

Clinical Trial Protocol

Iranian Registry of Clinical Trials

20 Jun 2026

The effect of peripheral blood mononuclear cells (PBMC) on pregnancy outcomes in patients with recurrent implantation failure (RIF): randomized control trial study

Protocol summary

Study aim

Investigation the effect of Intrauterine administration of autologous hCG- activated peripheral blood mononuclear cells (PBMC) on pregnancy outcomes in patients with recurrent implantation failure (RIF)

Design

This study is a double-blind, randomized control trial with parallel groups, that the sample size allocated to each group is equal. Each patient was first immunologically advised to receive treatment, and after flow cytometry tests were selected if they were eligible. The patient selected would then, after completing the informed consent form, took a random envelope from the box containing the envelopes and gave it to the scientist.

Settings and conduct

This study was conducted in Valiasr Hospital, Tabriz. The participants and data analyzer were blinded. After patients selection, blood sampling was done five days before embryo transfer. Then PBMCs were isolated using Ficol. PBMCs were administered into the uterine cavity after culturing 48 hours in the presence of hCG. PBS was inseminated in the control group as a placebo.

Participants/Inclusion and exclusion criteria

The target population in this study was 100 women less than 45 years old who experienced at least three repeated implantation failures and lower Th-17 to Treg ratio than the healthy women.

Intervention groups

There were 50 women in the treatment group who received intrauterine administration of PBMCs two days before embryo transfer (ET) and another 50 patients in the control group who received an intrauterine injection of PBS as placebo.

Main outcome variables

Pregnancy rate Live birth rate Miscarriage rate

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT2017081227520N8**

Registration date: **2017-09-15, 1396/06/24**

Registration timing: **prospective**

Last update: **2019-08-21, 1398/05/30**

Update count: **1**

Registration date

2017-09-15, 1396/06/24

Registrant information

Name

Mehdi Yousefi

Name of organization / entity

Department of Immunology, Faculty of Medicine,
Tabriz University of Medical Sciences, Tabriz, Iran

Country

Iran (Islamic Republic of)

Phone

+98 41 3336 4665

Email address

yousefime@tbzmed.ac.ir

Recruitment status

Recruitment complete

Funding source

Stem Cell And Regenerative Medicine Institute, Tabriz
University of Medical Sciences, Tabriz, Iran

Expected recruitment start date

2017-09-23, 1396/07/01

Expected recruitment end date

2018-05-22, 1397/03/01

Actual recruitment start date

2017-10-07, 1396/07/15

Actual recruitment end date

2018-09-25, 1397/07/03

Trial completion date

2018-09-27, 1397/07/05

Scientific title

The effect of peripheral blood mononuclear cells (PBMC) on pregnancy outcomes in patients with recurrent implantation failure (RIF): randomized control trial study

Public title

PBMC-therapy and treatment of recurrent implantation failure (RIF)

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Having at least three implantation failures after IVF
Having primary infertility Age under 45 years old
Having regular menstrual cycles BMI under 30

Exclusion criteria:

Having polycystic ovarian syndrome The presence of uterine pathology; Poor ovarian reserve
Having chromosomal abnormalities Presence of auto anti-bodies such as anti-TPO, anti-TG, ACA, APA, ANA, and anti-dsDNA
Presence of mutations involving the coagulation system such as deficiency of factor XII, Pro C, Pro S
Positive HIV, HCV or HBV tests

Age

From **20 years** old to **45 years** old

Gender

Female

Phase

1-2

Groups that have been masked

- Participant
- Data analyser

Sample size

Target sample size: **100**

Actual sample size reached: **100**

Randomization (investigator's opinion)

Randomized

Randomization description

At first, the sample size of 100 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 100. Even numbers were assigned to the treatment group and odd numbers to the placebo group. 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 opaqued 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

Used

Assignment

Parallel

Other design features

From 248 volunteer patients, after immunologic consultation and flow cytometry analysis, 100 women were finally selected. These 100 patients were randomly divided into two groups: 50 patients for intrauterine injection of PBMC activated by hCG before embryo transfer (ET) and 50 patients as control group undergoing intrauterine insemination of phosphate buffer saline (PBS) as a placebo before ET. One hundred healthy women were selected as the healthy control group for the selection of enrolled women

Secondary Ids**1****Registry name**

-WWW.clinicaltrial.gov

Secondary trial Id

-NCT03267797

Registration date

2017-08-30, 1396/06/08

Ethics committees**1****Ethics committee****Name of ethics committee**

Ethics committee of Tabriz University of Medical Sciences

Street address

Tabriz University of Medical Sciences , Daneshgah st, Tabriz,

City

Tabriz

Province

East Azarbaijan

Postal code

6446-14155

Approval date

2018-01-01, 1396/10/11

Ethics committee reference number

IR.TBZMED.REC.1396.937

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

Pregnancy rate

Timepoint

After positive beta-hCG test, clinical pregnancy was evaluated at 5-6 week

Method of measurement

Laboratory tests and ultrasound

Secondary outcomes

empty

Intervention groups

1

Description

Intervention group: blood sampling was done (20ml) five days before embryo transfer. Then PBMCs were isolated by Ficol and 20-30 million cells were cultured 48 hours in the presence of hCG. After 48 hours, 15-20 million PBMCs in 500 microliters PBS was administered into the uterine cavity two days before embryo transfer using embryo transfer catheter.

Category

Treatment - Other

2

Description

Control group: Similar to study group, blood sampling was done in this group but only 500 microliters PBS two days before embryo transfer was injected into uterine cavity.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Infertility center at Valiasr Hospital

Full name of responsible person

Dr. Mehdi Yousefi

Street address

Infertility center at Valiasr Hospital, Aflak-nama Sq, Zaferaniyeh Ave, Tabriz

City

Tabriz

Province

East Azarbaijan

Postal code

6446-14155

Phone

+98 41 3327 3000

Email

mehdi_yusefi@yahoo.com

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Stem Cell And Regenerative Medicine Institute, Tabriz University of Medical Sciences

Full name of responsible person

Mehdi Yousefi

Street address

Stem Cell And Regenerative Medicine Institute, Madani Hospital, Golbad Ave, Tabriz

City

Tabriz

Province

East Azarbaijan

Postal code

6446-14155

Phone

+98 41 3334 9525

Email

mehdi_yusefi@yahoo.com

Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

Stem Cell And Regenerative Medicine Institute, 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

Other

Person responsible for general inquiries

Contact

Name of organization / entity

Stem Cell And Regenerative Medicine Institute

Full name of responsible person

Mehdi Yousefi

Position

PhD in Medical Immunology

Latest degree

Ph.D.

Other areas of specialty/work

Immunology

Street address

Stem Cell And Regenerative Medicine Institute, Madani Hospital, Golbad Ave, Tabriz

City

Tabriz
Province
East Azarbaijan
Postal code
6446-14155
Phone
+98 41 3336 4665
Fax
Email
mehdi_yusefi@yahoo.com
Web page address

Person responsible for scientific inquiries

Contact

Name of organization / entity
Stem Cell And Regenerative Medicine Institute
Full name of responsible person
Mehdi Yousefi
Position
PhD in Immunology
Latest degree
Ph.D.
Other areas of specialty/work
Immunology
Street address
Stem Cell And Regenerative Medicine Institute,
Madani Hospital, Golbad Ave, Tabriz
City
Tabriz
Province
East Azarbaijan
Postal code
6446-14155
Phone
+98 41 3336 4665
Fax
Email
mehdi_yusefi@yahoo.com
Web page address

Person responsible for updating data

Contact

Name of organization / entity
Tabriz University of Medical Sciences

Full name of responsible person
Zahra Pourmoghadam
Position
MSc in Immunology
Latest degree
Master
Other areas of specialty/work
Immunology
Street address
Department of Immunology, Faculty of Medicine,
Tabriz University of Medical Sciences, Tabriz, Iran
City
Tabriz
Province
East Azarbaijan
Postal code
6446-14155
Phone
00
Fax
Email
Zahrapourmoghadam92@gmail.com
Web page address

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