Clinical Trial Protocol
Iranian Registry of Clinical Trials

30 Jun 2026

Evaluation of the effects of endometrial scratching on angiogenic and anti-angiogenic growth factors expression in unexplained repeated implantation failure (uRIF) patients

Protocol summary

Study aim

Determining the effect of endometrial scratching on the expression of angiogenic and anti-angiogenic growth factors

Design

A randomized clinical trial with control group, double blind, and two arm parallel group design of 20 patients. Randomization is performed using a computer-generated random assignment schedule for each patient. Sealed and numbered envelopes are used to conceal the treatment allocation until randomization.

Settings and conduct

Using a pipelle, endometrial scratching is performed by a gynecologist only in the intervention group in the clinic. In this study, the participating patients (creating the same conditions) and the researcher (through sample coding) will be blinded.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Women with Unexplained repeated implantation failure(uRIF), 20 to 40 years, Body max index less (BMI) than 25, good response to previous ovulation stimulation, at least two embryos with good grade in the current cycle, normal uterus. Exclusion criteria: Endometrial thickness is less than 7 mm, congenital anomalies,myoma,endometrioma, adhesions, hydrosalpinx, previous uterine or ovarian surgery, severe male factor infertility, number of embryos less than 2 in the current cycle, diabetes, thyroid disease, any endocrine, genetic, infection or autoimmune disorder

Intervention groups

Intervention: In the intervention group, endometrial sampling is obtained twice by Pipelle [one in the follicular phase and the last in the luteal phase of the same cycle preceding the embryo transfer cycle. Control group: In the control group endometrial sampling will be done only in the luteal phase of the cycle preceding the embryo transfer cycle.

Main outcome variables

Determination of angiogenic and anti-angiogenic growth factor gene expression in endometrial specimens in the intervention group compared with the control group

General information

Reason for update

According to the previous report, the actual recruitment end date of hospitalization is the same as 01/26/1401, and the only date of trial completion date is according to the examination of clinical pregnancy (5 weeks after embryo transfer) and live birth (9 months of pregnancy)in the participant's plan has increased. In addition, according to the evaluation of the secondary variables of implantation rate and clinical pregnancy, the variables related to them that are evaluated are added. A little rewriting has been done in the way the inclusion and exclusion criteria are expressed.

Acronym

IRCT registration information

IRCT registration number: **IRCT20210316050723N1**
Registration date: **2021-07-12, 1400/04/21**
Registration timing: **registered_while_recruiting**

Last update: **2024-01-27, 1402/11/07**
Update count: **4**

Registration date

2021-07-12, 1400/04/21

Registrant information

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Samaneh Aghajanpour

Name of organization / entity

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Recruitment status
Recruitment complete
Funding source

Expected recruitment start date
2021-06-20, 1400/03/30
Expected recruitment end date
2023-06-20, 1402/03/30
Actual recruitment start date
2021-06-20, 1400/03/30
Actual recruitment end date
2022-04-15, 1401/01/26
Trial completion date
2023-01-21, 1401/11/01

Scientific title
Evaluation of the effects of endometrial scratching on angiogenic and anti-angiogenic growth factors expression in unexplained repeated implantation failure (uRIF) patients

Public title
Evaluation of the effects of endometrial scratching on angiogenic and anti-angiogenic growth factors
Purpose
Other
Inclusion/Exclusion criteria
Inclusion criteria:
Infertile women with unexplained repeated implantation failure (unknown definite causes of RIF) failed to conceive after three or more embryo transfer cycles using high-quality transferred embryos (at least one blastocyst ET cycle) Age of 20 to 40 years Body mass index (BMI) less than 25 kg/m2 Good response to stimulation of previous ovulation Having at least two embryos with good grade normal uterus results of hysterosalpingography (HSG) or hysteroscopy Participant consent was required to join in the study and to complete the consent form
Exclusion criteria:
The thickness of the endometrium on the day of Human chorionic gonadotropin hormone injection is less than 7 mm Women with congenital anomalies, intramural and subserosal myomas(larger than 5 cm) Submucosal myoma Women with endometrioma larger than or equal to 3 cm With adhesions With hydrosalpinx Have previous uterine or ovarian surgery Severe male factor infertility (sperm extraction from the testis, sperm freezing, sperm DNA fragmentation index equal to or above 16%) Patients with any specific medication If the number of available embryos is less than 2 in the current cycle Women with endometrial tuberculosis and those undergoing tuberculosis treatment Have a history of diabetes, thyroid disease, any endocrine, genetic, infection or autoimmune disorder Abnormal Pre-implantation Genetic Test (PGT) Results Any specific medication Failure to return the patient to prepare an endometrial sample Women with severe pain during obtaining of tissue samples or the possibility of infection
Age
From **20 years** old to **40 years** old
Gender
Female

Phase
2
Groups that have been masked

- Participant
- Investigator

Sample size
Target sample size: **20**
Actual sample size reached: **20**
Randomization (investigator's opinion)
Randomized
Randomization description
Consecutive sampling until the required sample size is reached. Women by Balanced Block Randomization method are randomly divided into 2 equal groups of 10 people (intervention group and control group). Block randomization method is designed by epidemiologist using STATA software version 13 and the number of blocks considered is 4. Envelopes are prepared for 20 people and inside each envelope is written the group in which the patient should be placed. The envelopes are prepared in a way that the writing inside is not clear. A nurse before the patient enters the operating room, removes the envelope and sends the patients in one of the two groups.
Blinding (investigator's opinion)
Double blinded
Blinding description
In this study, a doctor scratches the endometrium in the intervention group on days 8-11. The biopsy specimen is prepared in the luteal phase of the same cycle during days 19-23 by the same doctor or other. Therefore, in this study, it is not possible to blind the doctor. In order to blind the patients participating in this study, all the conditions will be the same between the two groups, so the patients of the control group also referred to the center on the day of the scratching (8-11) and due to the blinding of the study, all the sampling steps were done except endometrial scratching will be done for the control group as well as the intervention group. Then, biopsy samples are prepared from both groups in the luteal phase on days 19-23. The endometrial biopsy sample of both groups is sent to the laboratory, which does not know whether the tissue sample received is for the intervention group or the control group, and only checks it based on the received code (blinding of the researcher).
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Research Ethics Committees of school of medicine
Street address
Tehran, Hemmat Highway next to Milad Tower, Iran University of Medical Sciences
City
Tehran
Province
Tehran
Postal code
۱۴۴۹۶۱۴۵۳۵
Approval date
2021-06-12, 1400/03/22
Ethics committee reference number
IR.IUMS.FMD.REC.1400.147

Health conditions studied

1

Description of health condition studied
Unexplained repeated implantation failure (uRIF)
ICD-10 code
N97.9
ICD-10 code description
Female infertility, unspecified

Primary outcomes

1

Description
Evaluation of gene expression
Timepoint
In the endometrial sample obtained in the luteal phase during days 19-23
Method of measurement
Using PCR Array method and based on the copy number

Secondary outcomes

1

Description
Clinical pregnancy
Timepoint
5 weeks after embryo transfer
Method of measurement
Vaginal ultrasonography (observing the gestational sac and fetal heart rate)

2

Description
Implantation
Timepoint
5 weeks after embryo transfer
Method of measurement
The number of observed sacs divided by the number of transferred embryos

3

Description
Total dose of gonadotropin (IU)
Timepoint
From ovarian stimulation to human chorionic gonadotropin (hCG) injection
Method of measurement
The number of international units (IU) received during the ovarian stimulation cycle

4

Description
Duration of ovarian stimulation (day)
Timepoint
From the start of gonadotropin administration to human chorionic gonadotropin (hCG) injection
Method of measurement
According to the patient's monitoring ultrasound chart (number of days receiving the medicine)

5

Description
Number of retrieved oocytes
Timepoint
On the day of oocyte pick-up
Method of measurement
The number of retrieved oocytes reported in the embryology chart

6

Description
Metaphase II oocytes
Timepoint
On the day of oocyte pick-up
Method of measurement
Based on the presence of the polar body reported by the embryologist

7

Description
Number of embryos
Timepoint
Three or five days after oocyte pick-up
Method of measurement
The number of cleavage embryos reported by the embryologist

8

Description
Embryo transfer cancelation
Timepoint
Three or five days after oocyte pick-up
Method of measurement
Participants with no embryo transfer

9

Description
Chemical pregnancy rate/Embryo transfer
Timepoint
2 weeks after embryo transfer
Method of measurement
Beta human chorionic gonadotropin (beta hCG) titer in blood serum by ELISA method

10

Description
Blighted ovum/Embryo transfer
Timepoint
5 weeks after embryo transfer
Method of measurement
Absence of fetus in gestational sac according to ultrasound report

11

Description
Ectopic pregnancy/Embryo transfer
Timepoint
5 weeks after embryo transfer
Method of measurement
According to the ultrasound report, there is a gestational sac outside the uterus with a positive Beta hCG titer

12

Description
Miscarriage rate/Embryo transfer
Timepoint
Pregnancy loss before 20 weeks
Method of measurement
Excretion of pregnancy remnants with vaginal bleeding (absence of heartbeat according to ultrasound report)

13

Description
Multiple Pregnancy (Twin)
Timepoint
5 weeks after embryo transfer
Method of measurement
Ultrasound report based on the number of gestational sacs with embryo

14

Description
Live birth rate/Embryo transfer
Timepoint
Time of delivery
Method of measurement
Birth of a live baby

15

Description
Fertilization rate
Timepoint
The day after the sperm injection
Method of measurement
number of oocytes with two pronuclei (2PN) divided by the number of injected oocytes

Intervention groups

1

Description
Intervention group: In the intervention group, endometrial sampling is obtained twice by Pipelle [one in the follicular phase (during 8-11 days and the last in the luteal phase (during 19-23 days) preceding the embryo transfer cycle. The endometrial scratching is induced with pipelle.
Category
Treatment - Other

2

Description
Control group: In the control group endometrial sampling will be done only in the luteal phase of the cycle preceding the embryo transfer cycle.
Category
Treatment - Other

Recruitment centers

1

Recruitment center
Name of recruitment center
Laleh Hospital
Full name of responsible person
Mehrdad Bakhtiyari
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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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Grant name

Grant code / Reference number

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

Title of funding source
Iran 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
Iran University of Medical Sciences

Full name of responsible person
Mehrdad Bakhtiyari

Position
Assistant professor

Latest degree
Ph.D.

Other areas of specialty/work
Anatomy

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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
Undecided - It is not yet known if there will be a plan to make this available

Clinical Study Report

Yes - There is a plan to make this available

Analytic Code

Not applicable

Data Dictionary

Not applicable

Title and more details about the data/document

Clinical study report (published article)

When the data will become available and for how long

After the publication of the article

To whom data/document is available

Available to the public

Under which criteria data/document could be used

Scientific use by citing the source

From where data/document is obtainable

Dr. Mehrdad Bakhtiyari

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

Request via e-mail

Comments