Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Evaluation of the effects of exosome therapy on the return of menstrual cycles and improvement of premature menopause symptoms in patients with premature ovarian failure (POF)

Protocol summary

Study aim
Evaluation of the therapeutic effects of stem cell exosomes on the return of the menstrual cycle and improvement of premature menopause symptoms in patients with premature ovarian failure (POF)

Design
This study is a randomized, single-blind, parallel-group clinical trial in which eligible participants are assigned to two groups of exosome and PRP in a 1:1 block randomization with variable block sizes using a sequence generated by statistical software. Allocation concealment is performed through opaque, sealed, and numbered envelopes. The study sample size is 18 people, divided equally between the two groups.

Settings and conduct
Location: Fatemeh Hospital, Hamadan. Participants: Premature ovarian failure (POF) patients with informed consent. Grouping: Randomized into two groups: exosome and PRP. Blinding: Single-blind; assessors and data analysts are blinded.

Participants/Inclusion and exclusion criteria
Inclusion criteria: definite POF/POI (high FSH, low estradiol), adequate ovarian reserve (AFC), informed consent. Exclusion criteria: genetic/chromosomal causes (Turner, mutations), active autoimmune diseases, hormonal cancers, or severe systemic diseases.

Intervention groups
Intervention group: Intraovarian injection of mesenchymal stem cell-derived exosomes (MSC-Exosomes). These exosomes are prepared from Wharton's gel mesenchymal cells and are injected by a gynecologist in an infertility clinic. Control group: Intraovarian injection of platelet-rich plasma (PRP). This group serves as an "active placebo" or "alternative standard of care" for comparison with exosomes and is administered in the same manner as the intervention group.

Main outcome variables
Return of menstrual cycle - spontaneous or clinical pregnancy

General information

Reason for update
Acronym
IRCT registration information
IRCT registration number: **IRCT20251118068036N2**
Registration date: **2026-05-16, 1405/02/26**
Registration timing: **registered_while_recruiting**

Last update: **2026-05-16, 1405/02/26**
Update count: **0**

Registration date
2026-05-16, 1405/02/26

Registrant information
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Recruitment status
recruiting
Funding source

Expected recruitment start date
2026-05-13, 1405/02/23
Expected recruitment end date
2027-05-13, 1406/02/23
Actual recruitment start date
empty

Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Evaluation of the effects of exosome therapy on the return of menstrual cycles and improvement of premature menopause symptoms in patients with premature ovarian failure (POF)

Public title
Effects of exosomes on premature menopause and return of menstruation in POF patients
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Definitive diagnosis of POF/POI: High FSH levels (usually greater than 25 or 40 IU/L on two occasions one month apart) and low estradiol levels. Ovarian reserve: The presence of a minimum number of antral follicles (AFC) on ultrasound. informed consent
Exclusion criteria:
Genetic or chromosomal causes: The presence of syndromes such as Turner Syndrome or specific mutations that are the main cause of ovarian failure. Underlying diseases: Active autoimmune diseases, hormone-dependent cancers, or severe systemic diseases (heart, kidney, liver).
Age
From **25 years** old to **40 years** old
Gender
Female

Phase
2
Groups that have been masked

- Outcome assessor

Sample size
Target sample size: **18**
Randomization (investigator's opinion)
Randomized
Randomization description
In this study, participants will be assigned to two intervention (exosome) and control (PRP) groups using a 1:1 block randomization. To avoid predictability of allocation, blocks of variable size (4 and 6) will be used. The randomization sequence will be prepared by statistical software and by an individual independent of the treatment team. The randomization unit in this study is the individual and each participant will be individually allocated to one of the two groups. For allocation concealment, opaque, closed, sealed and numbered envelopes will be used in the order of arrival. These envelopes will only be opened at the time of allocation and after the patient has been definitively entered the study to avoid selection bias.
Blinding (investigator's opinion)
Single blinded
Blinding description
The study will be conducted in a single-blinded manner; that is, the outcome assessor will be unaware of the group allocation of patients. Given the intrinsic differences between exosome and PRP interventions, blinding of the participant and the intervention provider is not possible. Patient allocation will be coded and performed using sealed envelopes.
Placebo
Used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Research Ethics Committee of Hamadan University of Medical Sciences
Street address
Shahid Fahmideh Street
City
Hamadan
Province
Hamadan
Postal code
6517835678
Approval date
2026-03-14, 1404/12/23
Ethics committee reference number
IR.UMSHA.REC.1404.991

Health conditions studied

1

Description of health condition studied
Evaluation of the effects of exosome therapy on the return of menstrual cycles and improvement of premature menopause symptoms in patients with premature ovarian failure (POF)
ICD-10 code
E28.3
ICD-10 code description
Primary ovarian failure

Primary outcomes

1

Description
Menstrual Cyclicity: Percentage of patients who show regular or significant return of menstruation during the follow-up period (3 to 6 months after injection).
Timepoint
Measurements will be taken at the beginning of the study (before treatment), the second month

(ultrasound), the third month (hormones, ultrasound, menstruation, pregnancy), the fourth month (ultrasound), and the sixth month (hormones, ultrasound, menstruation, pregnancy).

Method of measurement

Patient-reported outcome recording and confirmation by the physician based on observation of bleeding pattern and cycle regularity.

2

Description

Spontaneous or Clinical Pregnancy Rate: The percentage of patients who become pregnant during the study period (and up to 6 months after injection).

Timepoint

Follow-up in the third and sixth months. (If pregnancy symptoms appear earlier, an evaluation will be done at the appropriate time).

Method of measurement

Positive serum beta hCG test (≥25 IU/L) and confirmation of clinical pregnancy by visualization of the gestational sac via ultrasound.

Secondary outcomes

1

Description

AMH hormone level

Timepoint

AMH levels, as a secondary outcome, will be measured at three time points: baseline (before intervention), three months after intervention, and six months after intervention, using blood samples and ELISA. The unit of measurement is nanograms per milliliter (ng/mL).

Method of measurement

After serum separation, the venous blood sample is stored at -80°C and then measured using an ELISA kit (the name of the kit should be mentioned if known). The final results will be reported in nanograms per milliliter (ng/mL).

2

Description

Levels of FSH, LH, and estradiol (E2) hormones

Timepoint

It will be measured at three time points, including the beginning of the study (before the intervention), three months after the intervention, and six months after the intervention, using a blood sample and ELISA method. The unit of measurement is nanograms per milliliter (ng/mL).

Method of measurement

Blood sample and ELISA-based assays - measured on days 3 to 5 of the cycle if the cycle returns

Intervention groups

1

Description

Intervention group: Treatment type: Intraovarian injection of mesenchymal stem cell-derived exosomes (MSC-Exosomes).Technical details:Exosomes are prepared from mesenchymal cells extracted from Wharton’s Jelly tissue.Cells are cultured at passages 3 to 5 and exosomes are separated from the supernatant by ultracentrifuge.Purified exosomes are stored in PBS at -80°C until use.Administration: Intraovarian injection (by a gynecologist in an infertility clinic)

Category

Treatment - Drugs

2

Description

Control group: In this group, autologous platelet-rich plasma (PRP) is used as a comparative intervention. PRP is prepared from the subject's own venous blood sample and, after processing by centrifugation, is injected intraovarianly under transvaginal ultrasound guidance. The injection volume, frequency, and details of PRP preparation will be determined according to the study protocol.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center
Fatemeh Hospital, Hamadan

Full name of responsible person
Mahnaz Yavangi

Street address
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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?
Yes

Title of funding source
Hamedan 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
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Latest degree
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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