Clinical Trial Protocol
Iranian Registry of Clinical Trials

09 Jun 2026

Molecular evaluation of endometrium obtained from women with repeated implantation failure (RIF) after endometrial injury in compare to women without endometrial injury

Protocol summary

Study aim

Molecular evaluation of endometrium obtained from women with repeated implantation failure (RIF) after endometrial injury in compare to women without endometrial injury

Design

A randomized clinical trial with control group, double blind, 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

Female infertility Clinic of ROYAN institute.

Participants/Inclusion and exclusion criteria

- less thsn 40 years old - Patients had history of 3 failed consecutive cycles of IVF / ICSI. - Patients were good responders in prior ovulation induction cycle. - There were at least two embryos with grade A in each embryo transfer cycle. - Normal uterus in Hysterosalpingography (HSG) or ultrasound or hysteroscopy scans. - The minimum thickness of the endometrium is 7 mm in injection day.

Intervention groups

ntervention: Endometrial injury In the intervention group, endometrial sampling is obtained twice by Pipelle [one in the follicular phase (during 8-9 or 11- 13 day in the beginning of buserelin cycle) and the last in the luteal phase (during 19-21 or 20-23 day) of the same cycle preceding the embryo transfer cycle. No Intervention: Control In the control group endometrial sampling will be done only in the luteal phase (during 19-21 or 20-23 day) of the cycle preceding the embryo transfer cycle.

Main outcome variables

Determination of cytokine and chemokine genes expression in endometrial specimens in the intervention group (with local endometrial abrasion) compared with the control group (without local endometrial abrasion)

General information

Reason for update

Acronym

RIF-Injury

IRCT registration information

IRCT registration number: **IRCT20080831001141N28**
Registration date: **2020-11-25, 1399/09/05**
Registration timing: **retrospective**

Last update: **2020-11-25, 1399/09/05**
Update count: **0**

Registration date

2020-11-25, 1399/09/05

Registrant information

Name
Kiandokht Kiani
Name of organization / entity
Royan Institute
Country
Iran (Islamic Republic of)
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kiandokht.kiani@royaninstitute.org

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2014-06-30, 1393/04/09

Expected recruitment end date

2016-06-29, 1395/04/09

Actual recruitment start date

2014-06-30, 1393/04/09

Actual recruitment end date
2020-09-09, 1399/06/19
Trial completion date
2020-09-09, 1399/06/19

Scientific title
Molecular evaluation of endometrium obtained from women with repeated implantation failure (RIF) after endometrial injury in compare to women without endometrial injury

Public title
Molecular evaluation of endometrium after endometrial injury
Purpose
Other
Inclusion/Exclusion criteria
Inclusion criteria:
Infertile women with repeated implantation failure (RIF) refers to cases in which women have had three failed in vitro fertilization (IVF) attempts with good quality embryos.
Exclusion criteria:
Women with Sub mucosal myoma Women with Intramural and subserosal myomas larger than 5 cm Women with Endometrioma larger than or equal to 3 cm Women with Hydrosalpinx If the number of available embryos is less than 2 in the current cycle Women with endometrial tuberculosis and those undergoing tuberculosis treatment. Patients with any specific medication Patients with a history of thyroid disease, diabetes and other hormonal disorders and diseases Failure to return the patient to prepare an endometrial sample Inability to obtain tissue samples from patients due to severe pain or the possibility of infection
Age
From **18 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 8-9 or 11-13. The biopsy specimen is prepared in the luteal phase of the same cycle during days 19-21 or 20-23 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 conditions will be the same between the two groups, so patients in the control group also referred to the center on the day of scratching (on days 8-9 or 11-13) and due to the blindness of the study, all sampling steps except scratching The endometrium will be performed for the control group as well as the intervention group. The endometrial biopsy specimen of both groups is transferred to the Laboratory, which also does not know information about whether the tissue sample received is for the intervention or control group and examines it only based on the received code (researcher blindness).
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

1

Registry name
مرکز ثبت کارآزمائي هاي باليني ايالات متحده آمريکا (www.clinicaltrial.gov)
Secondary trial Id
NCT02480127
Registration date
2015-06-24, 1394/04/03

Ethics committees

1

Ethics committee
Name of ethics committee
Ethics Committee of Royan Institute
Street address
Royan Institute, Number 12, East Hafez Avenue, Banihashem Street, Resalat Highway.
City
Tehran
Province
Tehran
Postal code
148- 16635
Approval date
2014-08-12, 1393/05/21
Ethics committee reference number
EC/93/1070

Health conditions studied

1

Description of health condition studied
repeated implantation failure (RIF)
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 19-21 or 20-23
Method of measurement
Using PCR Array method and based on the copy number

Secondary outcomes

1

Description
clinical pregnancy rate
Timepoint
Only once; 6 weeks after embryo transfer.
Method of measurement
Vaginal ultrasound

Intervention groups

1

Description
Intervention group: In the intervention group, endometrial sampling is obtained twice by Pipelle [one in the follicular phase (during 8-9 or 11- 13 day in the beginning of buserelin cycle) and the last in the luteal phase (during 19-21 or 20-23 day) preceding the embryo transfer cycle.The endometrial injury which 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
Infertility Center of ROYAN
Full name of responsible person
Mahnaz Ashrafi
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Royan Institute, Number 12, East Hafez Avenue, Banihashem Street, Resalat Highway.
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
ROYAN Institute
Full name of responsible person
Parvaneh Afsharian
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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
ROYAN Institute
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
ROYAN Institute

Full name of responsible person
مهناز اشرفی

Position
Professor

Latest degree
Subspecialist

Other areas of specialty/work
Gynecology and Obstetrics

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is 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
Not applicable

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. Mahnaz Ashrafi

What processes are involved for a request to access data/document
Request via e-mail

Comments