Clinical Trial Protocol
Iranian Registry of Clinical Trials

02 Aug 2026

The effect of combination therapy of oral methylene blue and platelet-rich plasma-fibrin glue in patients with non-healing diabetic foot ulcer: a pilot study

Protocol summary

Study aim

Increasing the chance of healing diabetic wounds by improving the condition of lack of oxygen or hypoxia in the wound area caused by diabetes using methylene blue and also continuing to investigate the healing process with the synergistic treatment of methylene blue and platelet-rich plasma-fibrin glue as a method effective treatment in healing wounds

Design

A clinical trial with the control group, factorial, double-blind, randomized, phase 2 on 20 patients. Blocking will be used for randomization.

Settings and conduct

Wound clinic of Dr. Mohammad Hadi Saeed Mudaghq and Velayat Hospital

Participants/Inclusion and exclusion criteria

Having a Diabetic ulcer grade II and IV based on Wagner's classification on the sole, medial, or lateral part of the foot, not taking antidepressants, not having Glucose 6-phosphate dehydrogenase deficiency, the presence of a wound with a clear and severe infection, which is characterized by significant purulent secretions or extensive cellulitis, or gangrene requiring amputation, evidence of venous, ischemic, neurotrophic ulcers and traumatic wounds in the patient, failure to refer the patient more than two times to the mentioned center for follow-up and dressing change, hypersensitivity reaction to methylene blue, the patient's lack of consent to continue cooperation

Intervention groups

The first intervention group (group A) includes diabetic patients with chronic foot ulcers who, despite common treatments, will be undergone oral methylene blue intervention for 4 weeks, and their control group (group B) only will receive 200 ml of milk for 4 weeks. The second intervention group (group C) of diabetic patients with chronic foot ulcers will be treated with a 4-week synergistic treatment of oral methylene blue with fibrin glue, and their control group (group D) will be treated only with fibrin glue and 200 ml of milk for 4 weeks.

Main outcome variables

wound area

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20191228045924N3**
Registration date: **2023-02-09, 1401/11/20**
Registration timing: **prospective**

Last update: **2023-02-09, 1401/11/20**
Update count: **0**

Registration date

2023-02-09, 1401/11/20

Registrant information

Name

Daryoush Hamidi Alamdari

Name of organization / entity

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-04-04, 1402/01/15

Expected recruitment end date

2023-09-21, 1402/06/30

Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
The effect of combination therapy of oral methylene blue and platelet-rich plasma-fibrin glue in patients with non-healing diabetic foot ulcer: a pilot study

Public title
The effect of combination therapy of oral methylene blue and fibrin glue in the treatment of non-healing diabetic foot ulcer
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Having a Diabetic ulcer grade II and IV based on Wagner's classification on the sole, medial, or lateral part of the foot (including all surfaces of the toes) Having a single ulcer on the feet and extremities (toes, soles, heels) with no significant reduction in ulcer size (<20%) despite the use of best treatment methods for at least four weeks If there is more than one non-healing wound, choose the largest wound The size of the wound surface (length × width) between 2 cm2 and 20 cm2 No smoking, alcohol and drug addiction based on the patient's self-report Not taking drugs that may interfere with wound healing, such as Corticosteroids, immunosuppressants, and cytotoxic agents Not having a concurrent chronic disease that may cause problems in wound healing, such as cancers, vasculitis, no history of known severe kidney, liver, and heart disease, such as liver cirrhosis, active hepatitis, dialysis, etc. Not taking antidepressants Insensitivity to milk lactose Not having Glucose 6-phosphate dehydrogenase (G6PD) deficiency Confirmed, informed, signed consent form Ankle Brachial Index (ABI) higher than or equal to 0.7
Exclusion criteria:
Do not be treated with methylene blue Confirmed presence of osteomyelitis, or if there is suspicion of osteomyelitis The subject is pregnant or intends to become pregnant during the test period The patient is known to have mental, developmental, physical, and emotional disorders The occurrence of certain medical conditions The presence of a wound with a clear and severe infection, which is characterized by significant purulent secretions or extensive cellulitis, or gangrene requiring amputation Evidence of venous, ischemic, neurotrophic ulcers (numbness, tingling, lack of Achilles tendon reflex) and traumatic wounds in the patient Failure to refer the patient more than two times to the mentioned center for follow-up and dressing change Hypersensitivity reaction to methylene blue Platelet count less than 100,000 The patient's lack of consent to continue cooperation
Age
No age limit
Gender
Both

Phase
2
Groups that have been masked

- Participant
- Data analyser

Sample size
Target sample size: **20**
Randomization (investigator's opinion)
Randomized
Randomization description
In this study, permuted block randomization will be used to randomly allocate a participant to a treatment group while maintaining a balance across treatment groups. Each “block” has a specified number of randomly ordered treatment assignments. The sealed envelope is used as a means of randomization and allocation concealment.
Blinding (investigator's opinion)
Double blinded
Blinding description
First, the study will be explained to the participants that it is a double-blind study and includes two intervention groups and two control groups. One group will be given methylene blue along with milk for 4 weeks and one group will be received only milk for 4 weeks. The other group will be treated with a 4-week synergistic treatment of oral methylene blue with fibrin glue, and its control group will be treated with fibrin glue and milk for 4 weeks. Methylene blue is reduced when it dissolves in milk and the color of the milk does not change. The participants will not know about the content of the milk and which group they belong to. The statistical analyzer is not also informed about the groups.
Placebo
Used
Assignment
Factorial
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

2023-01-28, 1401/11/08

Ethics committee reference number

IR.MUMS.REC.1401.370

Health conditions studied

1

Description of health condition studied

Non-healing diabetic foot ulcer

ICD-10 code

E10-E14

ICD-10 code description

Diabetes mellitus with peripheral circulatory complications. Diabetic ulcer

Primary outcomes

1

Description

wound area

Timepoint

Every week for a month after dressing

Method of measurement

Paper ruler, digital camera, lab data and clinical observation

Secondary outcomes

1

Description

Need to amputation

Timepoint

Every week for a month after dressing

Method of measurement

Clinical observation, lab data

Intervention groups

1

Description

Intervention group: The first intervention group includes diabetic patients with chronic foot ulcers who, despite common treatments, will be undergone oral methylene blue intervention for 4 weeks, and the second intervention group consists of diabetic patients with chronic foot ulcers will be undergone synergistic 4-week treatment with oral methylene blue and fibrin glue.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Wound Clinic of Dr. Mohammad Hadi Saeed Mudaghq

Full name of responsible person

Dr. Mohammad Hadi Saeed Mudaghq

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No. 24, Pasdaran Ave., 3/1 Pasdaran

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Mashhad 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

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

Daryoush Hamidi Alamdari

Position
Associate Professor

Latest degree
Ph.D.

Other areas of specialty/work
Biochemistry

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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
There is no further information

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
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
The results of the clinical trial study will be made available to the public in the form of an article.

When the data will become available and for how long
After the completion of the study and data analysis, approximately 5 months after the completion of the interventions

To whom data/document is available
Researchers working in academic and scientific institutions and physicians

Under which criteria data/document could be used
According to the policies of the journal in which the article will be published, the data will be made available.

From where data/document is obtainable
the corresponding author of the article

What processes are involved for a request to access data/document
The request should be sent by email to the corresponding author and he will respond as soon as possible after reviewing the request.

Comments