Clinical Trial Protocol
Iranian Registry of Clinical Trials

29 Jul 2026

Comparsion of luteal estradiol administration during GnRH antagonist protocol versus microdose GnRH agonist protocol for patients with a history of poor IVF out come

Protocol summary

Study aim
Better ovarian stimulation in patients with poor ovarian responses

Design
Clinical trial with a randomized parallel control group with 116 patients, participating in the study between June 2011 to April 2012 (follow-up time is up to 20 weeks of pregnancy)

Settings and conduct
Clinical trial with a single-blind random control group , between June 2011 and April 2012 at Yazd Infertility Research and Treatment Center, Shahid Sadoughi University of Medical Sciences, Yazd

Participants/Inclusion and exclusion criteria
Inclusion criteria: a history of poor response in a prior cycle (≤3 oocytes retrieved, poor-quality oocytes; cycle cancellation due to inadequate ovarian response; Women anticipated to be a poor responder based on initial testing (third-day FSH level of 10 mIU/mL, or a basal antral follicle count <5). exclusion criteria: stage III–IV endometriosis; autoimmune or chromosomal disorders; endocrine or metabolic diseases; existence of only one ovary patients exhibiting a day 3 serum FSH level greater than 15 mIU/mL; Sever male factor (patients with azoospermia and normal morphology of sperm <4%); hydrosalpinx

Intervention groups
For fifty eight randomly estradiol (Aburaihan Pharmaceutical Co., Tehran, Iran) 2 mg is started orally twice a day on the 21st luteal day and continued until menstruation. Once menses began, estradiol was discontinued and gonadotropin stimulation was started on the2nd day of the menstrual cycle. Gonal-F (Gonal-F, Serono, Italy) at 225-300 IU/day was initiated from the second day of menses. When the leading follicle reached 14 mm in diameter, Cetrorelix (Merck- Serono Germany) 0.25 mg SC was added and continued every day until and including the day of hCG administration. Another group consisted of 58 women who underwent ovarian stimulation for IVF using micro dose agonist protocol.

Main outcome variables
Results of ovulation stimulation

General information

Reason for update
update as result

Acronym
IVF

IRCT registration information
IRCT registration number: **IRCT201108044339N8**
Registration date: **2011-09-15, 1390/06/24**
Registration timing: **registered_while_recruiting**

Last update: **2021-04-19, 1400/01/30**
Update count: **1**

Registration date
2011-09-15, 1390/06/24

Registrant information

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Recruitment status
Recruitment complete

Funding source
مرکز تحقیقاتی و درمانی ناباروری یزد

Expected recruitment start date
2011-03-01, 1389/12/10
Expected recruitment end date
2011-10-28, 1390/08/06
Actual recruitment start date
2011-03-01, 1389/12/10
Actual recruitment end date
2011-10-28, 1390/08/06
Trial completion date
2012-03-30, 1391/01/11

Scientific title
Comparsion of luteal estradiol administration during GnRH antagonist protocol versus microdose GnRH agonist protocol for patients with a history of poor IVF out come

Public title
Estradiol administration for patients with a history of poor IVFresponse
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
A history of poor response in a prior cycle (≤3 oocytes retrieved, poor-quality oocytes, Cycle cancellation due to inadequate ovarian response Women anticipated to be a poor responder based on initial testing (third-day FSH level of 10 mIU/mL, or a basal antral follicle count <5)
Exclusion criteria:
Stage III–IV endometriosis Autoimmune or chromosomal disorders Endocrine or metabolic diseases Existence of only one ovary Patients exhibiting a day 3 serum FSH level greater than 15 mIU/mL Sever male factor (patients with azoospermia and normal morphology of sperm <4%) Hydrosalpinx
Age
No age limit
Gender
Female

Phase
2
Groups that have been masked

- Investigator

Sample size
Target sample size: **116**
Actual sample size reached: **116**
Randomization (investigator's opinion)
Randomized
Randomization description
Patients are admitted to two groups of 58 patients based on permutation block method. Therapeutic tasks within the blocks are determined in such a way that they are random, but the desired allocation ratio is achieved in each block. 29 blocks of 4 are considered. Generate random codes using random block allocation method which will be generated with the help of Random allocation software version 1. The first person eligible to enter the study is given number one and so on until the last eligible person is given number 116. Using a table generated by random allocation software by number, people receive intervention A or B. In order to be blind, the random allocation of this list is given to another person outside the study, and by sending a text message before assigning the type of treatment, the eligible person is asked according to the number, and thus the people enter the study.
Blinding (investigator's opinion)
Single blinded
Blinding description
The physicians performing the follicular aspiration blinded to the stimulation protocol.
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Yazd Research and Clinical Center for Infertility
Street address
Yazd Research and Clinical Center for Infertility, Booali Street, Safaieh, Yazd
City
Yazd
Province
Yazd
Postal code
8916877391
Approval date
2011-06-20, 1390/03/30
Ethics committee reference number
933

Health conditions studied

1

Description of health condition studied
Female infertility
ICD-10 code
N97
ICD-10 code description
Female infertility

Primary outcomes

1

Description
The number of oocyte retrival
Timepoint
Day of punctuer
Method of measurement

Counting by microscope

2

Description
Clinical pregnancy rates
Timepoint
5 weeks after the embryo transfer
Method of measurement
Presence of a gestational sac with heart beat identified byultrasound

Secondary outcomes

1

Description
The cycle length
Timepoint
From the start of the drug until the day of the puncture
Method of measurement
Calendar

2

Description
The total dose of gonadotropin
Timepoint
From the start of the drug until the day of the puncture
Method of measurement
International unit

3

Description
The implantation rate
Timepoint
5 weeks after the embryo transfer
Method of measurement
The number of pregnancy sacs divided by the number of transferred embryos multiplied by 100

Intervention groups

1

Description
Fifty eight randomly selected women underwent IVF using the E2/antagonist protocol (E2/ANT group). In this group, estradiol (Aburaihan Pharmaceutical Co., Tehran, Iran) 2 mg was started orally twice a day on the 21st luteal day and continued until menstruation. Once menses began, estradiol was discontinued and gonadotropin stimulation was started on the2nd day of the menstrual cycle. Gonal-F (Gonal-F, Serono, Italy) at 225-300 IU/day was initiated from the second day of menses and was adjusted according to serum E2 concentrations and the ovarian response as noted by ultrasound. When the leading follicle reached 14 mm in diameter, Cetrorelix (Merck- Serono Germany) 0.25 mg SC was added and continued every day until and including the day of hCG administration. In both groups, 10,000 IU of hCG (pregnyl, Daropakhsh, Iran) was administered IM when at least two follicles reached ≥ 18 mm in diameter. The follicles were followed 36 hours later by ultrasound-guided transvaginal oocyte retrieval. The IVF and intracytoplasmic sperm injection (ICSI) procedures were performed, and the embryos were transferred on the third day after retrieval with a Labotect catheter (Labotect, Gotting, Germany). A good-quality embryo was defined as seven or more blastomeres on day 3,equally sized blastomeres and < 20% fragmentation' and poor-quality embryos consist of all the rest. The number of transferred embryos depended on the embryo quality and the patient's age. All the patients received 100 mg of progesterone (Aburaihan Pharmaceutical Co., Tehran, Iran) IM per day for luteal support, which was initiated on the day of oocyte retrieval. Serum B-hCG was checked 14 days after the embryo transfer .If the patient was pregnant, progesterone was continued until the 10th week of pregnancy. Chemical pregnancy was defined as serum B-hCG >50 IU/L after 14 days from embryo transfer. Clinical pregnancy was defined as the presence of a gestational sac with heart beat identified by ultrasound five weeks after the embryo transfer. The implantation rate was defined as the ratio of gestational sacs to the number of embryos transferred and Clinical abortion rate was determined as clinically recognized pregnancy losses before 20 weeks of gestation. Criteria for cycle cancellation due to poor ovarian response included the presence of fewer than two growing follicles on ultrasound' with an E2 level < 200 pg/ ml on day 7 of stimulation.
Category
Treatment - Drugs

2

Description
Control group consisted of 58 women who underwent ovarian stimulation for IVF using micro dose agonist protocol (micro dose group).In these patients, low-dose OCP (30 mcg Ethinyl Estradiol and 0.3mg Norgestrel, Aburaihan Pharmaceutical Co., Tehran, Iran) was started on the 2nd day of the previous cycle for 21 days. On the second day of menstruation, Suprefact (Buserelin acetate, Aventis Pharma Deutschland, Germany) 50 µg SC was started and continued twice a day until the day of hCG administration. After two days (on the fourth day of menstruation) Gonal-F was started at 225-300 IU/day .In these patients, like in the other group, the dose of Gonal –F was adjusted according to serum E2 concentrations and ovarian responses as noted by ultrasound. In both groups, 10,000 IU of hCG (pregnyl, Daropakhsh, Iran) was administered IM when at least two follicles reached ≥ 18 mm in diameter. The follicles were followed 36 hours later by ultrasound-guided transvaginal oocyte retrieval. The IVF and intracytoplasmic sperm injection (ICSI) procedures were performed, and the embryos were transferred on the third day after retrieval with a Labotect catheter (Labotect, Gotting, Germany). A good-quality embryo was defined as seven or more blastomeres on day 3,equally sized blastomeres and < 20% fragmentation'

and poor-quality embryos consist of all the rest. The number of transferred embryos depended on the embryo quality and the patient's age. All the patients received 100 mg of progesterone (Aburaihan Pharmaceutical Co., Tehran, Iran) IM per day for luteal support, which was initiated on the day of oocyte retrieval. Serum B-hCG was checked 14 days after the embryo transfer .If the patient was pregnant, progesterone was continued until the 10th week of pregnancy. Chemical pregnancy was defined as serum B-hCG >50 IU/L after 14 days from embryo transfer. Clinical pregnancy was defined as the presence of a gestational sac with heart beat identified by ultrasound five weeks after the embryo transfer. The implantation rate was defined as the ratio of gestational sacs to the number of embryos transferred and Clinical abortion rate was determined as clinically recognized pregnancy losses before 20 weeks of gestation. Criteria for cycle cancellation due to poor ovarian response included the presence of fewer than two growing follicles on ultrasound' with an E2 level < 200 pg/ ml on day 7 of stimulation.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Yazd Research and Clinical Center for Infertility, Shahid Sadoughi University of Medical Sciences

Full name of responsible person

Dr Robab Davar

Street address

Yazd Research and Clinical Center for Infertility, Booali Street, Safaieh, Yazd

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Yazd Research and Clinical Center for Infertility, Shahid Sadoughi University of Medical Sciences

Full name of responsible person

Vice-Chancellor for Research & Technology

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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

Yazd Research and Clinical Center for Infertility, Shahid Sadoughi 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

Yazd Research and Clinical Center for Infertility, Shahid Sadoughi University of Medical Sciences

Full name of responsible person

Dr Mozhgan Rahsepar

Position

Obestetrics and Gynecologist,Student of fellowship

Latest degree

Specialist

Other areas of specialty/work

Gynecology and Obstetrics

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Latest degree
Specialist
Other areas of specialty/work
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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
Yes - There is a plan to make this available
Statistical Analysis Plan
Yes - There is 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
No - There is not a plan to make this available
Analytic Code
No - There is not a plan to make this available
Data Dictionary
No - There is not a plan to make this available
Title and more details about the data/document
Information on the main outcome
When the data will become available and for how long
6 months after printing the results
To whom data/document is available
Editor-in-Chief
Under which criteria data/document could be used
Use in the retrospective study
From where data/document is obtainable
Yazd Research and Clinical Center for Infertility
What processes are involved for a request to access data/document
Request from the Research Deputy, submitted to the Research Council of the Center if the request accepts its referral to the security and after completion of the relevant forms, request is referred to the research experts and then get the data.
Comments

Trial results

Please tick if results have been published
Yes
Summary result posting date
2021-04-19, 1400/01/30
Table of baseline comparison

Archives of Gynecology and Obstetrics **volume 287**, pages149–153(2013)

Participant flow diagram
Table of variable outcomes' results
Table of adverse events
First publication date

2012-08-26, 1391/06/05

Abstract of published paper

Purpose This study aims to verify if luteal estradiol pre-treatment improves IVF/ICSI outcomes in a GnRH antagonist protocol as compared with a micro dose GnRH agonist protocol in poor-responding patients. Methods A total of 116 IVF/ICSI cycles were included in this prospective randomized single blind clinical trial. The selected women were randomly assigned to receive an estradiol pre-treatment in a GnRH antagonist protocol (daily oral Estradiol Valerate 4 mg preceding the IVF cycle from the 21st day until the first day of the next cycle) or in oral contraceptive pill micro dose GnRH agonist protocol. Results The patients in the luteal estradiol protocol required more days of stimulation (10.9 ± 1.6 vs. 10.2 ± 1.8) and a greater gonadotropin requirement (3,247.8 ± 634.6 vs. 2,994.8 ± 611 IU), yet similar numbers of oocytes were retrieved and fertilized. There was no significant difference between the two groups in terms of the implantation rates (9.8 vs. 7.9 %) and the clinical pregnancy rates per transfer (16.3 vs. 15.6 %). Conclusion This study demonstrates that the use of estradiol during a preceding luteal phase in a GnRH antagonist protocol can provide similar IVF outcomes when compared to a micro dose GnRH agonist protocol.