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 paitent recieve melatonin by does of 3 mg/day from 5'th day of sycle till pick-up day.in the control group ,the paitent recieve pelacebo capsule one every night from 5'th day of sycle till pick-up day .

Main outcome variables

The main outcomes in this plan arethe 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 onImproving 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 participatestudy 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 melatonin2. 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 Kosar 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 stereomicroscope7. Preparation of samples of granulosa cells and follicular fluid 8. Measurement of superoxide desmutase level in follicular fluid by spectrophotometric method using SOD Assay Kit9. 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-PCR10 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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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 emberyo 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 emberyo have received in each IVF cycle.

Timepoint
On day of emberyo insercion (IVF)

Method of measurement
quality of emberyo on the day of pick up in lab by pathologist under microscope (GV , MI , MII) and quality of emberyo 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 emberyo transfering

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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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