Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Nov 2026

Study the effect of ezetimibe along with metformin on changes in PPAR-γ and adiponectin expression, serum levels of liver enzymes, degree of hepatic steatosis, blood glycemic and lipids parameters in non-alcoholic fatty liver grade 2 patients suffering from diabetes: clinical trial

Protocol summary

Study aim

Comparison of metformin alone and combination of metformin with ezetimibe on PPAR-γ and adiponectin gene expression ,serum level of medical enzymes , degree of dietary steatosis , glycemic and blood lipid parameters in non- alcoholic fatty liver disease in grade 2 patients

Design

Clinical trial with 2 control and intervention groups, parallel groups, randomized, phase 4 on two groups of 80 people.

Settings and conduct

The participants in this project will be entered by the endocrinology and metabolism specialist from Nikbakht Clinic in Isfahan in 2023 based on the entry criteria of the study. Serum lipid profile (HDL and LDL-Cholesterol, Triglycerides) using commercial enzymatic method, serum level of GGT, AST and ALT by calorimetric method, insulin level by Cobas e411device, and interleukin 6 level by Imolite device method will be measured. Also serum MDA and TAC will be assayed using calorimetric method. Separation of mononuclear cells by PBMC and extraction of RNA and cDNA synthesis will be done with Fermantase kits. Gene expression of PPAR-γ and adiponectin will be assayed using Real time PCR method.

Participants/Inclusion and exclusion criteria

Diabetic patients with NAFLD

Intervention groups

The use of ezetimibe and metformin in the treatment of grade 2 non- alcoholic fatty liver patients with diabetes. The intervention group receives a daily dose of 10 mg ezetimibe from Hakim pharmaceutical company and between 500-2500 mg metformin tablets from Raha pharmaceutical company and the control group will take 500-2500 mg metformin tablets daily for 6 months.

Main outcome variables

In this study , the expression of adiponectin and PPAR-γ and the level of liver enzymes, the degree of steatosis, glycemic indices and lipid profile as the primary outcomes, as well as the serum levels of TAC, MDA and interleukin 6 and anthropometric indices will be considered as secondary outcomes

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20090305001745N3**
Registration date: **2023-12-03, 1402/09/12**
Registration timing: **prospective**

Last update: **2023-12-03, 1402/09/12**
Update count: **0**

Registration date

2023-12-03, 1402/09/12

Registrant information

Name

Mohamad Taghi Goodarzi

Name of organization / entity

Hamadan University of Medical Sciences

Country

Iran (Islamic Republic of)

Phone

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Email address

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date
2023-12-06, 1402/09/15
Expected recruitment end date
2024-06-04, 1403/03/15
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Study the effect of ezetimibe along with metformin on changes in PPAR-γ and adiponectin expression, serum levels of liver enzymes, degree of hepatic steatosis, blood glycemic and lipids parameters in non-alcoholic fatty liver grade 2 patients suffering from diabetes: clinical trial

Public title
A comparative study of the use of metformin and ezetimibe compared to the use of metformin in the treatment of non-alcoholic fatty liver disease
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Type 2 diabetes is known (under treatment) At least one year has passed since their diabetes NAFLD grade 2 or 3 has been diagnosed by ultrasound All patients should undergo non -pharmacological life style modification treatment
Exclusion criteria:
Newly diagnosed subjects Type 1 diabetes Receiving only insulin treatment Drug intolerance disorders Lack of consent to continue treatment Diagnosis of type 1 NAFLD Having a weight loss of more than 5 % Having Infectious diseases , cancer, allergy and immune - based diseases Smoking and alcohol consumption Appetite disorders such as anorexia or overeating Treatment with amphetamine, cyproheptadine, phenothiazine, appetite suppressants or appetite stimulants Chronic viral hepatitis (HBV-HCV-HDV), drug-induced liver disease , Wilson's disease , hereditary deficiency of antitrypsin 1, idiopathic hemochromatosis, history of complications from liver diseases including ascites , encephalopathy or variceal bleeding Uncontrolled cardiovascular or respiratory disease , active malignancy or active and chronic infections The use of agents such as vitamin E-omega 3 fatty acids or drugs with evidence of their effect on NAFLD (pioglitazon , GLP 1analog , dipeptidyl peptidase inhibitors IV ,ursodeoxycholic acid) Pregnancy or breastfeeding Use of corticosteroids Taking herbal medicines whose effect on fatty liver has been proven Taking any nutritional supplements in the last 3 months
Age
From **30 years** old to **60 years** old
Gender
Both

Phase
3
Groups that have been masked
No information
Sample size
Target sample size: **80**
Randomization (investigator's opinion)
Randomized
Randomization description
Simple randomization using individual method by the Endocrinologist. The patients will be divided into groups according the number of their registration in clinic: odd numbers in control group and even numbers in intervention group.
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 Islamic Azad University of Shahrood
Street address
Daneshgah Blvd.
City
Shahrood
Province
Semnan
Postal code
3614871151
Approval date
2023-09-07, 1402/06/16
Ethics committee reference number
IR.IAU.SHAHROOD.REC.1402.043

Health conditions studied

1

Description of health condition studied
Diabetes
ICD-10 code
E11.6
ICD-10 code description
Type 2 diabetes mellitus with other specified complications

Primary outcomes

1

Description

Liver steatosis

Timepoint

At the beginning of intervention and 6 months after that date.

Method of measurement

Sonography

2

Description

Adiponectin gene expression

Timepoint

At the beginning of intervention and 6 months after that date

Method of measurement

Real time PCR

3

Description

PPAR- gama Gene expression

Timepoint

At the beginning of intervention and 6 months after that

Method of measurement

Real time PCR

4

Description

Activity of liver enzymes in serum

Timepoint

At the beginning of intervention and 6 months after that date

Method of measurement

Spectrophotometry

5

Description

Patients lipid profile

Timepoint

At the beginning of intervention and 6 months after that date

Method of measurement

Autoanalyzer (Spectrophotometry)

6

Description

Serum Level of IL-6

Timepoint

At the beginning of intervention and 6 months after that date

Method of measurement

Enzyme Immunoassay

7

Description

Serum Level of Malone- di-aldehyde

Timepoint

At the beginning of intervention and 6 months after that date

Method of measurement

Spectrophotometry

Secondary outcomes

1

Description

Total Antioxidant Capacity

Timepoint

At the beginning of intervention and 6 months after that date.

Method of measurement

Spectrophotometry

2

Description

Fasting blood glucose

Timepoint

At the beginning of intervention and 6 months after that date.

Method of measurement

Autoanalyzer

3

Description

2 hours post prandial glucose

Timepoint

At the beginning of intervention and 6 months after that date.

Method of measurement

Autoanalyzer

4

Description

Glycated hemoglobin (HbA1c)

Timepoint

At the beginning of intervention and 6 months after that date.

Method of measurement

Spectrophotometry

5

Description

Insulin Resistance Index (HOMA-IR)

Timepoint

At the beginning of intervention and 6 months after that date.

Method of measurement

Calculation according to the related formula

Intervention groups

1

Description

Intervention group: grade 2 non- alcoholic fatty liver patients with diabetes receives a daily dose of 10 mg

ezetimibe (Hakim pharmaceutical company)and between 500-2500 mg metformin tablets (Raha pharmaceutical company) for 6 months.

Category

Treatment - Drugs

2

Description

Control group: grade 2 non- alcoholic fatty liver patients with diabetes receives 500-2500 mg metformin tablets (Raha pharmaceutical company) for 6 months.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Nikbakht Clinic

Full name of responsible person

Mohammad Reza Mirzaei

Street address

Nikbakht Clinic No 48, West Nikbakht St, Chaharbagh Bala St.

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Islamic Azad University of Shahrood

Full name of responsible person

Śahebali Manafi Dr.

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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

No

Title of funding source

There is no financial support for this project. It will be carried out in personal expenses.

Proportion provided by this source

100

Public or private sector

Private

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin

Type of organization providing the funding

Persons

Person responsible for general inquiries

Contact

Name of organization / entity

Islamic Azad University of Shahrood

Full name of responsible person

Mohammad Taghi Goodarzi

Position

Professor

Latest degree

Ph.D.

Other areas of specialty/work

Biochemistry

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Professor

Latest degree

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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
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
Not applicable