

Clinical Trial Protocol

Iranian Registry of Clinical Trials

05 Jul 2026

Evaluation of the Effect of Melatonin on the Follicular Oxidative Stress and Quality of Oocyte and Embryo in Women with Diminished Ovarian Reserve

Protocol summary

Study aim

Diminished ovarian reserve (DOR) significantly decreases the success rate of Assisted Reproductive techniques (ART). In this study we study the effect of melatonin on the follicular oxidative stress and quality of oocyte and embryo in women with Diminished ovarian reserve .

Design

This study is a randomized, double-blind, placebo-controlled clinical trial.

Settings and conduct

In this research, an intervention group including 38 patients with reduced ovarian reserve (based on entry and exit criteria) three months after taking one melatonin tablet (3 mg melatonin tablet Hakim) per day and a control group that received a placebo. The patient and the doctor do not know the contents of the package (melatonin tablets and placebo).

Participants/Inclusion and exclusion criteria

ART for the first time, normal male factor, normal uterine cavity and presence of two of the three following criteria first; summation of bilateral AFC ≤ 6 , second; AMH ≤ 1 and third; basal FSH on the 3rd day of menstrual cycle ≥ 10 . If the couple decline to participate, the protocol is not exactly followed or the ovaries showed poor responses to gonadotropins the cases are excluded from the study.

Intervention groups

In the case group ,the patient receive melatonin by does of 3 mg/day from 5'th day of cycle till pick-up day.in the control group ,the patient receive placebo capsule one every night from 5'th day of cycle till pick-up day .

Main outcome variables

The main outcomes in this plan are the level of sex hormones, the number of follicles, the number and quality of oocytes and embryos, measuring the level of superoxide dismutase, the expression of GDF9 (Growth Differentiation Factor 9), and BMP15(Bone

Morphogenetic Protein 15) and (nuclear factor erythroid 2-related factor 2)NRF -2genes which will be measured before and after the intervention.

General information

Reason for update

Acronym

DOR

IRCT registration information

IRCT registration number: **IRCT20170529034209N2**

Registration date: **2022-11-15, 1401/08/24**

Registration timing: **prospective**

Last update: **2022-11-15, 1401/08/24**

Update count: **0**

Registration date

2022-11-15, 1401/08/24

Registrant information

Name

Hojjat Ghasemnejad berenji

Name of organization / entity

Urmia University of Medical Sciences

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2022-12-01, 1401/09/10

Expected recruitment end date

2023-07-01, 1402/04/10

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Evaluation of the Effect of Melatonin on the Follicular Oxidative Stress and Quality of Oocyte and Embryo in Women with Diminished Ovarian Reserve

Public title

Effect of Melatonin on Improving Fertility in Women with Diminished Ovarian Reserve

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

ART for the first time normal uterine cavity presence of two of the three following criteria first; summation of bilateral AFC ≤ 6 , second; AMH ≤ 1 and third; basal FSH on the 3rd day of menstrual cycle ≥ 10 .

Exclusion criteria:

If the couple decline to participate in the study the protocol is not exactly followed the ovaries showed poor responses to gonadotropins the cases

Age

From **25 years** old to **50 years** old

Gender

Female

Phase

2-3

Groups that have been masked

- Participant
- Outcome assessor

Sample size

Target sample size: **38**

Randomization (investigator's opinion)

Randomized

Randomization description

Individuals will be randomly assigned to one of two study groups with the help of a random number table and will receive the intervention of the allocated group. For allocation concealment, the method of sealed opaque envelopes which are numbered sequentially will be used. In this method, each random sequence is recorded on a card. Finally, the lids of the letter envelopes will be glued and placed inside a box. At the beginning of the study, according to the order of entry of eligible participants to study, one of the envelopes will be opened in order and the assigned group of the participant will be revealed.

Blinding (investigator's opinion)

Double blinded

Blinding description

This study is a randomized, double-blind, placebo-controlled clinical trial. In this research, an intervention group including 38 patients with reduced ovarian reserve (based on inclusion and exclusion criteria) three months after consuming one melatonin pill (Melatonin 3 mg Hakim pill) per day and a control group receiving a

placebo (placebo) Figure by Department of Pharmacy, Urmia University of Medical Sciences) suffering from reduced ovarian reserve, referred to the infertility center of Kausar Hospital, Urmia, enter the cycle of ovulation stimulation.

Placebo

Used

Assignment

Parallel

Other design features

Patients are advised to take one pill every night before going to sleep from the night of menstruation until the oocyte retrieval is done. Before starting the study, ultrasound will be done to evaluate the ovary. All patients start the gonadotropin-releasing hormone agonist protocol from day 21 of the same cycle. After 7 days, an ultrasound is performed and the level of estradiol is measured, which is repeated every 3 days, and when we have at least two eggs of 17-18 mm, 10,000 units of human chorionic gonadotropin are injected. 34 to 36 hours later, egg maturation occurs when 100 mg of progesterone intramuscular injection is performed to support the luteal phase and continues vaginally. Patients are followed up and their results are recorded. Then, after opening the codes, the data is analyzed. The patient and control groups are compared in terms of duration of stimulation, gonadotropin dose, estradiol level on the day of the trigger, the number and quality of eggs and embryos, and chemical or clinical pregnancy. The first group (treatment): women with reduced ovarian reserve treated with melatonin who enter the cycle of ovulation stimulation after three months of supplementation. The second group (control): women with reduced ovarian reserve who enter the cycle of ovulation stimulation. They will be divided. After selecting the subjects to be studied, the work steps will be carried out in the following order: 1. Measurement of serum levels of FSH, LH and E2 hormones in the control group and the treatment group before and three months after taking melatonin 2. Measurement of the serum level of FSH, LH and E2 hormones in the treatment group before ovulation stimulation 3. Beginning of ovulation stimulation courses according to the protocols of the infertility center of Kausar Hospital in Urmia 4. Examining the number of follicles in all groups 5. Oocyte collection from all groups according to the protocols of the infertility center of Kausar Hospital in Urmia 6. Investigating the number and quality of oocytes obtained from ovarian stimulation using a stereomicroscope 7. Preparation of samples of granulosa cells and follicular fluid 8. Measurement of superoxide desmutase level in follicular fluid by spectrophotometric method using SOD Assay Kit 9. Measuring NRF2 gene expression as a marker of oxidative stress suppression and GDF9 and BMP15 genes as markers of oocyte maturation in granulosa cells by qRT-PCR 10 method. Measuring the quality of embryos obtained on the third and fifth day

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics Committee of Urmia University of Medical Sciences

Street address

Jahad St., Resalat Blvd., Urmia University of Medical Sciences, Urmia, Iran

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urmia

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West Azarbaijan

Postal code

5715833631

Approval date

2022-09-21, 1401/06/30

Ethics committee reference number

IR.UMSU.REC.1401.262

Health conditions studied

1

Description of health condition studied

Diminished ovarian reserve (DOR)

ICD-10 code

E28.3

ICD-10 code description

Primary ovarian failure

Primary outcomes

1

Description

Number of ovum have received in each IVF cycle

Timepoint

On day of ovum pick up

Method of measurement

Measuring number of ovumes on the day of pick up in lab by the embryologist under microscope (GV , MI , MII) and quality of embryo also by the same pathologist due to kind of cell division (Grade I , II , III , IV)

2

Description

Quality of ovum have received in each IVF cycle.

Timepoint

On day of ovum pick up

Method of measurement

evaluation quality of ovumes on the day of pick up in lab by an embryologist under the microscope (GV , MI , MII) and quality of embryo also by the same pathologist due to kind of cell division (Grade I , II , III , IV)

3

Description

Quality of embryo have received in each IVF cycle.

Timepoint

On day of embryo insercion (IVF)

Method of measurement

quality of embryo on the day of pick up in lab by pathologist under microscope (GV , MI , MII) and quality of embryo also by the same pathologist due to kind of cell division (Grade I , II , III , IV)

4

Description

expression of the GDF9,BMP15, NRF -2 genes

Timepoint

On day of ovum pick up

Method of measurement

QRT-PCR

5

Description

Superoxide dismutase enzyme

Timepoint

On day of ovum pick up

Method of measurement

spectrophotometry

6

Description

the level of luteinizing hormone (LH),FSH,E2

Timepoint

menstrual cycle

Method of measurement

ELISA

Secondary outcomes

1

Description

Clinical pregnancy

Timepoint

4 - 6 weeks after embryo transferring

Method of measurement

Serum BHCG and TVS

Intervention groups

1

Description

The intervention group of 38 patients with Diminished Ovarian Reserve (based on Inclusion and exclusion criteria) three months after taking one melatonin tablet (3 mg melatonin tablet Hakim) per day.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Kowsar Hospital

Full name of responsible person

Dr. Hojjat Ghasemnejad- berenji

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

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Full name of responsible person

Dr. Saber Golizadeh

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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

Oroumia 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

Oroumia University of Medical Sciences

Full name of responsible person

Dr. Hojjat Ghasemnejad- berenji

Position

Assistant Professor

Latest degree

Ph.D.

Other areas of specialty/work

Reproductive Biology

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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

Not applicable

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

Not applicable

Data Dictionary

Not applicable