Clinical Trial Protocol
Iranian Registry of Clinical Trials

18 Sep 2026

The effect of probiotics on fertility in women with recurrent implantation failure based on Th1 to Th2 ratio

Protocol summary

Study aim

Determining the effect of probiotics on fertility in women with recurrent implantation failure based on Th1 to Th2 ratio.

Design

Before administering the drug, heparinized blood is taken from the patients, and PBMC are isolated. Then, flow cytometry technique will be used to count the number of Th1 and Th2 cells. In order to investigate the secretion of cytokines, ELISA will be used. QRT-PCR method will be used to measure transcription factors. After performing these steps according to the protocol, the probiotic dose (2 tablets per day) is adjusted based on the ratio of Th1 to Th2. At this stage and after the treatment protocol, all the factors that were measured before prescribing the drug will be measured again to determine the effects of the probiotic drug on the immune system of the patients. Finally, after 9 months, in order to check the number of babies born by people with RIF, we will continuously monitor the people whose β-HCG test was positive after taking the medicine with the help of gynecologists.

Settings and conduct

The study will be conducted in Valiasr International Hospital, Tabriz. Subjects will receive probiotic pills according to the protocol.

Participants/Inclusion and exclusion criteria

Patients will be selected only from Azerbaijan people. Patients who have experienced at least 3 consecutive implantation failures.

Intervention groups

The studied groups are including 3 groups of patients with RIF who receive probiotics, patients who do not receive any type of treatment despite the history of RIF problem as a control group and a group of healthy women with a history of successful pregnancy and delivery are also considered as a control group.

Main outcome variables

The frequency of Th1 and Th2 cells The expression level of cytokines (IL-4, IL-10,IFNγ ,TNFα) and transcription factors (T-bet و GATA3) Secretory levels of cytokines (IL-4, IL-10,IFNγ ,TNFα) Pregnancy rate

General information

Reason for update

Acronym

RIF

IRCT registration information

IRCT registration number: **IRCT20160422027520N20**
Registration date: **2023-01-23, 1401/11/03**
Registration timing: **prospective**

Last update: **2023-01-23, 1401/11/03**
Update count: **0**

Registration date

2023-01-23, 1401/11/03

Registrant information

Name

Mehdi Yousefi

Name of organization / entity

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2023-02-20, 1401/12/01

Expected recruitment end date

2024-08-22, 1403/06/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

The effect of probiotics on fertility in women with recurrent implantation failure based on Th1 to Th2 ratio

Public title

The effect of probiotics on fertility

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Patients from East Azerbaijan Having at least three implantation failures Do not have any type of immunotherapy in their medical history. Having regular menstrual cycles

Exclusion criteria:

Patients under 18 years old and over 41 years old Patients with coagulation problems. Patients with intrauterine anomalies. Having chromosomal abnormalities

Age

From **18 years** old to **40 years** old

Gender

Female

Phase

2

Groups that have been masked

- Participant
- Data analyser

Sample size

Target sample size: **50**

Randomization (investigator's opinion)

Randomized

Randomization description

At first, the sample size of 50 patients with RIF that met our inclusion criteria was considered as the total sample size. 'Random allocation rule' method was used for randomization, where numbers were randomly assigned to cards on a random order of one to 50. Even numbers were assigned to the treatment group and odd numbers to the control group (who did not receive any treatment). In this method, the balance will be reached at the end of the study in the number of people assigned to each group. Each card was placed in sealed and opaque envelopes to hide the random assignment.

Blinding (investigator's opinion)

Double blinded

Blinding description

The participants and the person who analyzed the results were blinded in this study. Participants were aware of the study before being randomized and informed consent was obtained from them. It should be noted that the person analyzing the results had no other role in this study.

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Tabriz University of Medical Sciences

Street address

Tabriz University of Medical Sciences , Daneshghah st, Tabriz,

City

Tabriz

Province

East Azarbaijan

Postal code

6446-14155

Approval date

2023-01-21, 1401/11/01

Ethics committee reference number

IR.TBZMED.REC.1401.798

Health conditions studied

1

Description of health condition studied

Recurrent implantation failure

ICD-10 code

N98.9

ICD-10 code description

Complication associated with artificial fertilization, unspecified

Primary outcomes

1

Description

The frequency of Th1 and Th2 cells

Timepoint

Before and after interference

Method of measurement

By using flow cytometry

2

Description

Investigating the expression level of transcription factors T-bet and GATA3

Timepoint

Before and after interference

Method of measurement

By using Quantitative Real time PCR

3

Description
Examining the expression level of cytokines IL-4, IL-10, IFNγ, TNFα
Timepoint
Before and after interference
Method of measurement
By using Quantitative Real time PCR

4

Description
Investigating the secretion of cytokines IL-4, IL-10, IFNγ, TNFα
Timepoint
Before and after interference
Method of measurement
using sandwich ELISA method.

Secondary outcomes

1

Description
Pregnancy rate
Timepoint
After positive beta-hCG test, clinical pregnancy was evaluated at 5-6 week
Method of measurement
Examining the formation of gestational sac using Sonography method

Intervention groups

1

Description
Intervention group: probiotic tablets (2 tablets per day) orally
Category
Treatment - Drugs

2

Description
Control group: receive no intervention
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Infertility center at Valiasr Hospital
Full name of responsible person
Dr. Mehdi Yousefi
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Sponsors / Funding sources

1

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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
Tabriz 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
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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