

Clinical Trial Protocol

Iranian Registry of Clinical Trials

18 Sep 2026

Effects of extract of *Foeniculum vulgare* on serum levels of estrogen, progesterone, LH and FSH hormones and miR-499, BMP15 and GDF9 genes expression in granulosa cells of patients with polycystic ovary syndrome (PCOS)

Protocol summary

Study aim

To evaluate the effects of an extract of *Foeniculum vulgare* on serum levels of estrogen, progesterone, LH, and FSH hormones and miR-499, BMP15, and GDF9 genes expression in granulosa cells of patients with the polycystic ovarian syndrome(PCOS)

Design

Randomized, parallel-group, single-blind, controlled, phase 2-3 clinical trial on 45 patients.

Settings and conduct

The study was conducted in the infertility treatment center of Besat Hospital, Sanandaj, where 45 patients were randomly divided into three groups. In this study, only the laboratory technician did not know about the grouping of patients.

Participants/Inclusion and exclusion criteria

Inclusion criteria: PCOS patients (experimental group): at least 10 cysts with a diameter of 2-8 mm around the central stroma, (Adams criteria), menstrual cycle disorder, clinical symptoms, and detection of polycystic ovaries in ultrasound(Rotterdam diagnostic criteria).
Exclusion criteria: over 35 and under 20 years of age, Cushing's syndrome, weight-induced amenorrhea, pituitary diseases, congenital adrenal hyperplasia , prolactinoma, thyroid disorders, androgen-secreting tumors, hypertension, chronic kidney disease, alcoholics, and smokers.

Intervention groups

3 groups of 15 people (1: control group 2: experimental group). The experimental group: women with PCOS were treated with ICSI/ IVF and then they were divided into two groups (treated with fennel extract and not treated with fennel extract).

Main outcome variables

1) Change in the serum level of FSH hormone 2) Changes in the serum level of LH hormone 3) Change in

progesterone serum level 4) Changes in serum estrogen levels 5) Changing the expression of miRNA-499 6) Changing the expression of GDF9 7) Changing the expression of BMP-15

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20200908048665N1**

Registration date: **2023-06-01, 1402/03/11**

Registration timing: **retrospective**

Last update: **2023-06-01, 1402/03/11**

Update count: **0**

Registration date

2023-06-01, 1402/03/11

Registrant information

Name

Azra allahveisi

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

2020-10-22, 1399/08/01

Expected recruitment end date

2023-07-23, 1402/05/01
Actual recruitment start date
 2020-11-21, 1399/09/01
Actual recruitment end date
 2023-05-22, 1402/03/01
Trial completion date
 2023-06-22, 1402/04/01

Scientific title
 Effects of extract of *Foeniculum vulgare* on serum levels of estrogen, progesterone, LH and FSH hormones and miR-499, BMP15 and GDF9 genes expression in granulosa cells of patients with polycystic ovary syndrome (PCOS)

Public title
 Effects of extract of *Foeniculum vulgare* on patients with polycystic ovary syndrome (PCOS)

Purpose
 Treatment

Inclusion/Exclusion criteria
Inclusion criteria:
 According to the Adams criteria based on ovarian ultrasound manifestations is to have at least 10 cysts with a diameter of 2-8 mm around the central stroma, densely and in the form of a necklace. Having Rotterdam diagnosis criteria (menstrual cycle disorder, clinical symptoms, and diagnosis of polycystic ovary in ultrasound diagnosed by a radiology specialist and infertility fellowship). BMI between 18-22 Age between 20-35 years
Exclusion criteria:
 Patients with Cushing's syndrome and weight-induced amenorrhea Pituitary disorders Congenital Adrenal Hyperplasia (CAH) Prolactinoma Thyroid disorders Androgen-secreting tumors Hypertension Chronic kidney disease Alcoholics and smokers Previous miscarriage Infertility in their husbands

Age
 From **20 years** old to **35 years** old

Gender
 Female

Phase
 2-3

Groups that have been masked

- Outcome assessor
- Data analyser

Sample size
 Target sample size: **45**
 More than 1 sample in each individual
 Number of samples in each individual: **15**
 The studied participants included 3 groups of 15 people. The intervention group included patients with polycystic ovary syndrome who were treated with fennel extract. A control group including women who had infertility problems in their spouses and another group including women with polycystic ovaries without treatment with fennel were selected as the second control group.
 Actual sample size reached: **45**

Randomization (investigator's opinion)
 Randomized

Randomization description
 Individual block randomization was considered by considering fifteen blocks and within each block three groups (A, B, and C) whose order was set randomly. So, finally, the list of 45 people who were assigned to each group was placed in 45 sealed envelopes, with numbers 1 to 45 written on the envelopes, and the study group was recorded inside the envelopes. The arrangement of the groups was done based on the block allocation by the website <https://www.sealedenvelope.com>.

Blinding (investigator's opinion)
 Single blinded

Blinding description
 In this study, only the person investigating the results (hormones and expression of desired genes) in the laboratory did not know about the grouping of the patients, but the patients and the researchers were aware of the grouping.

Placebo
 Used

Assignment
 Parallel

Other design features
 In this study, the level of hormones LH, FSH, estrogen, progesterone and the expression level of 499-miR and BMP15 and GDF9 genes in granulosa cells of women with polycystic ovary syndrome as well as two healthy groups and patients without intervention were investigated. The desired measurements were performed before and after the intervention group, but only baseline values were measured in the other two groups. All measurements were among the routine measures for patients presenting with infertility complaints.

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics Committee of Kurdistan University of Medical Sciences

Street address

Sanandaj - Pasdaran Ave

City

Sanandaj

Province

Kurdistan

Postal code

66177-13446

Approval date

2021-02-17, 1399/11/29

Ethics committee reference number

IR.MUK.REC.1399.141

Health conditions studied

1

Description of health condition studied

polycystic ovary syndrome (PCOS)

ICD-10 code

E28.2

ICD-10 code description

Polycystic ovarian syndrome

Primary outcomes

1

Description

Serum level of estrogen hormone

Timepoint

Before starting the study and before IVF in three groups and after the intervention in the experimental group (After taking 45 days of ethanol extract of fennel plant)

Method of measurement

ELISA test

2

Description

Serum levels of progesterone

Timepoint

Before starting the study and before IVF in three groups and after the intervention in the experimental group (After taking 45 days of ethanol extract of fennel plant)

Method of measurement

ELISA test

3

Description

FSH serum level

Timepoint

Before starting the study and before IVF in three groups and after the intervention in the experimental group (After taking 45 days of ethanol extract of fennel plant)

Method of measurement

ELISA test

4

Description

LH serum level

Timepoint

Before starting the study and before IVF in three groups and after the intervention in the experimental group (After taking 45 days of ethanol extract of fennel plant)

Method of measurement

ELISA test

5

Description

The expression level of 499-miR

Timepoint

Before starting the study and before IVF in three groups and after the intervention in the experimental group (After taking 45 days of ethanol extract of fennel plant)

Method of measurement

Real time PCR

6

Description

BMP15 gene expression

Timepoint

Before starting the study and before IVF in three groups and after the intervention in the experimental group (After taking 45 days of ethanol extract of fennel plant)

Method of measurement

Real time PCR

7

Description

GDF9 gene expression

Timepoint

Before starting the study and before IVF in three groups and after the intervention in the experimental group (After taking 45 days of ethanol extract of fennel plant)

Method of measurement

Real time PCR

Secondary outcomes

empty

Intervention groups

1

Description

Intervention group: women with polycystic ovary syndrome (PCOS) treated with fennel extract in the amount of 100 mg twice a day in the form of capsules made by the research group.

Category

Treatment - Other

2

Description

Control group: This group was given a placebo in the form of capsules similar to the intervention group, which contained starch, twice a day for 45 days.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Besat hospital

Full name of responsible person

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1

Sponsor

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Grant name

Maleki

Grant code / Reference number

1399.141

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

Sanandaj 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

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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

Not applicable

Data Dictionary

Not applicable

Title and more details about the data/document

Row data will be available.

When the data will become available and for how long

After publication

To whom data/document is available

Researchers

Under which criteria data/document could be used

For systematic review and meta-analysis.

From where data/document is obtainable

Research deputy at Kurdistan University of Medical Sciences

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

Send a request to the research deputy at the University

Comments