

Clinical Trial Protocol

Iranian Registry of Clinical Trials

16 Sep 2026

Investigating the effect of injecting the combination of exosomes extracted from follicular fluid, stem cells extracted from Wharton's jelly, platelets enriched from blood plasma and gonadotropins into the ovaries of poi, pof patients.

Protocol summary

Study aim

Stimulation of follicular growth in patients and recovery of menstrual cycle and sex hormone levels followed by the birth of a live child Investigating the effect of exosomes with gonadotropins and PRP

Design

20 qualified patients refers to Tahoor cilinic(QOM) will be selected. Medical history, general, abdominal and local examinations, clinical tests (general status using CBC, liver, kidney, thyroid and ovarian function tests by FSH, LH, E2, AMH, ultrasound and chromosomal examination to confirm karyotype) Healthy typing will be checked. Exosomes is extracted from follicular fluid by PEG method, then they will be injected together with enriched plasma (PRP) into the ovarian tissue of POF and POI patients.

Settings and conduct

This study will be conducted in Tahura Infertility Center, for this purpose 10 qualified clients of Tahura Infertility Center will be selected. All cases in terms of medical history, general, abdominal and local examinations, clinical tests (general condition using CBC, test, kidney, thyroid and ovarian function by FSH, LH, E2, AMH, ultrasound and chromosomal examination to confirm karyo) . Healthy typing will be checked

Participants/Inclusion and exclusion criteria

Women with premature menopause POF Women with premature ovarian failure POI Normal women with Grade(A) eggs Non-entry conditions: Idiopathic infertile women

Intervention groups

This study was conducted on eight groups: 1.The first group will not receive any stimulus as a control. 2.Only exosome. 3.Only PRP. 4.only gonadotropin. 5. Exosome and PRP. 6. Exosome and gonadotropin. 7.Gonadotropin and PRP 8. Exosome, gonadotropin and PRP, they will

receive.

Main outcome variables

increase ovarian reserve; proper ovarian function; The possibility of fertility of POF, POI women; recovery of menstrual cycle and sex hormone levels; Birth of a live child

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20230528058312N3**

Registration date: **2024-02-19, 1402/11/30**

Registration timing: **prospective**

Last update: **2024-02-19, 1402/11/30**

Update count: **0**

Registration date

2024-02-19, 1402/11/30

Registrant information

Name

Seyed Reza Tabatabaee Qomi

Name of organization / entity

Tahoor Infertility Treatment & limited surgery Clinic

Country

Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2024-02-20, 1402/12/01

Expected recruitment end date

2025-02-19, 1403/12/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Investigating the effect of injecting the combination of exosomes extracted from follicular fluid, stem cells extracted from Wharton's jelly, platelets enriched from blood plasma and gonadotropins into the ovaries of poi, pof patients.

Public title

Exosome and stem cells therapy

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Women with premature menopause POF Women with premature ovarian failure POI Normal women with Grade A eggs

Exclusion criteria:

Women with idiopathic infertility Women with adequate ovarian reserve

Age

From **20 years** old to **40 years** old

Gender

Female

Phase

1

Groups that have been masked

No information

Sample size

Target sample size: **20**

Randomization (investigator's opinion)

N/A

Randomization description

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

Islamic Azad University, Qom branch

Street address

15 Khordad St., Islamic Azad University, next to Social Security Insurance, Qom branch, Iran

City

Ghoum

Province

Ghoum

Postal code

3747113135

Approval date

2024-02-19, 1402/11/30

Ethics committee reference number

IR.IAU.QOM.REC.1402.206

Health conditions studied

1

Description of health condition studied

Premature Ovarian failure(POF) / Premature Ovarian Insufficiency (POI)

ICD-10 code

N97.0

ICD-10 code description

Female infertility associated with anovulation

Primary outcomes

1

Description

Absence of eggs in the ovaries of women under 40 years and primary or secondary amenorrhea for more than 4 months in women under 40 years with an elevated serum level of Follicular Stimulated Hormone(higher than 25 mIU/mL

Timepoint

15 days after the injection and then every month at the time of ovulation during one year

Method of measurement

Transvaginal ultrasound device, Hormonal Test by Elisa Kit.

Secondary outcomes

1

Description

Absence of eggs in the ovaries of women under 40 years and primary or secondary amenorrhea for more than 4 months in women under 40 years with an elevated serum level of Follicular Stimulated Hormone(higher than 25 mIU/m

Timepoint

15 days after the injection and then every month at the time of ovulation during one year

Method of measurement

Transvaginal ultrasound device, Hormonal Test by Elisa Kit.

Intervention groups

1

Description

Intervention group: Infertile women with primary or secondary amenorrhea for more than 4 months under 40 years old with an elevated serum level of FSH (higher than 25 mIU/mL). This group only autologous PRP (plate rich plasma) will be received. PRP was prepared from 40 mL of peripheral blood by the buffy coat protocol. In brief, whole blood was divided into two aliquots and centrifuged at 3,000 rpm for 8 min at room temperature to form three layers. The top platelet poor plasma and the middle layer were transferred to another two sterile tube and then centrifuged again at 4,000 rpm for 5 min. After removal of upper portion of the supernatant, each pellet was reconstituted with 2.5 ml of supernatant. patient is lying in the dorsal lithotomy position, and a needle (Towako Trans myometrial Set 18 GA× 325 mm, Cook, Australia) with an angle of 15 to 30 degrees is advanced into ovarian stroma under vaginal ultrasound guidance (Honda 2000). Under intravenous sedation using 100 mg propofol (Fresenius Kabi Austria GmbH, Graz, Austria). No antibiotic will not be used, and the patient withstood the process without painful sensation.

Category

Treatment - Other

2

Description

Intervention group: Infertile women with primary or secondary amenorrhea for more than 4 months under 40 years old with an elevated serum level of FSH (higher than 25 mIU/mL). this group receive exosome (100µg/ml) from the follicular fluid of fertile women referred to Tahura infertility center for IVF due to male factor infertility, who have been examined for HIV, HCV and HPV health and have grade A eggs, will be extracted according to the protocol provided by Eswaran with the help of Andreu Polyethylene glycol (PEG) (600 kDa). In order to check the presence of exosomes with the Mrestro brand nanodrop spectrophotometer, the concentration of DNA and RNA, with the ZEISS brand SEM electron microscope, the presence of exosomes will be checked. In addition, CD9, CD 63, CD81, CD82 factors will be checked with the help of Beckman brand flow cytometry. on the second and fifth day of the participants' menstrual cycle will be injected into their superficial layer of the ovary, only once during the treatment cycle. The patient is lying in the dorsal lithotomy position, and a needle (Towako Trans myometrial Set 18 GA× 325 mm, Cook, Australia) with an angle of 15 to 30 degrees is advanced into ovarian stroma under vaginal ultrasound guidance (Honda 2000). Under intravenous sedation using 100 mg propofol (Fresenius Kabi Austria GmbH, Graz, Austria). No antibiotic will be used, and the patient withstood the process without painful sensation.

Category

Treatment - Other

3

Description

Intervention group: Infertile women with primary or secondary amenorrhea for more than 4 months under 40 years old with an elevated serum level of FSH (higher than 25 mIU/mL) only gonadotropin, 1 ml of 150 IU of FSH/75 IU of LH (Pergoveris, Merck Serono, Aubonne, Switzerland) was slowly infused into ovarian tissue, 0.5 ml in each ovary, under intravenous sedation using 100 mg propofol (Fresenius Kabi Austria GmbH, Graz, Austria). No antibiotic is used, and the patient withstood the process without painful sensation. No visible side effect will be noted in the whole procedure.

Category

Treatment - Other

4

Description

Intervention group: nfertile women with primary or secondary amenorrhea for more than 4 months under 40 years old with an elevated serum level of FSH (higher than 25 mIU/mL). this group receive exosome (100µg/ml) and autologous PRP (4ml), under intravenous sedation using 100 mg propofol (Fresenius Kabi Austria GmbH, Graz, Austria). No antibiotic will be used, and the patient withstood the process without painful sensation.

Category

Treatment - Other

5

Description

Intervention group: Infertile women with primary or secondary amenorrhea for more than 4 months under 40 years old with an elevated serum level of FSH (higher than 25 mIU/mL) will be received gonadotropin 1 (150 IU rFSH/75 IU rLH, Pergoveris, Merck Serono, Aubonne, Switzerland) and exosome (100µg/ml) extracted from Follicular fluid of fertile woman injected under intravenous sedation using 100 mg propofol (Fresenius Kabi Austria GmbH, Graz, Austria). No antibiotic is used, and the patient withstood the process without painful sensation. No visible side effect is noted in the whole procedure.

Category

Treatment - Other

6

Description

Intervention group: Infertile women with primary or secondary amenorrhea for more than 4 months under 40 years old with an elevated serum level of FSH (higher than 25 mIU/mL) receive gonadotropin 1 ml (150 IU rFSH/75 IU rLH) (Pergoveris, Merck Serono, Aubonne, Switzerland) and autologous PRP (4mL) prepared by the buffy coat protocol be injected under intravenous sedation using 100 mg propofol (Fresenius Kabi Austria GmbH, Graz, Austria). No antibiotic is used, and the patient withstood the process without painful sensation.

Category

Treatment - Other

7**Description**

Intervention group: infertile women with primary or secondary amenorrhea for more than 4 months under 40 years old with an elevated serum level of FSH (higher than 25 mIU/mL) received gonadotropin 1ml(150IU rFSH/75IU rLH) (Pergoveris, Merck Serono, Aubonne, Switzerland), autologous PRP (4mL) prepared by the buffy coat Protocol and exosome (100µg/ml) extracted from Follicular fluid of fertile woman injected under intravenous sedation using 100 mg propofol (Fresenius Kabi Austria GmbH, Graz, Austria). No antibiotic is used, and the patient withstood the process without painful sensation.

Category

Treatment - Other

8**Description**

Intervention group: Infertile women under the age of 40 for at least 4 months with primary or secondary amenorrhea with an increase in FSH serum level (above 25 mIU/mL) for this group, UC-MSC stem cells from human umbilical cord tissue, obtained from normal healthy deliveries, were donated for this group. They have come to be separated. Finally, Wharton jelly mesenchymal stem cells will be obtained through enzymatic digestion of umbilical cord cells using 1.67% collagenase (Sigma, C9891, Saint Louis, MO, USA) at 37°C. After dissociation, cells were lysed up to passage 5 using α-MEM (Gibco, 32561-102, Carlsbad, CA, USA) supplemented with 4 mM Glutamax (Gibco, 35050-079, Carlsbad, CA, USA) and bovine serum. Inactivated 10% will multiply. (Gibco, 16000044, Grand Island, NY, USA). Finally, vials containing pure UC-MSC mesenchymal stem cells using 6% hydroxyethyl starch (Claris, G/LVP-5, Ellisbridge, Ahmedabad, India) with 10% dimethyl sulfoxide (Sigma, D2650, Irvine, England). which will be frozen and quarantined by the vitrification method. Finally, randomly vials (before freezing and after thawing), in terms of life; Proliferation, mycoplasma, endotoxin, growth and differentiation will be reviewed. Before each treatment, cell vials will be selected according to the total number of viable cells obtained by quality controls (using flow cytometry and the Cell Counter device) after freezing and thawing (following the syringe preparation steps) to determine the required cell dose. need the protocol. Finally, to reach the therapeutic goal of 9 million stem cells in each infusion, vials containing stem cells will be adjusted. In addition, factors CD9, CD 63, CD81, CD82 will be evaluated with the help of Beckman Coulter brand flow cytometry. Finally, the stem cells extracted with the required concentration on day 2 and 5 will be added to the surface layer of the ovary if the patient is in dorsal lithotomy mode. Lying down with the help of a puncture needle (Towako (Transmyometrial Set 18 GA x 325 mm, Cook) with an angle of 15 to 30 degrees towards the ovary and with the

guidance of the 2000 Honda vaginal ultrasound machine, it will be done only once during the treatment cycle. Before the injection, the patient will be put into artificial sleep with the help of an intravenous sedative using 100 mg of propofol (Fresenius Kabi Austria GmbH, Graz, Austria). No antibiotics will be used. According to previous studies, this process is painless and has no visible side effects.

Category

Treatment - Other

Recruitment centers**1****Recruitment center****Name of recruitment center**

Tahoor, Specialized Infertility Treatment And limited Surgery Center

Full name of responsible person

Dr. seyed Reza Tabatabaee Qomi

Street address

Tahoor infertility treatment and limited surgery clinic, Tahoor street, Jamkaran

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3747113135

Phone

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Email

taba_1359@yahoo.com

Sponsors / Funding sources**1****Sponsor****Name of organization / entity**

Tahoor infertility treatment and limited surgery clinic

Full name of responsible person

Seyed Reza Tabatabaee Qomi

Street address

Superspecialized Infertility Treatment And surgery center, Tahoor street, Jamkaran,

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Province

Ghoum

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Phone

+98 912 746 0016

Email

taba_1359@yahoo.com

Grant name**Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

Title of funding source

Tahoorra infertility treatment and limited surgery clinic

Proportion provided by this source

90

Public or private sector

Private

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin**Type of organization providing the funding**

Persons

Person responsible for general inquiries**Contact****Name of organization / entity**

Tahoorra infertility treatment and limited surgery clinic

Full name of responsible person

Seyed Reza Tabatabaee Qomi

Position

Treatment Manager

Latest degree

Ph.D.

Other areas of specialty/work

Infertility

Street address

Tahoorra infertility treatment and limited surgery clinic, Tahoorra street, Jamkaran

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Email

taba_1359@yahoo.com

Person responsible for scientific inquiries**Contact****Name of organization / entity**

Tahoorra infertility treatment and limited surgery clinic

Full name of responsible person

Seyed Reza Tabatabaee Qomi

Position

Treatment Manager

Latest degree

Ph.D.

Other areas of specialty/work

Infertility

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Person responsible for updating data**Contact****Name of organization / entity**

Tahoorra infertility treatment and limited surgery clinic

Full name of responsible person

Tahoorra infertility treatment and limited surgery clinic

Position

Treatment Manager

Latest degree

Ph.D.

Other areas of specialty/work

Infertility treatment and limited surgery clinic

Street address

Tahoorra infertility treatment and limited surgery clinic, Tahoorra street, Jamkaran

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Sharing plan**Deidentified Individual Participant Data Set (IPD)**

Yes - There is a plan to make this available

Study Protocol

Yes - There is a plan to make this available

Statistical Analysis Plan

Yes - There is a plan to make this available

Informed Consent Form

Yes - There is a plan to make this available

Clinical Study Report

Yes - There is a plan to make this available

Analytic Code

Yes - There is a plan to make this available

Data Dictionary

Yes - There is a plan to make this available

Title and more details about the data/document

All data obtained after identification of study cases can be shared.

When the data will become available and for how long

All information is accessible in April 2025.

To whom data/document is available

Our data will be available for all researchers and Doctors

Under which criteria data/document could be used

All information related to the performed ultrasounds, tests related to exosome and stem cell extraction will be accessible

From where data/document is obtainable

Applicants can contact one of the following email addresses to receive documents or data:
asalighe@yahoo.com taba_1359@yahoo.com

What processes are involved for a request to access**data/document**

Three weeks after sending the applicant's message, the requested documents and files will be sent.

Comments