Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

Comparative study of the effect of immunotherapy with hydroxychloroquine and vitamin D3 compared to vitamin D3 alone in patients with recurrent miscarriage

Protocol summary

Study aim

Comparison of the results of using a combination of hydroxychloroquine and vitamin D3 compared to vitamin D alone on live birth in women with a history of recurrent miscarriage

Design

The clinical trial will be conducted in a controlled, double-blind, randomized, phase 2 and 3, parallel-group design on 80 eligible subjects. The sealed envelope method will be used for randomization.

Settings and conduct

Eligible women aged 18–40 years at Imam Reza and Ghaem hospitals in Mashhad will be divided into two groups after randomization: Intervention group: 200 mg of hydroxychloroquine every 12 hours + 1000 units of vitamin D3 daily from 6 to 20 weeks of pregnancy. Control group: Routinely receive 1000 units of vitamin D3 daily. Examinations will be performed by ultrasound. The study is double-blind, and the assessors and analysts are unaware of the groups.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Women aged 18 to 40 years, trying to conceive, with at least 2 consecutive first-trimester miscarriages of unknown origin, a normal parental karyotype, no uterine abnormalities, serum vitamin D level 30 to 100, and consent to participate in the study. Exclusion criteria: Pregnancy at entry or normal pregnancy after the last miscarriage, antiphospholipid syndrome (persistent positive APL + Myakis criteria), contraindications for hydroxychloroquine or vitamin D, other chronic diseases, history of epilepsy or psychotic disorders, recent use of hydroxychloroquine or vitamin D in the past two months.

Intervention groups

Control group: A group of 40 people is eligible for inclusion and receives 1000 units of oral vitamin D3 daily. Intervention group: A group of 40 people is eligible for inclusion and receives 200 mg of oral hydroxychloroquine twice daily, every 12 hours, along with 1,000 units of oral vitamin D3 daily.

Main outcome variables

Frequency of ongoing pregnancy

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20250507065634N3**
Registration date: **2025-08-24, 1404/06/02**
Registration timing: **prospective**

Last update: **2025-08-24, 1404/06/02**
Update count: **0**

Registration date

2025-08-24, 1404/06/02

Registrant information

Name

mahnaz shafaei fallah

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone

+98 915 930 0704

Email address

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2025-09-17, 1404/06/26

Expected recruitment end date

2025-11-21, 1404/08/30

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

Scientific title
Comparative study of the effect of immunotherapy with hydroxychloroquine and vitamin D3 compared to vitamin D3 alone in patients with recurrent miscarriage

Public title
Comparing the effect of immunotherapy with hydroxychloroquine and vitamin D3
Purpose
Prevention
Inclusion/Exclusion criteria
Inclusion criteria:
Women between the ages of 18 and 40 Women who are trying to conceive Women with a history of at least two consecutive first-trimester miscarriages of unknown origin, with normal parental karyotype, absence of uterine abnormalities associated with recurrent miscarriage Normal serum vitamin D levels (above 30) and less than 100 Consent to participate in the study
Exclusion criteria:
Pregnancy at the time of study entry Normal pregnancy since last miscarriage Antiphospholipid syndrome with persistently positive APL antibodies and the presence of clinical conditions of APS based on Myakis criteria Known contraindications for the use of hydroxychloroquine or vitamin D Other chronic diseases History of epilepsy or psychotic disorders History of recent use of hydroxychloroquine or vitamin D in the past two months
Age
From **18 years** old to **40 years** old
Gender
Female

Phase
2-3
Groups that have been masked

- Care provider
- Outcome assessor
- Data analyser

Sample size
Target sample size: **80**
Randomization (investigator's opinion)
Randomized
Randomization description
Experimental and control groups: After selecting the sample, in the next step, people are divided into experimental and control groups using a random method. How to perform randomization: First step: After selecting the voluntary sample, all selected people are placed on a list (numbers from one to 80 are assigned to people). Second step: From these individuals, a random method is used to divide them into two experimental groups and a control group, using sealed and opaque (numbered) envelopes. Each person randomly selects an envelope and is divided into the corresponding group.
Blinding (investigator's opinion)
Double blinded
Blinding description
The study was double-blind. Participants were assigned to groups using sealed, opaque envelopes containing an allocation code (A and B). These envelopes were opened as individuals arrived, and each participant's unique code was recorded. The main study coordinator was responsible for maintaining the allocation list and did not interfere with the assessment or care process. Participants and caregivers were unaware of their assigned group. Information about the type of possible intervention, medications, and possible drug side effects was explained to participants, and consent was obtained from participants. The outcome assessors also only saw the participant identification code and did not have access to information about the groups. The intervention and control packages were identical in appearance and packaging to prevent their identification.
Placebo
Used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Research Ethics Committees of Imam Reza Hospital Educational, Research and Treatment Center-Mashhad
Street address
Basement Floor (-1), Educational Complex Building, Imam Reza Hospital, Mashhad, Khorasan Razavi, Iran
City
Mashhad
Province
Razavi Khorasan
Postal code
9137913316
Approval date
2025-08-04, 1404/05/13
Ethics committee reference number
IR.MUMS.IRH.REC.1404.111

Health conditions studied

1

Description of health condition studied
Recurrent Pregnancy Loss
ICD-10 code
O26.2
ICD-10 code description
Pregnancy care for patient with recurrent pregnancy loss

2

Description of health condition studied
Spontaneous abortion
ICD-10 code
O03
ICD-10 code description
Spontaneous abortion

Primary outcomes

1

Description
Frequency of ongoing pregnancy
Timepoint
Week 20 onwards
Method of measurement
Ultrasound

Secondary outcomes

1

Description
Repeated miscarriage
Timepoint
Before week 20
Method of measurement
Fetal loss before 20 weeks with Ultrasound

2

Description
Gestational age at the time of miscarriage
Timepoint
Number of weeks of pregnancy
Method of measurement
Ultrasound

3

Description
Fetal abnormalities
Timepoint
Weeks 6-8, 11-13, 18-22 of pregnancy
Method of measurement
Ultrasound

Intervention groups

1

Description
Control group: They will receive oral vitamin D3 1000 units daily after a positive pregnancy test and confirmation of intrauterine pregnancy with serial pregnancy tests or vaginal ultrasound until the 20th week of pregnancy. Ultrasound will be performed at 6-8, 11-13, and 18-22 weeks of pregnancy.
Category
Placebo

2

Description
Intervention group: Receive oral hydroxychloroquine 200 mg twice daily every 12 hours along with oral vitamin D3 1000 units daily after a positive pregnancy test and confirmation of intrauterine pregnancy with serial titration of pregnancy test or vaginal ultrasound until the 20th week of pregnancy. Ultrasound will be performed at 6-8 weeks, 11-13 weeks, and 18-22 weeks of pregnancy.
Category
Diagnosis

Recruitment centers

1

Recruitment center
Name of recruitment center
Imam Reza Hospital
Full name of responsible person
Salman Soltani
Street address
Imam Reza Educational, Research and Treatment Center, Imam Reza Hospital Square, Avicenna (Ibn Sina) Street, Mashhad, Khorasan Razavi, Iran
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2

Recruitment center
Name of recruitment center
Ghaem Hospital
Full name of responsible person
Mostafa Dastan
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Qaem Hospital, Ahmadabad Street, Mashhad, Khorasan Razavi, Iran
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
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Full name of responsible person
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Research Affairs Management, Central Building, Mashhad University of Medical Sciences, Daneshgah Street, Mashhad, Khorasan Razavi, Iran
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RAMResearch@mums.ac.ir
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
Shaghayegh Jahantigh
Position
Resident
Latest degree
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Other areas of specialty/work
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Person responsible for updating data

Contact
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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

Demographic data and the main outcome results of the research can be shared after de-identification and preserving the privacy of individuals.

When the data will become available and for how long

Data can be made available 4 months after the results are published and after personally identifiable information is removed.

To whom data/document is available

The study data and documentation will be available to researchers and scholars working at reputable academic and scientific institutions.

Under which criteria data/document could be used

Research data and documentation may be used for scientific and research purposes. Users must undertake to keep non-identifiable data confidential.

From where data/document is obtainable

If you need data, please contact jahantigh.sh71@gmail.com

What processes are involved for a request to access data/document

After receiving and reviewing the request from the researcher, the request will be responded to as soon as possible.

Comments