Clinical Trial Protocol
Iranian Registry of Clinical Trials

10 Jun 2026

Effect of adding long-acting GnRH agonist plus Letrozole to endometrial preparation method with Estradiol on pregnancy outcome in frozen embryo transfer cycles among women with recurrent implantation failure: A clinical trial

Protocol summary

Study aim

Determining the effect of adding long-acting GnRH agonist plus Letrozole to endometrial preparation method with estradiol on pregnancy outcome in frozen embryo transfer cycles among women with recurrent implantation failure.

Design

Phase 3 clinical trial is with two parallel groups and the sample size is 64 people. Randomization will be done using random allocation1 software. Block randomization method will be done. Blinding will not be done.

Settings and conduct

Clinical trial is random and without blinding. In Yazd Reproductive Research Center, 64 infertile women referred to this center who had a history of at least two repeated implantation failures despite quality A and B embryo transfer, were randomly divided into control group and case group. Blinding was not performed in this study.

Participants/Inclusion and exclusion criteria

Infertile 18 to 42 years old women with a history of at least two implantation failure of good quality embryos (A and B) who are candidate for frozen thawed embryo transfer cycle. Male factors are normal and the patient has no anomalous problems, no adenomyosis, no ectopic endometriosis.

Intervention groups

The control group just receive 6 mg of Estradiol valerate daily from the second day of the menstrual cycle. Patients in the case group will receive a monthly dose of Triptorelin 3.75 for up to two months plus 5 mg of Letrozole daily, and immediately after the end of two months of treatment they will enter the freeze embryo transfer cycle and start taking 6 mg of estradiol daily. In both groups, transvaginal sonography is performed on day 13 of the menstrual cycle, and after reaching an endometrial thickness of at least 7 mm, 400 mg of vaginal Progesterone twice daily with 6 mg of estradiol daily for three days until the day of embryo transfer will consume.

Main outcome variables

Chemical and clinical pregnancy rate, chemical abortion

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20220104053629N1**
Registration date: **2022-02-13, 1400/11/24**
Registration timing: **prospective**

Last update: **2022-02-13, 1400/11/24**
Update count: **0**

Registration date

2022-02-13, 1400/11/24

Registrant information

Name

Sara Naghibzadeh

Name of organization / entity

Country

Iran (Islamic Republic of)

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+98 35 3824 7085

Email address

sara_naghib848@yahoo.com

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2022-02-19, 1400/11/30

Expected recruitment end date

2022-07-21, 1401/04/30

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Effect of adding long-acting GnRH agonist plus Letrozole to endometrial preparation method with Estradiol on pregnancy outcome in frozen embryo transfer cycles among women with recurrent implantation failure: A clinical trial

Public title

Effect of adding long-acting GnRH agonist plus Letrozole to frozen embryo transfer cycles

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

18 to 42 years old infertile women The history of at least two implantation failure of good quality embryos (A and B) Frozen thawed embryo transfer cycle Candidate for embryo transfer with A and B grade

Exclusion criteria:

Severe male factor or sperm retrieval except ejaculation Endometriosis in previous sonography or laparascopy Severe adenomiosis in sonography History of myoma surgery or any interfering myoma with implantatio History of implantation failure because of thin endometrium

Age

From **18 years** old to **42 years** old

Gender

Female

Phase

3

Groups that have been masked

No information

Sample size

Target sample size: **64**

Randomization (investigator's opinion)

Randomized

Randomization description

Randomization of samples in the two groups will be done using permutation block method using Random allocation 1 software. 8 blocks with a size of 8 samples are considered. For allocation concealment, sealed envelopes for each person is used.

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Yazd Reproductive Institute, Shahid Sadoughi University of medical sciences

Street address

Bouali Ave, Safaeiyeh

City

Yazd

Province

Yazd

Postal code

8916877391

Approval date

2021-12-19, 1400/09/28

Ethics committee reference number

IR.SSU.RSI.REC.1400.022

Health conditions studied

1

Description of health condition studied

Female infertility

ICD-10 code

N97

ICD-10 code description

Female infertility

Primary outcomes

1

Description

Rate of chemical pregnancy

Timepoint

2 weeks after embryo transfer

Method of measurement

pregnancy blood test

Secondary outcomes

1

Description

Rate of clinical pregnancy

Timepoint

4 weeks after embryo transfer

Method of measurement

Seeing gestational sac in sonography

2

Description

Rate of chemical abortion

Timepoint
4 weeks after embryo transfer
Method of measurement
Positive pregnancy blood test without gestational sac

Intervention groups

1

Description
Control group: This group just receive 6 mg of Estradiol valerate daily from the second day of the menstrual cycle. Transvaginal sonography is performed on day 13 of the menstrual cycle, and after reaching an endometrial thickness of at least 7 mm, 400 mg of vaginal Progesterone twice daily with 6 mg of estradiol daily for three days until the day of embryo transfer will consume.
Category
Treatment - Drugs

2

Description
Intervention group: Patients in the case group will receive a monthly dose of Triptorelin 3.75 for up to two months plus 5 mg of Letrozole daily, and immediately after the end of two months of treatment they will enter the freeze embryo transfer cycle and start taking 6 mg of estradiol daily. Transvaginal sonography is performed on day 13 of the menstrual cycle, and after reaching an endometrial thickness of at least 7 mm, 400 mg of vaginal Progesterone twice daily with 6 mg of estradiol daily for three days until the day of embryo transfer will consume.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Yazd Research and Clinical Center for Infertility
Full name of responsible person
Behnaz Gandom
Street address
Bouali ave, Safaeiyeh
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Web page address

Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Yazd University of Medical Sciences
Full name of responsible person
Amir Houshang Mehrparvar
Street address
Bahonar Square, Central Building of Yazd Shahid Sadoughi University of Medical Sciences
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Yazd
Province
Yazd
Postal code
8916978477
Phone
+98 35 3726 3733
Email
dvc.research@ssu.ac.ir
Web page address
http://ssu.ac.ir/cms
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Yazd 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
Yazd University of Medical Sciences
Full name of responsible person
Razieh Dehghani Firoozabadi
Position
Professor
Latest degree
Subspecialist
Other areas of specialty/work
Gynecology and Obstetrics
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Person responsible for updating data

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Latest degree
Medical doctor
Other areas of specialty/work
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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
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
Yes - There is a plan to make this available
Analytic Code
No - There is not a plan to make this available
Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available
Title and more details about the data/document
All participant data sets are to be shared.
When the data will become available and for how long
2 months after the result publication.
To whom data/document is available
A journal in which the results are published
Under which criteria data/document could be used
Submission of an official application via the agent that is legally in charge
From where data/document is obtainable
Yazd Reproductive Sciences Institute, Bouali Ave, Yazd, Iran. yazd-rsi@ssu.ac.ir
What processes are involved for a request to access data/document
Request from the Research Deputy, submitted to the Research Council of the Center if the request accepts its referral to the security and after completion of the relevant forms, the request is referred to the research experts and then get the data.
Comments