Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Comparison of Combined Vitamin B12 and Folic Acid Supplementation with Placebo for the Prevention of Thrombocytopenia in Patients Receiving Concomitant Treatment with Meropenem and Linezolid: A Randomized Double-Blind Clinical Trial

Protocol summary

Study aim

To compare vitamin B12 and folic acid with placebo for preventing platelet count reduction and thrombocytopenia in adults receiving concomitant meropenem and linezolid.

Design

A phase 3 randomized, double blind, placebo controlled, parallel group clinical trial involving 36 participants allocated in a one to one ratio using permuted blocks of four.

Settings and conduct

The study will be conducted at Shahid Sadoughi Hospital in Yazd. Blood counts will be measured at baseline and on days 3 and 7. An independent pharmacist will code identical packages and retain the allocation key.

Participants/Inclusion and exclusion criteria

Hospitalized adults aged at least 18 years, with a baseline platelet count above 150,000 per microliter and an indication for at least seven days of concomitant linezolid and meropenem, will be included. Exclusions include hematologic disease, severe hepatic or renal impairment, underlying causes of thrombocytopenia, severe sepsis or septic shock with low platelets before treatment, active bleeding, platelet affecting medicines, piperacillin, and recent vitamin B12 or folic acid use.

Intervention groups

The intervention group will receive oral vitamin B12, 1,000 micrograms daily, and oral folic acid, 1 milligram daily, for seven days plus standard treatment. The control group will receive matching oral placebo for seven days plus standard treatment.

Main outcome variables

Change in platelet count from baseline to days 3 and 7; incidence and severity of thrombocytopenia by day 7.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20260914071059N1**
Registration date: **2026-09-16, 1405/06/25**
Registration timing: **prospective**

Last update: **2026-09-16, 1405/06/25**
Update count: **0**

Registration date

2026-09-16, 1405/06/25

Registrant information

Name
Alireza Haddadi
Name of organization / entity
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Iran (Islamic Republic of)
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+98 35 3822 4000
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haddadialireza80@gmail.com

Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-10-07, 1405/07/15

Expected recruitment end date

2026-12-06, 1405/09/15

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Comparison of Combined Vitamin B12 and Folic Acid Supplementation with Placebo for the Prevention of Thrombocytopenia in Patients Receiving Concomitant Treatment with Meropenem and Linezolid: A Randomized Double-Blind Clinical Trial

Public title

Effect of Vitamin B12 and Folic Acid on Preventing Platelet Count Reduction in Patients Receiving Concomitant Meropenem and Linezolid Treatment

Purpose

Prevention

Inclusion/Exclusion criteria

Inclusion criteria:

Age 18 years or older Baseline platelet count greater than 150,000 per microliter Hospitalization and a clinical indication for concomitant treatment with linezolid and meropenem for at least 7 days Provision of written informed consent to participate in the study

Exclusion criteria:

History of hematologic disorders Severe hepatic impairment defined as Child-Pugh class C Severe renal impairment defined as an estimated glomerular filtration rate below 30 mL/min/1.73 m² or need for dialysis Advanced bone marrow failure Concomitant use of medications affecting platelet count such as aspirin or clopidogrel Presence of an underlying cause of thrombocytopenia such as immune thrombocytopenia, bone marrow aplasia, leukemia, hematologic malignancy, known megaloblastic anemia, or hypersplenism Severe sepsis or septic shock with thrombocytopenia before antibiotic administration Concomitant use of piperacillin Active bleeding Recent use of vitamin B12 or folic acid

Age

From **18 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size

Target sample size: **36**

Randomization (investigator's opinion)

Randomized

Randomization description

The individual participant will be the unit of randomization. After confirmation of eligibility and obtaining written informed consent, 36 participants will be allocated in a 1:1 ratio to either the intervention group with 18 participants or the placebo control group with 18 participants. Before the beginning of recruitment, the allocation sequence will be generated by the independent research pharmacist using permuted block randomization with a fixed block size of four and the Sealed Envelope web-based randomization tool available at https://www.sealedenvelope.com/simple-randomiser/v1/lists. No stratification will be used. Each allocation will be linked to a unique sequential code, and the independent pharmacist will prepare identically appearing, sequentially numbered intervention and placebo packages according to the randomization sequence. Each eligible participant will receive the next consecutively numbered package in the order of enrollment. The allocation list and the code key will be securely retained by the independent pharmacist and will not be accessible to recruiters, participants, clinical care providers, investigators, outcome assessors, or the data analyst until completion of the final analysis. This procedure will ensure allocation concealment

Blinding (investigator's opinion)

Double blinded

Blinding description

The random allocation sequence will be provided to an independent research pharmacist. The pharmacist will prepare, package, and code the intervention products, including vitamin B12 and folic acid, and the matching placebo so that they are identical in appearance, color, size, shape, and packaging. Participants, clinical care providers, principal investigators, outcome assessors and data collectors, and the data analyst will remain unaware of group allocation and the meaning of the codes. The allocation code will be kept exclusively by the independent research pharmacist and will be disclosed to the research team after completion of the final data analysis. No independent data safety and monitoring committee will be established for this study

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Research Ethics Committee of the School of Medicine, Shahid Sadoughi University of Medical Sciences

Street address

School of Medicine, Shahid Sadoughi University of Medical Sciences, Shohadaye Gomnam Boulevard, Alem Square

City

Yazd

Province

Yazd

Postal code

8915173143

Approval date

2026-06-16, 1405/03/26

Ethics committee reference number

IR.SSU.MEDICINE.REC.1405.124

Health conditions studied

1

Description of health condition studied

Thrombocytopenia associated with meropenem and linezolid treatment

ICD-10 code

D69.5

ICD-10 code description

Secondary thrombocytopenia

Primary outcomes

1

Description

Occurrence of thrombocytopenia, defined as at least one platelet count below 150,000 per microliter after initiation of the intervention

Timepoint

At baseline before initiation of the intervention and on days 3 and 7 after initiation of the intervention

Method of measurement

Platelet count will be measured in a venous blood sample using an automated hematology analyzer as part of a complete blood count

Secondary outcomes

1

Description

Platelet count expressed as the number of platelets per microliter of venous blood

Timepoint

At baseline before the intervention and on days 3 and 7 after initiation of the intervention

Method of measurement

Measurement in a venous blood sample using an automated hematology analyzer as part of a complete blood count

2

Description

Severity of thrombocytopenia classified as mild for a platelet count from 100,000 to less than 150,000 per microliter, moderate for a count from 50,000 to less than 100,000 per microliter, and severe for a count below 50,000 per microliter

Timepoint

On days 3 and 7 after initiation of the intervention

Method of measurement

Classification according to platelet count measured in venous blood using an automated hematology analyzer

3

Description

Discontinuation of linezolid or meropenem due to platelet count reduction, recorded as yes or no

Timepoint

From initiation of the intervention through day 7

Method of measurement

Review of medication orders and the treating physician's documented reason for discontinuation in the medical record

4

Description

Total duration of hospitalization in days from hospital admission to discharge

Timepoint

At hospital discharge

Method of measurement

Calculation from the admission and discharge dates recorded in the hospital information system and medical record

5

Description

Occurrence of at least one suspected adverse reaction to the study products, recorded as yes or no

Timepoint

Daily from initiation of the intervention through day 7

Method of measurement

Daily clinical assessment and review of nursing notes, medication records, and the medical record

Intervention groups

1

Description

Intervention group: Participants will receive 1,000 micrograms of oral vitamin B12 once daily and 1 milligram of oral folic acid once daily for seven days, starting concurrently with meropenem and linezolid treatment. Standard treatment with meropenem and linezolid will be administered according to the treating physician's judgment and the hospital protocol

Category

Treatment - Drugs

2

Description

Control group: Participants will receive matching oral placebo for seven days with the same number of dosage units, appearance, color, size, shape, packaging, and administration schedule as the active supplements. Standard treatment with meropenem and linezolid will be administered according to the treating physician's judgment and the hospital protocol

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center
Shahid Sadoughi Hospital

Full name of responsible person
Jamshid Ayatollahi

Street address
Shahid Sadoughi Hospital, Ebne Sina Boulevard, Shahid Ghandi Boulevard, Safaieh

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
Yazd University of Medical Sciences

Full name of responsible person
Mehran Karimi

Street address
Vice Chancellery for Research and Technology, Imam Reza Educational and Research Complex, Beginning of Daneshjoo Boulevard, Imam Hossein Square

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dvc.research@ssu.ac.ir

Web page address
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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
Yazd 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
Yazd University of Medical Sciences

Full name of responsible person
Mohammadreza Heidarzadeh

Position
Infectious Diseases Resident

Latest degree
Medical doctor

Other areas of specialty/work
Infectious diseases

Street address
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Person responsible for scientific inquiries

Contact

Name of organization / entity
Yazd University of Medical Sciences

Full name of responsible person
Alireza Haddadi

Position
Intern

Latest degree
A Level or less

Other areas of specialty/work
Infectious diseases

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Person responsible for updating data

Contact

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Position
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Latest degree
A Level or less

Other areas of specialty/work
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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is 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
Yes - There is a plan to make this available

Data Dictionary
Yes - There is a plan to make this available

Title and more details about the data/document
Deidentified individual participant data underlying the published results will be shared, including demographic variables, baseline characteristics, intervention allocation, platelet counts, occurrence and severity of thrombocytopenia, antibiotic discontinuation, length of hospital stay, and adverse events. The study protocol, statistical analysis plan, blank informed consent form, clinical study report, data dictionary, and statistical analysis syntax will also be available. Direct identifiers, signed consent forms, and information that could reasonably identify participants will not be shared.

When the data will become available and for how long
Access will begin six months after publication of the main study results and will remain available for five years.

To whom data/document is available
Qualified researchers affiliated with recognized academic, healthcare, or scientific research institutions may request access to the data and documents.

Under which criteria data/document could be used
The data and documents may be used for replication of the study findings, secondary analyses, systematic reviews, or meta analyses after approval of a scientifically and ethically sound proposal. Applicants must provide their institutional affiliation, research proposal, analysis plan, and ethics approval when applicable. They must sign a data use agreement prohibiting participant reidentification, unauthorized use, and onward sharing. Proper acknowledgment and citation of the original study will be required.

From where data/document is obtainable
Requests should preferably be submitted by email to Mohamadreza Heidarzadeh, Infectious Diseases Resident, Department of Infectious Diseases, Shahid Sadoughi Hospital, Yazd, Iran, at mohamadrezaheidarzadeh0776@gmail.com. Postal correspondence may be sent to the Department of Infectious Diseases, Shahid Sadoughi Hospital, Ebne Sina Boulevard, Shahid Ghandi Boulevard, Safaieh, Yazd, Iran. Telephone: +98 35 38224000. The principal investigator may also be contacted at jamshidayatollahi@yahoo.com.

What processes are involved for a request to access data/document
The applicant must submit a written request including their name, institutional affiliation, research question, proposed analyses, requested variables, ethics approval when applicable, funding source, and conflicts of interest. Receipt of the request will be confirmed within seven working days. The research team will review the request within 30 working days and may request additional information. If approved, a data use agreement will be signed and the requested files will be transferred securely within 15 working days after completion of the agreement. The reason for rejection will be communicated to the applicant.

Comments
All shared participant data will be coded and deidentified. Access will be limited to the approved applicants, purposes, variables, and access period. The participant identification key and signed consent forms will remain confidential and will not be shared. Data sharing will be subject to the approved informed consent form and applicable ethics committee requirements.