Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Evaluation of effect of the autologous exosomes derived from menstrual blood mesenchymal cells on the ovarian reserve follicles and the rate of pregnancy in patients with Diminished Ovarian Reserve (DOR)

Protocol summary

Study aim
Evaluation the effect of exosomes derived from autologous menstrual blood stem cells on ovarian reserves and pregnancy rate

Design
Randomized controlled clinical trial phase 1-2, with parallel groups on 30 patients

Settings and conduct
This clinical trial will be performed on infertile women with DOR in infertility department in Imam Khomeini Hospital, Sari, Iran. Patients will be randomly assigned into two groups of control (IVF) and autologous exosomes derived from menstrual blood mesenchymal cells(Men-MCs). Collecting 5 ml of menstrual blood. Isolation, culture and identification (flow cytometry) of Men-MCs. Isolation of autologous exosomes (chromatography). Injection of autologous exosome. Assessment of outcomes.

Participants/Inclusion and exclusion criteria
Inclusion criteria:Patients aged 20-42 Years, Body mass index below 30, Diagnosed diminished ovarian reserve(DOR), Antral follicles below 7, Anti Mullerian Hormone below 1.1 nanogram per mililiter Exclusion criteria:Chronic malignancies, chronic pelvic pain, Infertility due to severe male factor, Obstruction of fallopian tubes

Intervention groups
Intervention group:Single intraovarian injection of 2 mililiter(ml) of autologous exosome with a total protein of 20 micrograms per microliter with a puncture needle under ultrasound guide Control group: Vaginal ultrasound during day 1-3 of cycle. Prescribing Follicle Stimulating Hormone(FSH) recombinant ampoule. Observing follicle above 12 millimeter(mm), initiating antagonist therapy. Observing follicle size 17-18 mm. Human Chorionic Gonadotropin(HCG) injection. Ovarian puncture. In vitro fertilization(IVF) of oocytes. Transfer of embryos in the hormonal cycle to the patient

Main outcome variables
Hormonal change, Ovarian follicle growth change, Oocyte quality change, Pregnancy, Live birth, Abortion

General information

Reason for update

Acronym

IRCT registration information
IRCT registration number: **IRCT20210228050535N1**
Registration date: **2022-02-27, 1400/12/08**
Registration timing: **registered_while_recruiting**

Last update: **2022-02-27, 1400/12/08**
Update count: **0**

Registration date
2022-02-27, 1400/12/08

Registrant information

Name
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Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2022-02-04, 1400/11/15

Expected recruitment end date
2022-05-22, 1401/03/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Evaluation of effect of the autologous exosomes derived from menstrual blood mesenchymal cells on the ovarian reserve follicles and the rate of pregnancy in patients with Diminished Ovarian Reserve (DOR)

Public title

Exosome therapy in infertility

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Patients aged 20-42 Years Body mass index (BMI) below 30 (kilograms per square meters) Diagnosed diminished ovarian reserve (DOR) Antral follicles below 7 Anti Mullerian Hormone (AMH) below 1.1 nanogram per mililiter (ng/ml) Premature ovarian insufficiency (POI) Unovulation or amnehorreha

Exclusion criteria:

Abnormal shape of the uterus on Hysterosalpingography (HSG) or hysteroscopy Hematologic or immunologic diseases Hormonal disturbances Chromosomal and genetics abnormalities Pregnant patients Obstruction of fallopian tubes on Hysterosalpingography or laparoscopy Patients affected by Thyroid disease Patients affected by diabetes Chronic malignancies Chronic pelvic pain Infertility due to severe male factor

Age

From **20 years** old to **42 years** old

Gender

Female

Phase

1-2

Groups that have been masked

No information

Sample size

Target sample size: **30**

Randomization (investigator's opinion)

Randomized

Randomization description

A random series of 30 individuals were produced for eligible patients. In each sequence, the intervention group with autologous exosome and the control group would be considered by a 1:1 ratio; thus, 15 patients will be allocated to each group. Random Sequence will be provided using Sealed Envelope web site with block size of 4.

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

Research Ethics Committees of Imam Hospital-Mazandaran University of Medical Sciences

Street address

Imam Hospital, Amir Mazandarani St, Imam Sq, Sari

City

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Province

Mazandaran

Postal code

4816633131

Approval date

2021-10-13, 1400/07/21

Ethics committee reference number

IR.MAZUMS.IMAMHOSPITAL.REC.1400.041

Health conditions studied

1

Description of health condition studied

Diminished ovarian reserve

ICD-10 code

N97.0

ICD-10 code description

Female infertility associated with anovulation

Primary outcomes

1

Description

Estradiol rate of change

Timepoint

2 weeks before injection and 1 to 3 months after injection

Method of measurement

ELISA diagnostic kit

2

Description

The ovarian follicle growth rate of change

Timepoint

2 weeks before injection and 1 to 3 months after injection

Method of measurement

Ultrasound

3

Description

Oocyte quality rate of change

Timepoint
2 weeks before injection and 1 to 3 months after injection
Method of measurement
Oocyte classification based on presence or absence of polar body and nucleolus

4

Description
Follicle Stimulating Hormone (FSH) rate of change
Timepoint
2 weeks before injection and 1 to 3 months after injection
Method of measurement
ELISA diagnostic kit

5

Description
Anti Mullerian Hormone (AMH) rate of change
Timepoint
2 weeks before injection and 1 to 3 months after injection
Method of measurement
ELISA diagnostic kit

Secondary outcomes

1

Description
Pregnancy rate
Timepoint
1 to 3 months after injection and 12 weeks after pregnancy
Method of measurement
Beta-Human Chorionic Gonadotropin(B HCG) test, Ultrasound

2

Description
Live newborn birth rate
Timepoint
9 to 12 months after injection
Method of measurement
Follow up

3

Description
Abortion rate
Timepoint
1 to 9 month after pregnancy
Method of measurement
Ultrasound, follow up

Intervention groups

1

Description
Intervention group: 5 mililiter of menstrual blood sample will be collected from patients with menstrual cup. Mesenchymal cells will be isolated and cultured from a menstrual blood sample. After culturing menstrual blood-derived mesenchymal cells, in the fifth passages, the cells will be identified by Flow cytometry.Then exosomes will be isolated from the culture medium by Chromatography. Intra-ovarian injection of autologous exosomes will be performed in the intervention group. On the day of injection (follicular phase of menstrual cycle until day 14) 2 mililiter (ml) of autologous exosome with 1 percent phosphate buffered saline(PBS) with a total protein of 20 micrograms per microliter will be injected into the ovary with a puncture needle from the cortex to the medulla in several areas under ultrasound guide.
Category
Treatment - Other

2

Description
Control group: For patients in the control group, the in vitro fertilization (IVF) cycle with antagonist will be performed, then after 1 to 3 months, the freeze embryo will be transferred. From day 1 to 3 cycles, vaginal ultrasound will be performed. FSH recombinant ampoule (2-4 pieces) will be prescribed. Then ultrasound is performed every other day and depending on the number and size of the follicle, Human Menopausal Gonadotropins (HMG) will be added or subtracted to the drugs.If a follicle above 12 millimeter (mm) is observed, the antagonist is started and will be prescribed daily. Whenever 17-18 millimeter (mm) follicle is observed, Human Chorionic Gonadotropin (HCG) is injected and an ovarian puncture will be performed 34-48 hours later, and the ovums will be delivered to a laboratory for in vitro fertilization. 1 to 3 months later, 1 to 3 grade A or B embryos will be transferred to the patient during the hormonal cycle.
Category
Treatment - Other

Recruitment centers

1

Recruitment center
Name of recruitment center
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Sponsors / Funding sources

1

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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
Mazandaran 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

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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