lipid profiles (TC, TG, HDL-c LDL-c), oxidative status (total antioxidant capacity, glutathione peroxidase and superoxide dismutase and Malondialdehyde), inflammatory status (hs-CRP, IL-6 and TNF-α), serum levels of L-citrulline and NOx (nitrate and nitrite)

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20100209003320N16**
Registration date: **2019-06-26, 1398/04/05**
Registration timing: **prospective**

Last update: **2019-11-28, 1398/09/07**
Update count: **2**

Registration date

2019-06-26, 1398/04/05

Registrant information

Name

Mehrangiz Ebrahimi mamagani

Name of organization / entity

Health & Nutrition faculty of Tabriz university of medical sciences

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2019-07-11, 1398/04/20

Expected recruitment end date

2019-09-22, 1398/06/31

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

The effect of L-citrulline supplementation on nutrirtional, metabolic, oxidative and inflammatory status and serum levels of L-citrulline and NOx in type 2 diabetes patients: A randomized controlled clinical trial

Public title

The effect of L-Citrulline in type 2 Diabetes

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Suffering from type 2 diabetes that have passed at least 6 months since diagnosis and having HbA1c less than 9. Men and non-menopausal women Age 25 to 55 years BMI 25 to 35 kg/m2 People who control their diabetes just by using metformin and sulfonylurea Willingness to participate in the study

Exclusion criteria:

Pregnancy, lactation or menopause in women Smoking or alcohol use A history of following a particular diet (at the time of the study or 3 months before the study) Change in the type or dosage of medications consumed, the type and amount of physical activity, changes in the diet at the start and during the study Using synthetic or herbal drugs for weight loss Use of any supplement (L-arginine, glutamine, multivitamin, antioxidant supplement, etc.) during the three months before or during the study. Taking insulin Suffering from cardiovascular disease, liver, intestinal, thyroid and parathyroid dysfunction, polycystic ovary syndrome, cancers and malignant diseases such as sprue and Crohn's disease Having symptoms of infectious or inflammatory disease or recent surgery The use of hypotensive and lipid-lowering drugs Use of corticosteroids and non-steroidal anti-inflammatory drugs for 3 months before the study.

Age

From **25 years** old to **55 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Investigator

Sample size

Target sample size: **46**

Randomization (investigator's opinion)

Randomized

Randomization description

46 eligible patients will be randomly allocated to intervention and placebo groups using a software generated random permuted blocks. The generated random sequence will be kept in a protected location and administered by an independent third party who is blind to the trial throughout the study.

Blinding (investigator's opinion)

Double blinded

Blinding description

In this study, the main investigators (including the student and her supervisors and adviser professors), as well as the patients will be blinded to the type of the supplement (L-citrulline or placebo) received by each group. The person responsible for preparing the supplement sachets (who is completely unrelated to the study) will be asked to assign a three-digit code to each of the two powders (L-citrulline and placebo) and keep the codes for himself until the end of the study and data analysis.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

The Research Ethics Committee of Tabriz University of Medical Sciences

Street address

Tabriz University of Medical Sciences, Attar Neishabouri Ave., Golgasht St.

City

Tabriz

Province

East Azarbaijan

Postal code

5166/1573113

Approval date

2019-06-11, 1398/03/21

Ethics committee reference number

IR.TBZMED.REC.1398.216

2

Ethics committee

Name of ethics committee

The Research Ethics Committee of Tabriz University of Medical Sciences

Street address

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5166/1573113

Approval date

2019-10-21, 1398/07/29

Ethics committee reference number

IR.TBZMED.REC.1398.739

Health conditions studied

1

Description of health condition studied

Type 2 diabetes

ICD-10 code

E11

ICD-10 code description

Type 2 diabetes mellitus

Primary outcomes

1

Description

Anthropometric Indices

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

Measurement of height and weight without shoes and with minimum clothes on, by Seca stadiometer and scale, respectively. Measurement of waist and hip circumference by a tape measure and body mass index (BMI) by dividing weight (kg) by height squared (m2)

2

Description

Calorie and macronutrients intake

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

The intake of calorie and macronutrients from the diet of the subjects with using a 3 day food record questionnaire and analysis by the nutritionist 4 program.

3

Description

Fasting blood sugare

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

Enzymatic method

4

Description

Insulin

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

ELISA

5

Description

HbA1c

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

Enzymatic method

6

Description

Lipid profile

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

Measurement of total cholesterol, HDL- cholesterol and triglyceride through enzymatic methods and calculation of LDL- cholesterol by Friedewald equation

7

Description

Insulin resistance

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

Insulin resistance with HOMA-IR and calculation by this equation : [fasting insulin (mU / ml) × fasting glucose (mg / dl)] / 405

8

Description

Oxidative stress indices

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

Measurement of total antioxidant capacity, glutathione peroxidase, superoxide dismutase and malondialdehyde through spectrophotometric method

9

Description

Inflammatory indices

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

Measurement of serum hs-CRP by immunoturbidometry method and serum IL-6, TNF-α, MCP1 and TLR4 by ELISA

10

Description

Serum levels of L-Citrulline

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

ELISA

11

Description

Serum nitrate and nitrite (NOx)

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

Colorimetric with Griess Reagent

Secondary outcomes

1

Description

Physical activity level

Timepoint

Baseline and 8 weeks after intervention

Method of measurement

Via IPAQ questionnaire

Intervention groups

1

Description

Intervention group: Patients in this group will receive L-citrulline supplement for 8 weeks. The supplement is a sachet containing 3 grams of L-Citrulline (a product by Bulk Supplements Co. and made in the United States) which will be dissolved in a glass of water and used once a day before breakfast.

Category

Treatment - Drugs

2

Description

Control group: Patients in this group will receive placebo for 8 weeks. The placebo is a sachet containing 3 grams of microcrystalline cellulose (a product by Linyi Jindi Chemical Co. and made in China) which will be dissolved in a glass of water and used once a day before breakfast.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Tabriz Diabetes Control Center

Full name of responsible person

Dr. Majid Mobasseri

Street address

Sina Hospital, Between the Maralan and Hafez Roads,. Azadi St.

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Tabriz University of Medical Sciences

Full name of responsible person

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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

Tabriz 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

Tabriz University of Medical Sciences

Full name of responsible person

Samaneh Azizi

Position

Ph.D. student of nutrition sciences

Latest degree

Master

Other areas of specialty/work

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Person responsible for scientific inquiries

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Other areas of specialty/work
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Person responsible for updating data

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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
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
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
Title and more details about the data/document
Data collected for the primary outcomes will be shared.
When the data will become available and for how long
Access starting 12 months after publication
To whom data/document is available
The data will only be available for people working in academic institutions.
Under which criteria data/document could be used
The data of the present study will only be accessible by other researchers, for conducting meta-analysis.
From where data/document is obtainable
Ms. Samaneh Azizi, E-mail address: s.azizi296@gmail.com, cellphone number: 0098 9177200691
What processes are involved for a request to access data/document
The applicant should provide a brief description of the aims and methods of his his Meta-analysis. His request will be assessed and, if agreed, the data will be emailed to the applicant. All these procedures will take no longer than 15 days.
Comments