Clinical Trial Protocol
Iranian Registry of Clinical Trials

29 May 2026

Investigating the additional effect of methylene blue to empagliflozin on nephropathy in patients with type II diabetes

Protocol summary

Study aim

Determination of the additional effect of Methylene Blue to Empagliflozin on nephropathy in patients with Type 2 Diabetes and its comparison with the control Group"

Design

A clinical trial with the control group, parallel, blinding in assessors, analysts, and sample allocators, randomized, phase 2 on 50 patients. Blocking will be used for randomization

Settings and conduct

Patients with early-stage nephropathy and microalbuminuria, confirmed by two urine tests with a ratio of 30-300 mg/g, are treated by an endocrinologist at Qaem Hospital. The attending physician's criteria determine admission and discharge, with willing patients randomly assigned to the control or intervention group using block randomization.

Participants/Inclusion and exclusion criteria

age:25 to 65, and having a GFR between 25 and 90. They must not have liver insufficiency, active liver disease, active infection, sepsis, or polycystic kidney disease. Inclusion criteria also involve non-professional athletes, individuals not receiving insulin treatment, no acute kidney failure unrelated to diabetes, no history of heart or vascular diseases, G6PD deficiency, well-controlled blood pressure, and no prior cancer or endocrine diseases

Intervention groups

Diabetic patients in whom microalbuminuria has been confirmed, despite standard treatments (Empagliflozin) , will be undergone oral methylene blue intervention for 6 months. Methylene blue is given to the patient in the form of a sachet to be dissolved in 200 ml of Milk and drunk after one hour.

Main outcome variables

Primary Outcome : Reduction in microalbuminuria. Improvement in GFR rate. Secondary Outcome: Improvement in creatinine levels. Reduction in blood glucose, HbA1C, and blood pressure. Decreased incidence of urinary tract infections. Decreased serum levels of NO metabolites. Reduction in levels of inflammatory markers."

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20191228045924N7**
Registration date: **2023-11-12, 1402/08/21**
Registration timing: **prospective**

Last update: **2023-11-12, 1402/08/21**
Update count: **0**

Registration date

2023-11-12, 1402/08/21

Registrant information

Name

Daryoush Hamidi Alamdari

Name of organization / entity

Country

Iran (Islamic Republic of)

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+98 51 3882 8574

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-11-21, 1402/08/30

Expected recruitment end date

2025-03-18, 1403/12/28

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Investigating the additional effect of methylene blue to empagliflozin on nephropathy in patients with type II diabetes

Public title

additional effect of methylene blue to empagliflozin on diabetic nephropathy

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Individuals diagnosed with type 2 diabetes between the ages of 25 and 65 are eligible for inclusion in the study. Patients with a Glomerular Filtration Rate (GFR) greater than 25 and less than 90 Absence of liver insufficiency or active liver disease Absence of active infection and sepsis. Exclusion of professional athletes and individuals who have not engaged in intense physical exercise in the 9 days leading up to the sample collection. Patients not currently undergoing treatment with insulin. Patients with no history of polycystic kidney disease. Absence of acute kidney failure due to causes other than diabetes, such as infection. No history of cardiovascular diseases No history of uncontrolled high blood pressure. Absence of cancer or any other endocrine diseases. Not having Glucose 6-phosphate dehydrogenase (G6PD) deficiency

Exclusion criteria:

Patient's non-consent for continued cooperation. Absence of cancer or any other endocrine diseases.

Age

From **25 years** old to **65 years** old

Gender

Both

Phase

2

Groups that have been masked

No information

Sample size

Target sample size: **50**

Randomization (investigator's opinion)

Randomized

Randomization description

This method is used to prevent noticeable imbalances in the number of participants assigned to each group. Randomized blocking ensures that no significant imbalance occurs between groups at any point during randomization, and that the number of participants in each group is equal at specific points. To implement this method, the block size must be determined initially (e.g., a block of four). In order to reduce the predictability of the randomization process, various block sizes are employed in blocked randomization. For this purpose, we consider 10 blocks of four and 5 blocks of two for the 50 patients who are to be included in the study. The list of four-person blocks is created, and numbers from 1 to 6 are assigned to them (AABB(1)- ABAB(2)-ABBA(3)- BBAA(4)- BABA(5)- BAAB(6)). Additionally, the list of two-person blocks consists of AB and BA. Finally, treatment allocation is carried out based on the obtained sequences (..., AABB-BBAA-BABA).

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Research Ethics committees of Mashhad University of Medical Sciences

Street address

Daneshgah street, the central organization of University, Quraishi construction

City

mashhad

Province

Razavi Khorasan

Postal code

9138813944

Approval date

2023-10-27, 1402/08/05

Ethics committee reference number

IR.MUMS.REC.1402.203

Health conditions studied

1

Description of health condition studied

Diabetic nephropathy

ICD-10 code

E11.2

ICD-10 code description

Type 2 diabetes mellitus with renal complications

Primary outcomes

1

Description

Reduction in microalbuminuria

Timepoint

At time point zero (prior to drug administration), three months, and six months after drug administration.

Method of measurement

laboratory test

2

Description
Enhancement in GFR (Glomerular Filtration Rate)
Timepoint
At time point zero (prior to drug administration), one month, three months, and six months after drug administration.
Method of measurement
Laboratory test and Calculation of the Glomerular Filtration Rate (GFR)

Secondary outcomes

1

Description
Improvement in creatinine levels
Timepoint
At time point zero (prior to drug administration), one month, three months, and six months after drug administration.
Method of measurement
Laboratory test

2

Description
Reduction in blood glucose
Timepoint
At time point zero (prior to drug administration), one month, three months, and six months after drug administration.
Method of measurement
Laboratory test

3

Description
Reduction in blood pressure
Timepoint
At time point zero (prior to drug administration), one month, three months, and six months after drug administration.
Method of measurement
Barometer

4

Description
Reduction in HbA1C
Timepoint
At time point zero (prior to drug administration), three months, and six months after drug administration.
Method of measurement
laboratory test

5

Description
Reduction in the incidence of urinary tract infections
Timepoint
At time point zero (prior to drug administration), one month, three months, and six months after drug administration.
Method of measurement
laboratory test

6

Description
Decrease in serum levels of NO (its metabolites)
Timepoint
At time point zero (prior to drug administration), three months, and six months after drug administration
Method of measurement
ELISA

7

Description
Reduction in the levels of inflammatory factors((TNF)-α, (IL)-6, (IL)-1β
Timepoint
At time point zero (prior to drug administration), three months, and six months after drug administration
Method of measurement
ELISA

Intervention groups

1

Description
Intervention group: The intervention group includes Diabetic patients in whom microalbuminuria has been confirmed, despite standard treatments (Empagliflozin) , will be undergone oral methylene blue intervention for 6 months. Methylene blue is given to the patient in the form of a sachet to be dissolved in 200 ml of Milk and drunk after one hour.
Category
Treatment - Drugs

2

Description
Control group: This group comprises diabetic patients in whom the presence of microalbuminuria has been confirmed. These patients will receive standard treatment with empagliflozin. Additionally, these patients will be administered 200 milliliters of milk.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Qaem Hospital
Full name of responsible person
Dr.Shokoufeh Bonakdaran
Street address

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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
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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
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
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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
Undecided - It is not yet known if there will be a plan to make this available