Clinical Trial Protocol
Iranian Registry of Clinical Trials

28 Jul 2026

Investigating the effect of estradiol administration duration on pregnancy outcomes of frozen embryo transfer cycles: a double-blind randomized clinical trial

Protocol summary

Study aim

Determining the effectiveness of estradiol treatment duration

Design

219 women who applied for the transfer of gynecological freeze, referring to the infertility treatment center and meeting the conditions for entering the study, will be included; From the second or third day of the menstrual cycle, estradiol is given orally at a dose of 4 to 6 mg; After one week, people will go for the first transvaginal ultrasound to get the thickness of the endometrium. If the thickness of the endometrium is 7 or more and suitable, they will be divided into three groups of 73 people in a double-blind manner. Each person will be placed in one of the groups by one of the randomization methods (combination of random number table and random block method). Selection of blocks will be done using a table of random numbers. Finally, cards will be prepared according to the number of patients, and the type of treatment is specified in these cards. The size of the block and the number of blocks are for the masked therapist and they will not know

Settings and conduct

This study is carried out in the infertility treatment center of Zainab Hospital in Shiraz. In this study, both patients and doctors will be blind; Patients know the type of intervention, but they do not know the characteristics of the groups.

Participants/Inclusion and exclusion criteria

Patients under 45 years of age with at least two embryos of good quality in the stage of cleavage or blastocyst for transfer and with a healthy uterine cavity that has been confirmed by hysterosalpingograph and hysteroscopy or saline ultrasound

Intervention groups

• This study includes 3 groups of 73 people, in the first group, progesterone is started from day 8-11 of receiving estradiol, in the second group, from day 12-14 of receiving estradiol, and in the third group, from day 15-18 of receiving.

Main outcome variables

Biochemical and clinical pregnancy rates

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20220906055898N1**
Registration date: **2022-09-28, 1401/07/06**
Registration timing: **registered_while_recruiting**

Last update: **2022-09-28, 1401/07/06**
Update count: **0**

Registration date

2022-09-28, 1401/07/06

Registrant information

Name

Ameneh Keshavarz

Name of organization / entity

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2022-09-22, 1401/06/31

Expected recruitment end date

2022-11-21, 1401/08/30

Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Investigating the effect of estradiol administration duration on pregnancy outcomes of frozen embryo transfer cycles: a double-blind randomized clinical trial

Public title
Comparing the effectiveness of estradiol administration on endometrial thickness and pregnancy outcome in infertile women applying for frozen embryo transfer
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
• Patients under 45 years of age • Normal BMI • Patients with at least two good quality embryos for transfer • Patients with a healthy uterine cavity confirmed by hysterosalpingograph and hysteroscope or saline ultrasound
Exclusion criteria:
Patients with Uncontrolled Chronic Disease Patients with Donated Ovum or Embryos Patients with surrogacy Patients who Could Not Achieve an Endometrial Thickness of 7 to 10 mm Patients with More Than Three Unsuccessful Transplants (RIF) Poor Responder Patients with Endometriosis Patients with Adenomyosis Patients whose Embryos are the Result of TESE or Severe male PGD candidate patients
Age
From **20 years** old to **45 years** old
Gender
Female

Phase
3
Groups that have been masked

- Participant
- Care provider

Sample size
Target sample size: **219**
Randomization (investigator's opinion)
Randomized
Randomization description
In this study, firstly, the samples were selected based on the conditions for entering the study and based on the purpose, from among the women referring to the infertility treatment center of Hazrat Zainab (PBUH) who referred to transfer their frozen embryos using the easy sampling method and in available are selected. After that, the researcher obtains the informed consent form by referring to the selected people and introducing himself and briefly stating the type of study and the objectives of the study; Then the women participating in the study are randomly assigned to three short-term, medium-term and long-term intervention groups. All patients are included in the study voluntarily and with the knowledge of random assignment of the intervention. It will be explained to all participants before the start of the study that they will be randomly divided into three intervention groups: short-term (A), medium-term (B) and long-term (C) to randomly divide the samples using the random block allocation method. Bandi is used. In this trial, we will have three groups of 6 blocks (including 2 people participating in drug group A, 2 people participating in drug group B, and 2 people participating in drug group C). The randomization tool is also used from random sequence generation software (random allocation software), which in addition to simple randomization, these random sequence generation software are capable of generating random sequence by block method. The randomization process is done by the study methodology consultant and the clinical researchers are not aware of the randomization process. For concealment, we use Concealment Allocation, which refers to the method used to perform a random sequence on the participants in the study, in such a way that the allocated group is not known before the allocation of the individual. By using sealed opaque letter envelopes with a random sequence (Sequentially numbered, seale, opaque envelopes (, in this method, each of the random sequences created is recorded on a card and the cards are placed inside the letter envelopes in order. In order to maintain a random sequence, the outer surface of the envelopes is numbered in the same order. Finally, the lid of the letter envelopes is glued and placed in a box. At least one week after starting estradiol and when the thickness of the endometrium is 7 or higher; Participants, based on the order of entry of eligible participants into the study, one of the envelopes will be opened and the assigned group of that participant will be revealed.
Blinding (investigator's opinion)
Double blinded
Blinding description
In this study, after selecting the patients, none of the sample will know about the randomization and allocation process to the groups, and the patients will not have contact with each other and will be visited at separate times. Doctors are given envelopes with coded numbers in advance and patients are entered into study groups in the order of the envelope numbers. Therefore, the present study is double-blind. After receiving estradiol from the second or third day of the menstrual cycle for one week, the patients are divided into three groups receiving progesterone: A- from day 8-11 B- from day 12-14 C- from day 15-18. The doctor who performs the embryo transfer on the day of the end of receiving progesterone does not know which group the patients are in, and only the supervisor of this proposal manages the day of the transfer
Placebo
Not used
Assignment
Other
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics Committee of Shiraz University of Medical Sciences

Street address
شیراز - خیابان زند - ساختمان مرکزی دانشگاه علوم پزشکی شیراز

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Shiraz

Province
Fars

Postal code
3478671946

Approval date
2022-07-31, 1401/05/09

Ethics committee reference number
IR.SUMS.REC.1401.342

Health conditions studied

1

Description of health condition studied
Infertility

ICD-10 code
N97

ICD-10 code description
Female infertility

Primary outcomes

1

Description
• Biochemical and clinical pregnancy rates

Timepoint
• 2 weeks after embryo transfer

Method of measurement
• By doing the B-HCG test• By transvaginl sonography

Secondary outcomes

1

Description
pregnancy

Timepoint
• 2 weeks after embryo transfer

Method of measurement
• By transvaginl sonography

Intervention groups

1

Description
Intervention group: All patients are given oral estradiol at a dose of 4 to 6 mg from the second or third day of the menstrual cycle, and after a week, the patients return for the first transvaginal ultrasound to measure the thickness of the endometrium; If the thickness of the endometrium is 7 and above, and suitable, they are divided into three groups in the form of two blind strains.

Category
Treatment - Drugs

2

Description
Intervention group: In the first intervention group, from day 8-11 of receiving estradiol, after measuring the level of estradiol, if there is a suitable response, progesterone is started, and then the embryos are transferred in the cleavage or blastocyst stage.

Category
Treatment - Drugs

3

Description
Intervention group: In the second intervention group, from day 12-14 of receiving estradiol, after measuring the level of estradiol, if there is a suitable response, progesterone is started, and then the embryos are transferred in the cleavage or blastocyst stage.

Category
Treatment - Drugs

4

Description
Intervention group: In the third intervention group, from day 15-18 of receiving estradiol, after measuring the level of estradiol, if there is a suitable response, progesterone is started, and then the embryos are transferred in the cleavage or blastocyst stage.

Category
Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center
Zeinabiyyeh Hospital infertility Clinic

Full name of responsible person
Ameneh Keshavarzi

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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?
No
Title of funding source
Shiraz 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
Shiraz University of Medical Sciences
Full name of responsible person
Ameneh Keshavarzi
Position
Infertility Fellowship
Latest degree
Specialist
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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