Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Jun 2026

Comparison of sildenafil and isorbid effects on embery transfer outcome in patients with recurrent implantation failure

Protocol summary

Study aim
1. Evaluation of implantation ،endometrial thickness and pregnancy in women with recurrent implant failure

Design
The trial has two intervention groups, double-blind, randomized, phase ۲ on 90 patients. Chi-square test will be used to compare clinical fertility and statistical analysis will be performed using SPSS.26 software.

Settings and conduct
IVF Clinic of Tabriz Al-Zahra Hospital Endometrial preparation begins with estradiol valerate tablets. In first group Simultaneously with estradiol،sildenafil 50 mg vaginally and in the second group isosorbide dinitrate 10 mg with estradiol is administered vaginally. After embryo transfer luteal phase support is provided with progesterone injections.The facilitator will be aware of the study groups, and the researcher, data collector, and data analyst will be blinded to the study groups.

Participants/Inclusion and exclusion criteria
Patients with a history of infertility and twice implantation failure will be included in the study with consent Exclusion criteria 1. Treatment with antihypertensive drugs 2. Myoma, adenomyosis, congenital malformation of the uterus, endometriosis 3. History of cardiovascular or kidney or liver disease or the use of nonsteroidal anti-inflammatory drugs and any chronic disease 3. Reluctance to participate in the study

Intervention groups
Endometrial preparation begins with estradiol valerate tablets at a dose of 4 mg and increases to 6 mg per day after 3 days. In the first group, in addition to standard treatment, isosorbide dinitrate 10 mg vaginal tablets (group 1) at the same time as estradiol It is started and continued for one day before embryo transfer. In the other group (group II), sildenafil 50 mg tablets daily are prescribed from the day of estradiol onset until one day before embryo transfer.

Main outcome variables
Endometrial thickness examination, BHCG titer examination pregnancy

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20110301005942N8**
Registration date: **2021-11-15, 1400/08/24**
Registration timing: **registered_while_recruiting**

Last update: **2021-11-15, 1400/08/24**
Update count: **0**

Registration date
2021-11-15, 1400/08/24

Registrant information

Name
Aliye Ghasemzadeh

Name of organization / entity
Tabriz University of Medical Sciences

Country
Iran (Islamic Republic of)

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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2021-08-29, 1400/06/07

Expected recruitment end date
2022-08-29, 1401/06/07

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
Comparison of sildenafil and isorbid effects on embery transfer outcome in patients with recurrent implantation failure

Public title
Comparison of sildenafil and isorbid effects on embery transfer outcome in patients with recurrent implantation failure

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
15 to 40 years Patients with a history of double implantation failure who have at least 2 frozen embryos for transfer will be included in the study with consent.

Exclusion criteria:
1.Treatment with hypertension drugs 2.Myoma, adenomyosis, congenital malformations of the uterus, endometriosis 3.History of cardiovascular or renal or liver disease or use of nonsteroidal anti-inflammatory drugs and any chronic disease Reluctance to participate in the study

Age
From **15 years** old to **40 years** old

Gender
Female

Phase
2

Groups that have been masked

- Participant
- Investigator
- Outcome assessor
- Data analyser

Sample size
Target sample size: **90**

Randomization (investigator's opinion)
Randomized

Randomization description
In this study, there will be two intervention groups. Assignment of patients to study groups after their arrival will be done using closed letter envelopes with numbers 1 to the maximum sample size on the envelopes and AB groups in the envelopes and written in them and mixed randomly. . After the package is selected by the patient recipient, patients will be divided into desired groups.

Blinding (investigator's opinion)
Double blinded

Blinding description
The facilitator (supervisor) who is not involved in the collection and analysis of study data will be aware of the study groupings and the researcher, the data collector and the data analyzer will be blinded to the study groups. The subjects will not be aware of their behaviors during treatment. Patients will be assigned to study groups after their arrival using closed letter envelopes with numbers 1 to 90 on the envelopes and groups A and B written on the envelopes and mixed randomly. After the package is selected by the patient recipient, patients will be divided into desired groups. Envelopes will be arranged by the facilitator (supervisor) and study groups will be selected. Envelopes will be selected by the female resident. Envelopes will be numbered from number 1 to the end. The first person will be given the first envelope and this will continue until the last desired number, where 45 people will be in group A and 45 people in group B.

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
33357313

Approval date
2021-08-29, 1400/06/07

Ethics committee reference number
IR.TBZMED.REC.1400.503

Health conditions studied

1

Description of health condition studied
Infertility

ICD-10 code
N97.1

ICD-10 code description
Female infertility of tubal origin

Primary outcomes

1

Description
evaluation of endometrial thickness

Timepoint
The initial evaluation of endometrial thickness is performed on day 1 to 3 and then 10 days later.

Method of measurement

Trans vaginal sonograghy

2

Description
BHCG titer examination
Timepoint
Chemical pregnancy 2 weeks after embryo transfer
Method of measurement
Chemical pregnancy with BHCG

Secondary outcomes

1

Description
Clinical pregnancy
Timepoint
4 weeks after embryo transfer
Method of measurement
Trans vaginal sonography

Intervention groups

1

Description
Intervention group 1: Intervention group 1. For patients on day 1-3 of the menstrual cycle, vaginal ultrasound is performed and in the absence of ovarian cysts and space-occupying lesions in the uterine cavity, the standard treatment required for endometrial preparation is started. Endometrial preparation with 4 mg estradiol valerate tablets The gram starts and increases to 6 mg per day after 3 days. In the first group, at the same time as estradiol sildenafil is started, 50 mg daily is administered vaginally and fetal transfer is continued until the day before.
Category
Treatment - Drugs

2

Description
Intervention group 2: For patients on day 1-3 of the menstrual cycle, vaginal ultrasound is performed and in the absence of ovarian cysts and space-occupying lesions in the uterine cavity, the standard treatment required for endometrial preparation is started. Endometrial preparation begins with estradiol valerate tablets at a dose of 4 mg and increases to 6 mg per day after 3 days. In the second group, in addition to standard treatment, the administration of isosorbide dinitrate 10 mg vaginal tablets is started from the day of estradiol onset and continues until one day before embryo transfer. The initial ultrasound control for endometrial thickness is performed 10 days later.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Alzahra Hospital
Full name of responsible person
Aliyeh Ghasemzadeh
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Alzahra Hospital, South Artesh St.
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Tabriz University of Medical Sciences
Full name of responsible person
Mohammad Samei
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Third Floor, Central Building of Number2, Golgasht Street
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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
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
Dr. Aliye Ghasemzadeh
Position
Fellowship of Infertility
Latest degree
Subspecialist
Other areas of specialty/work
Gynecology and Obstetrics
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Golgasht Street, Tabriz University Of Medical Sciences
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Person responsible for scientific inquiries

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Person responsible for updating data

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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