Clinical Trial Protocol
Iranian Registry of Clinical Trials

03 Jul 2026

Comparison of freeze embryo transfer cycle results in modified natural cycle versus hormone replacement therapy

Protocol summary

Study aim
Comparison of freeze embryo transfer cycle results in modified natural cycle versus hormone replacement therapy

Design
An open-label, randomized clinical trial study with parallel groups and phases 3 on 150 patients.Randomization will be done according to block randomization method using Random allocation software.

Settings and conduct
This study will be conducted on 150 patients referred to the infertility clinic of Al-Zahra Hospital with frozen embryos for embryo transfer without blinding.

Participants/Inclusion and exclusion criteria
Patients will be included in the study, aged between 20 and 39 years, if they have regular periods and a history of one unsuccessful transfer, if no cysts are seen in the ovary, and if they have congenital anomalies of the uterus, fibroids or any intrauterine lesions, severe endometriosis. And previous history of unsuccessful transfer more than twice and endometrial thickness less than 7.5 mm will be prohibited from entering the study.

Intervention groups
. Estradiol tablets will be ordered in HRT group and 10 -12 days later, trans vaginal ultrasonography will be performed and if endometrial thickness ≥7.5 mm, progesterone will be added to regimen. Embryos in cleavage stage will be transferred in the uterus on the fourth day of progesterone administration. Luteal phase support will be provided with 400 mg progesterone suppository twice a day and 50 mg injectable progesterone once every two days.In condition of visible mature follicle in ovary and endometrial thickness ≥7.5 and serum progesterone ≤ 1.5 ng/ml, 5000-unit HCG will be administrated and in the fifth day, embryo in cleavage stage will be transferred to uterus. Progesterone suppository (400 mg) will be administrated for luteal phase support.

Main outcome variables
Successful pregnancy has been considered as the main outcome of this study.

General information

Reason for update
Acronym
IRCT registration information
IRCT registration number: **IRCT20130603013566N11**
Registration date: **2023-03-12, 1401/12/21**
Registration timing: **prospective**

Last update: **2023-03-12, 1401/12/21**
Update count: **0**

Registration date
2023-03-12, 1401/12/21

Registrant information

Name
Kobra Hamdi
Name of organization / entity
Tabriz University of Medical Sciences
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Recruitment status
Recruitment complete
Funding source

Expected recruitment start date
2023-03-16, 1401/12/25
Expected recruitment end date
2024-03-15, 1402/12/25
Actual recruitment start date
empty

Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Comparison of freeze embryo transfer cycle results in modified natural cycle versus hormone replacement therapy

Public title
Comparison of two methods of estrogen and progesterone hormone administration and endometrial preparation in normal ovarian cycle in endometrial preparation for embryo transfer.
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Age between 20 and 39 years Having regular periods History of one failed transfer
Exclusion criteria:
Congenital uterine anomalies Uterine fibroids Severe endometriosis Previous history of failed transfer more than twice Endometrial thickness less than 7.5 mm
Age
From **20 years** old to **39 years** old
Gender
Female

Phase
3
Groups that have been masked
No information
Sample size
Target sample size: **150**
Randomization (investigator's opinion)
Randomized
Randomization description
Patients will be divided into intervention and control groups using block randomization based on generated numbers by Random allocation software. Thus, in this software, first the number of groups and the total number of the sample size will be entered, and then in the block section, the Block randomization method will be implemented. Patients will be allocated to intervention or control groups based on generated numbers.
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 Tabriz University Of Medical Sciences
Street address
Third Floor; Central Building of Number2; Golgasht Street
City
Tabriz
Province
East Azarbaijan
Postal code
5166616471
Approval date
2023-03-06, 1401/12/15
Ethics committee reference number
IR.TBZMED.REC.1401.1081

Health conditions studied

1

Description of health condition studied
Infertility
ICD-10 code
N97.0
ICD-10 code description
Female infertility associated with anovulation

Primary outcomes

1

Description
Chemical pregnancy
Timepoint
14 days after embryo transfer
Method of measurement
HCG β blood test

2

Description
Number of gestational sacs
Timepoint
From week 5 of pregnancy
Method of measurement
Vaginal ultrasound

Secondary outcomes

1

Description
Fetal growth
Timepoint
From the beginning of the intervention to the end of

pregnancy

Method of measurement

Ultrasound

Intervention groups

1

Description

In the patients of the intervention group, where the preparation of the endometrium will be done by the administration of estrogen and progesterone hormones (artificial or HRT), the 2 mg estradiol pill will start from the second day of the menstrual cycle. On the second and third day, one number every 12 hours and then one number every 8 hours.10 to 12 days after taking estradiol, the next visit will be done and the thickness of the endometrium will be measured by transvaginal ultrasound. If the thickness of the endometrium is equal to or higher than 7.5 mm, injectable progesterone with a dose of 50 mg will be started, first one and then two daily.On the fourth day of starting progesterone, the transfer will be done.Luteal phase support will be done with 400 mg rectal progesterone suppositories every 12 hours and 50 mg progesterone ampoules every three days. In the 10th to 12th day visit, if the thickness of the endometrium is less than 7.5 mm, estradiol will be continued with the same dose or, if needed, higher doses, and the patient will be visited 3 to 4 days later and the endometrial examination will be repeated with ultrasound, and this work will be repeated until reaching The endometrium will continue to be 7.5 mm or more thick.If the thickness of the endometrium does not increase after a maximum of 20 days of taking estradiol, the treatment cycle will be stopped and the patient will be excluded from the study. The information related to the interrupted cycles will be mentioned in the results, but it will not be included in the examination of the results of the embryo transfer cycles.

Category

Treatment - Drugs

2

Description

Control group:In the control group, the endometrium preparation method will be modified with a normal menstrual cycle.On the first to third day of the menstrual cycle, the patient will be visited and transvaginal ultrasound will be performed.Patients will be visited again on the 10th to 12th day of the menstrual cycle and the size of the ovarian follicles and the thickness of the endometrium will be evaluated with transvaginal ultrasound.If the follicle is 17 mm or larger, the ampoule and the thickness of the endometrium is higher than 7.5 mm and the serum progesterone is below 1.5 nanograms/ml, the HCG ampoule will be prescribed with a dose of 5000 units.If there is no dominant follicle of 17 mm or larger, re-visit every 1-2 days will continue until the mentioned results are achieved.If the desired results are not achieved, the cycle will be canceled up to 20 days, and if the serum progesterone level is higher than 1.5 ng/ml on the 10-12 day visit, the embryo transfer cycle will be stopped due to the impossibility of detecting the exact time of ovulation. became .The day of HCG injection is considered as day zero. From the second day, 400 mg progesterone suppository or 50 mg progesterone ampoule will be prescribed to the patient once a day. And on the fifth day, 2 grade A embryos will be transferred to the uterus in the cleavage stage. Luteal phase support will continue with one 400 mg rectal suppository. 14 days after the embryo transfer, a pregnancy test will be performed, and if pregnancy is achieved, two weeks later, an ultrasound will be performed to check the pregnancy status.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Alzahra Hospital

Full name of responsible person

Kobra Hamdi

Street address

Alzahra Hospital, South Artesh St.,Tabriz, iran

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Vice chancellor for Research,Tabriz University Of Medical Sciences

Full name of responsible person

Dr.Mohammad Samiei

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No. 2 Central Building,Tabriz University of Medical Sciences, Golgasht Street, Tabriz

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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
Vice chancellor for Research,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
Kobra Hamdi

Position
Associate Professor of Obstetrics Gynecology

Latest degree
Subspecialist

Other areas of specialty/work
Gynecology and Obstetrics

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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