

Clinical Trial Protocol

Iranian Registry of Clinical Trials

31 May 2026

Intradermal lymphocyte therapy in recurrent pregnancy loss patients with immunologic abnormalities

Protocol summary

Study aim

This study investigates the immunomodulatory effects of intradermal lymphocyte therapy in patients with RPL with immunological abnormalities such as imbalance of immune system cells including Treg and Th17, as well as other immunological parameters such as transcription factors related to these cells. Changes in the cytokine production and microRNAs involved in their function compared to before treatment will be examined in this study.

Design

200 patients with RPL with immunological disorders are randomly divided into two groups of 100, one group will receive intradermal lymphocyte therapy and other group will not receive intervention.

Settings and conduct

Tabriz Valiasr Hospital

Participants/Inclusion and exclusion criteria

After receiving informed consent from people with RPL and also a control group consisting of healthy and fertile women with a history of successful previous pregnancies, heparinized blood is taken and mononuclear blood cells are isolated. Flow cytometry technique will then be used to count the number of T reg, Th-17, NK and B cells. The results of flow cytometry studies will be compared, and 200 patients with RPL with immunological disorders and 100 people as a healthy control group will be included in this study. The group of 200 patients with RPL was randomly divided into two groups of 100, one group receiving lymphocyte therapy and the other group not receiving treatment.

Intervention groups

According to the standard protocol, 2×10^7 of the husband's lymphocytes will be injected subcutaneously on the forearm or arms of patients with recurrent miscarriages. The number of injections is three times and at intervals of one month.

Main outcome variables

Immunological parameters such as Treg and Th17 cell

frequency, gene and protein expression of Foxp3 and RORyt, gene expression of cytokines and the expression of microRNAs, including mir-146a, mir-155 and mir-326.

General information

Reason for update

Acronym

RPL

IRCT registration information

IRCT registration number: **IRCT20160422027520N19**

Registration date: **2021-10-12, 1400/07/20**

Registration timing: **prospective**

Last update: **2021-10-12, 1400/07/20**

Update count: **0**

Registration date

2021-10-12, 1400/07/20

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

Expected recruitment start date

2021-10-22, 1400/07/30

Expected recruitment end date

2022-05-20, 1401/02/30

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Intradermal lymphocyte therapy in recurrent pregnancy loss patients with immunologic abnormalities

Public title

Intradermal injection of lymphocytes in recurrent pregnancy loss patients

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Having at least three consecutive abortions Having regular menstrual cycles BMI of people below 30 Have no uterine pathology Our patients will be selected only from Azerbaijan. Patients were selected whose semen analysis and DNA fragmentation test were normal.

Exclusion criteria:

Patients under the age of 18 and over 40 years Patients who themselves or their spouse have abnormal karyotypes or genetic or chromosomal abnormalities. Patients with chronic underlying disease who have to take certain medications. Patients with intrauterine anomalies. Having polycystic ovary syndrome Patients who test positive for HIV, HCV or HBV

Age

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

Gender

Both

Phase

1-2

Groups that have been masked

- Participant
- Data analyser

Sample size

Target sample size: **200**

Randomization (investigator's opinion)

Randomized

Randomization description

At first, the sample size of 200 patients with RPL 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 200. 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**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

5166614766

Approval date

2021-10-06, 1400/07/14

Ethics committee reference number

IR-TBZMED.REC.1400.597

Health conditions studied**1****Description of health condition studied**

Recurrent Pregnancy Loss(RPL)

ICD-10 code**ICD-10 code description****Primary outcomes****1****Description**

Frequency of Treg and Th17 cells

Timepoint

Before and after the intervention

Method of measurement

Flow cytometry

2**Description**

Gene expression levels of Foxp3 and RORyt

Timepoint

Before and after the intervention

Method of measurement

Real-time PCR

3

Description

Protein expression levels of Foxp3 and RORyt

Timepoint

Before and after the intervention

Method of measurement

Western blot

4

Description

Gene expression levels of IL-10, IL-17, IL-21, IL-23, TGF- β

Timepoint

Before and after the intervention

Method of measurement

Real-time PCR

5

Description

Secretion levels of IL-10, IL-17, IL-21, IL-23, TGF- β

Timepoint

Before and after the intervention

Method of measurement

ELISA

6

Description

Gene expression levels of mir-146a , mir-155 , mir-326

Timepoint

Before and after the intervention

Method of measurement

real-time PCR

Secondary outcomes

empty

Intervention groups

1

Description

Intervention group: The group of 200 patients with recurrent miscarriage was randomly divided into two groups of 100, one group receiving lymphocyte therapy and the other group not receiving treatment. Is injected. According to the standard protocol, 2 × 10⁷ of husband's lymphocytes are injected subcutaneously into patients with recurrent miscarriages. The number of injections is three times and at intervals of one month.

Category

Treatment - Other

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, Zafarianiyeh Ave, Tabriz

City

Tabriz

Province

East Azarbaijan

Postal code

5166614766

Phone

+98 41 3327 3000

Email

mehdi_yusefi@yahoo.com

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Tabriz University of Medical Sciences

Full name of responsible person

Mehdi Yousefi

Street address

Stem Cell Research Center, Tabriz University of Medical Sciences, Tabriz

City

Tabriz

Province

East Azarbaijan

Postal code

5166614766

Phone

+98 41 3334 9525

Email

mehdi_yusefi@yahoo.com

Web page address

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

Tabriz University of Medical Sciences

Full name of responsible person

Mehdi Yousefi

Position

PhD in Medical Immunology

Latest degree

Ph.D.

Other areas of specialty/work

Immunology

Street address

Tabriz University of Medical Sciences , Daneshgah st, Tabriz,

City

Tabriz

Province

East Azarbaijan

Postal code

5166614766

Phone

+98 41 3336 4665

Email

mehdi_yusefi@yahoo.com

Person responsible for scientific inquiries

Contact

Name of organization / entity

Tabriz University of Medical Sciences

Full name of responsible person

Mehdi Yousefi

Position

PhD in Immunology- Associate professor

Latest degree

Ph.D.

Other areas of specialty/work

Immunology

Street address

Tabriz University of Medical Sciences , Daneshgah st, Tabriz,

City

Tabriz

Province

East Azarbaijan

Postal code

5166614766

Phone

+98 41 3336 4665

Email

mehdi_yusefi@yahoo.com

Person responsible for updating data

Contact

Name of organization / entity

Tabriz University of Medical Sciences

Full name of responsible person

Sanam Dolati

Position

Assistant Professor of Immunology

Latest degree

Ph.D.

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

5166614766

Phone

00

Email

sanam.dolati@gmail.com

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