Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Evaluation of the effects of astaxanthin on markers related to autophagy and study of inflammatory activity by expression of microRNAs in type ۲ diabetic patients are treated with metformin

Protocol summary

Study aim
Determination of the effect of astaxanthin on autophagic pathway and study of inflammatory activities by gene expression of inflammatory-related microRNAs in patients with type 2 diabetes treated with metformin

Design
The clinical trial has a control group. A double-blind, randomized study. 1. metformin is prescribed with placebo. 2. metformin is prescribed with astaxanthin.

Settings and conduct
The study population was from patients referring to Endocrine and Metabolism Research Center of Isfahan and conducted tests at the Faculty of Pharmacy of Isfahan University of Medical Sciences. The following biochemical parameters are measured in two groups of treatment and control before and 8 weeks after treatment: blood glucose and glycosylated sugar, blood lipids, uric acid, serum creatinine, and blood urea Evaluation of autophagic gene expression on PBMC by RT-PCR method Expression of autophagic proteins (Atg-5, ATg-7) by Western blotting method Evaluation of serum levels of inflammatory markers (TNF-a, IL-6, IL-1B) Expression of inflammatory-related microRNAs (MiR-155,21,34a) Evaluation of insulin resistance and oxidative markers (aHB, LysoPC)

Participants/Inclusion and exclusion criteria
Inclusion criteria: type 2 diabetic patients treated by metformin nonInclusion criteria: patients with type 1 diabetes, Pregnant women. Women in lactation, Taking any antidiabetic drug other than metformin, Patients with other endocrine disorders, Take any other antioxidant supplement

Intervention groups
One group will be taken metformin (1000-1500 mg/day) plus astaxanthin supplementation 10 mg/day and other groups will be taken metformin 1500-1000 mg/day plus astaxanthin placebo For 8 weeks All steps for the treatment process are under the supervision of a doctor.

Main outcome variables
Increasing the efficacy of treatment in improving inflammatory, autophagic, insulin resistance and oxidative indexes

General information

Reason for update
Evaluation of the effects of astaxanthin on markers related to autophagy and study of inflammatory activity by expression of microRNAs in type ۲ diabetic patients are treated with metformin (Continued study on available samples)

Acronym

IRCT registration information
IRCT registration number: **IRCT20190305042939N1**
Registration date: **2019-06-17, 1398/03/27**
Registration timing: **registered_while_recruiting**

Last update: **2022-04-23, 1401/02/03**
Update count: **2**

Registration date
2019-06-17, 1398/03/27

Registrant information

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Name of organization / entity

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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2019-05-21, 1398/02/31
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
Evaluation of the effects of astaxanthin on markers related to autophagy and study of inflammatory activity by expression of microRNAs in type ۲ diabetic patients are treated with metformin

Public title
Evaluating the effect of astaxanthin supplement in patients with type 2 diabetes Treated by metformin
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Patients with type 2 diabetes Treated by metformin Age: 20-60 years
Exclusion criteria:
Patients with type 1 diabetes Pregnant women Women in lactation Taking any antidiabetic drug other than metformin Patients with other endocrine disorders Take any other antioxidant supplement
Age
From **20 years** old to **60 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Data analyser

Sample size
Target sample size: **50**
More than 1 sample in each individual
Number of samples in each individual: **2**
Get 2 blood sample from the patient before and after the intervention
Randomization (investigator's opinion)
Randomized
Randomization description
from among patients in the Isfahan Endocrine and Metabolism Center, 50 patients with type 2 diabetes who are merely treated with metformin are selected available and easy to use.Then, the names of the patients were entered into the SPSS software and using the software, they are randomly divided into two groups of 25 intervention and placebo groups.
Blinding (investigator's opinion)
Double blinded
Blinding description
For this purpose, based on the supplement we used in this intervention, which is the softgel, the placebo is designed and the investigator is aware of the difference between the two, but the patients and the statistical counselor do not know this difference.
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
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Deputy of Research & Technology, Headquarters Building No. 4, Isfahan University of Medical Sciences & Health Services, Isfahan
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Approval date
2019-05-18, 1398/02/28
Ethics committee reference number
IR.MUI.RESEARCH.REC.1398.103

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2021-01-06, 1399/10/17
Ethics committee reference number
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Ethics committee
Name of ethics committee
Ethics committee of shiraz University of Medical

Sciences

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Approval date

2022-03-29, 1401/01/09

Ethics committee reference number

IR.SUMS.REC.1401.029

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

Glycemic Indexes: Following the intervention, we expect the glycemic indexes of the patients (treated with astaxanthin and metformin) to differ from the control group (placebo and metformin).

Timepoint

Initially (before the intervention) and at the end (8 weeks after the intervention)

Method of measurement

(Glycemic indexes in this study include fasting blood sugar, glycated hemoglobin, and insulin). Fasting blood Glucose: Colorimetric Method - Glycated Hemoglobin: High Performance Liquid Chromatography - Insulin: ELISA Technique

2

Description

Oxidative stress: Following the intervention, we expect the oxidative stress markers of the patients (treated with astaxanthin and metformin) to differ from the control group (placebo and metformin).

Timepoint

Initially (before the intervention) and at the end (8 weeks after the intervention)

Method of measurement

The oxidative stress in this study is measured by markers that are: total antioxidant capacity, malondialdehyde, catalase and superoxide dismutase, all of which are measured by Spectrophotometry and with relevant reagents.

3

Description

Tubular and glomerular Indexes: Following the intervention, we expect the tubular and glomerular Indexes of the patient group (treated with astaxantin and metformin) to differ from the control group (placebo and metformin)

Timepoint

Initially (before the intervention) and at the end (8 weeks after the intervention)

Method of measurement

Tubular and glomerular markers in this study are: cystatin C, microalbumin, creatinine and lipocalin-associated neutrophil gelatinase: ELISA technique

4

Description

Oxidative stress: Following the intervention, we expect the oxidative stress markers of the patients (treated with astaxanthin and metformin) to differ from the control group (placebo and metformin)

Timepoint

Initially (before the intervention) and at the end (8 weeks after the intervention)

Method of measurement

The oxidative stress in this study is measured by markers that are:Total protein, malondialdehyde, 8-hydroxy deoxyguanosine and protein products oxididation by Bradford methods and ELISA technique

5

Description

Inflammation, insulin resistance and oxidative Indexes: Following the intervention, we expect the inflammation Indexes of the patient group (treated with astaxantin and metformin) to differ from the control group (placebo and metformin)

Timepoint

Initially (before the intervention) and at the end (8 weeks after the intervention)

Method of measurement

The methods of measuring inflammatory, insulin resistance and oxidative markers variables in this study were: use of ELISA technique for interleukin-6, interleukin-1B and TNF-a and aHB using RT-PCR method for gene expression of inflammatory microRNAs including MiR-155, MiR-21, MiR-34a, using photometric method for lysoPC

6

Description

Autophagic Indexes: Following the intervention, we expect the autophagic Indexes of the patient group (treated with astaxantin and metformin) to differ from the control group (placebo and metformin)

Timepoint

Initially (before the intervention) and at the end (8 weeks

after the intervention)

Method of measurement

The method of measuring the variables of autophagic indexes in this study were: using RT-PCR technique for mTOR, Becline-1, LC3-II, western blotting method for protein level Atg-5, Atg-7

Secondary outcomes

empty

Intervention groups

1

Description

Control group: Metformin /Placebo treated diabetic group.

Category

Placebo

2

Description

Intervention group: Intervention group: Diabetic group treated with metformin / astaxanthin.This intervention is intended to evaluate the efficacy of treatment for diabetic patients. Based on the explanation given in the proposed text Astaxanthin (3,3'-dihydroxy-β, β'-carotene-4,4'-dione) is a natural red or orange carotenoid compound that exists in different microorganisms and seafood.The main source of food is Astaxanthin, the hematococcus pluvialis (Haematococcus pluvialis), which is a green microalgae and enters the human body by eating fish and sea animals. It has an antioxidant strength of 550 times the antioxidant value of vitamin E (32).Astaxanthin has been reported to play an important role in lipid and sugar intake, in addition to anti-inflammatory effects, and the protection of the nervous system and the cardiovascular system.Various action mechanisms have been proposed for this antioxidant such as:activation of AMPK 2. regulating the PI3K / Akt signaling path in the liver 3. Increased glucose uptake by tissues (increased insulin sensitivity).It is expected that the use of this carotenoid in combination with metformin, which is almost the same mechanism of action, can be effective in increasing the efficacy of treatment. Also, considering the role of oxidative stress in the development of chronic diabetes complications and the role of diminished glucose lowering drugs in reducing these complications including renal complications, Using this antioxidant can be taken to reduce the complications of diabetes in these patients.The subjects were divided into two equal groups and each group was divided into 25 patients.1. Metformin / placebo group: This metformin (glucophage) group is given at a dose of 1000-1500 mg / day plus one placebo daily.2. Group treated with metformin / astaxanthin: This group of metformin (glucophage) with a dose of mg / day 1000-1500 with astaxanthin with a dose of 10 mg/day is given as a softgel (WAKA TANI Astaxanthin Supplement)

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Endocrinology and Metabolism Research Center of Isfahan University of Medical Sciences

Full name of responsible person

Mohammadhosein Aarabi

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Sponsors / Funding sources

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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

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

2

Sponsor

Name of organization / entity

Shiraz 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

Shiraz 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

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Position

Professor

Latest degree

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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

Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary

Not applicable