Clinical Trial Protocol
Iranian Registry of Clinical Trials

13 Jun 2026

effect of progesterone in natural frozen – thawed embryo transfer cycles

Protocol summary

Study aim
Better endometrial development and increased pregnancy rate

Design
A clinical trial with a randomized parallel control group with 102 patients. Participants participated in the study between March 2011 and March 2012 and were followed up to 20 weeks of gestation.

Settings and conduct
En Yazd Research and Clinical Center for infertility affiliated to Shahid Sadoughi University of Medical Sciences

Participants/Inclusion and exclusion criteria
Inclusion critera: cryopreserved embryos after conventional in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI); maternal age of 20-40 years (on the day of embryo freezing); regular menstrual cycle of 25-35 days; body mass index of 20-27 kg/m2 Exclusion critera:the use of testicular sperm for ICSI (ejaculated sperm only); basal follicle stimulating hormone; stage III-IV endometriosis; polycystic ovarian syndrome (PCOS)

Intervention groups
The progesterone group received 100mg/day of progesterone (Aburaihan Pharmaceutical Co., Tehran, Iran) IM, that began 36 hours after the hCG administration and continued until ten weeks of gestation if pregnancy occurred. Control patients received no progesterone. In both groups, cryopreserved embryo transfer was performed with a Cook catheter (Cook Ireland Ltd.) five days after hCG administration. Serum β-hCG level was measured 14 days after the transfer.

Main outcome variables
The main outcome measures concerned clinical pregnancy and implantation rates

General information

Reason for update
update as result

Acronym
IVF

IRCT registration information
IRCT registration number: **IRCT201108044339N6**
Registration date: **2011-09-22, 1390/06/31**
Registration timing: **registered_while_recruiting**

Last update: **2021-03-27, 1400/01/07**
Update count: **2**

Registration date
2011-09-22, 1390/06/31

Registrant information

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Recruitment status
Recruitment complete

Funding source
Yazd research and clinical center for infertility

Expected recruitment start date
2011-03-01, 1389/12/10

Expected recruitment end date
2011-11-02, 1390/08/11

Actual recruitment start date
2011-03-01, 1389/12/10

Actual recruitment end date
2011-11-02, 1390/08/11

Trial completion date
2012-03-30, 1391/01/11

Scientific title
effect of progesterone in natural frozen – thawed embryo

transfer cycles

Public title
natural frozen – thawed embryo transfer cycles
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
cryop reserved embryos after conventional in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) maternal age of 20-40 years (on the day of embryo freezing) regular menstrual cycle of 25-35 days body mass index of 20-27 kg/m2
Exclusion criteria:
the use of testicular sperm for ICSI (ejaculated sperm only) basal follicle stimulating hormone stage III-IV endometriosis polycystic ovarian syndrome (PCOS)
Age
From **20 years** old to **40 years** old
Gender
Female

Phase
2
Groups that have been masked
No information
Sample size
Target sample size: **109**
Actual sample size reached: **102**
Randomization (investigator's opinion)
Randomized
Randomization description
Patients were randomized to either group in a ratio of 1:1 by means of computer-generated random numbers on the day of participation. Group selection and randomization were performed by a nurse not involved in the study, by using opaque sealed envelopes. Both the patients and the clinicians were aware of the allocated arm.
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
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
929

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
chemical pregnancy
Timepoint
14 days after embryo transfer
Method of measurement
BHCG TEST

Secondary outcomes

1

Description
Clinical pregnancy
Timepoint
4-5 weeks after embryo transfer
Method of measurement
Obestetrics sonography

2

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

3

Description
Clinical abortion
Timepoint
before20 weeks of gestation
Method of measurement
as clinically

Intervention groups

1

Description
On the second or third days of the menstrual cycle, all patients underwent transvaginal ultrasounds and serum hormone analysis for FSH. Then, a vaginal ultrasonographic examination was performed on cycle days 10 and repeated as necessary. Final oocyte maturation was achieved by intramuscular (IM) administration of 10000 IU of hCG (Pregnyl, Daropakhsh, Iran) when an endometrial thickness of 8 mm or more and a follicle of 18 mm were present on the ultrasound. On the day of the hCG administration, we measured serum estradiol, progesterone and LH levels.The progesterone group received 100mg/day of progesterone (Aburaihan Pharmaceutical Co., Tehran, Iran) IM, that began 36 hours after the hCG administration and continued until ten weeks of gestation if pregnancy occurred. In both groups, cryopreserved embryo transfer was performed with a Cook catheter (Cook Ireland Ltd.) five days after hCG administration. Serum β-hCG level was measured 14 days after the transfer.

Category
Treatment - Drugs

2

Description
In control group :On the second or third days of the menstrual cycle, all patients underwent transvaginal ultrasounds and serum hormone analysis for FSH. Then, a vaginal ultrasonographic examination was performed on cycle days 10 and repeated as necessary. Final oocyte maturation was achieved by intramuscular (IM) administration of 10000 IU of hCG (Pregnyl, Daropakhsh, Iran) when an endometrial thickness of 8 mm or more and a follicle of 18 mm were present on the ultrasound. On the day of the hCG administration, we measured serum estradiol, progesterone and LH levels.Control patients received no progesterone. In both groups, cryopreserved embryo transfer was performed with a Cook catheter (Cook Ireland Ltd.) five days after hCG administration. Serum β-hCG level was measured 14 days after the transfer.

Category
Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center
Yazd research and clinical center for infertility

Full name of responsible person
Dr Maryam Eftekhar

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
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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 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 University of Medical Sciences

Full name of responsible person
Dr Mozhgan Rahsepar

Position
Obestetrics and Gynecologist,Student of fellowship
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Person responsible for scientific inquiries

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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
Yes - There is 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

2021-03-08, 1399/12/18

Table of baseline comparison

Table 1

Characteristics of patients

Outcome variable	Progesterone N=51	No progesterone N=51	P value
Age (Years)	29.0 ± 3.8	28.7 ± 4.6	0.71
BMI (kg/m^2)	23.8 ± 2.8	24.3 ± 2.4	0.35
Duration of infertility (Years)	6.0 ± 3.8	6.7 ± 4.5	0.71
Basal FSH (IU/L)	5.8 ± 1.9	6.0 ± 2.0	0.90
Previous ART attempts n (%)	14 (27.5)	17 (33.3)	0.51
Etiology of infertility n (%)			0.62
Male factor	35 (68.6)	32 (62.7)	
Tubal factor	7 (13.8)	6 (11.8)	
Unexplained	9 (17.6)	13 (25.5)	

Participant flow diagram

Table of variable outcomes' results

Table 2

Patients’ previous fresh cycle characteristics

Outcome variable	Progesterone N=51	No progesterone N=51	P value
Type of previous stimulation n (%)			0.84
Agonist protocol	29 (56.9)	31(60.8)	
Antagonist protocol	22 (43.1)	20 (39.2)	
Fertilization procedure n (%)			
IVF	11 (21.6)	19 (37.3)	
ICSI	40 (78.4)	32 (62.7)	
No. of oocytes retrieved	10.0 ± 4.3	9.6 ± 3.4	0.16
No. of mature oocytes	8.3 ± 3.4	7.6 ± 2.8	0.22
No. of embryos obtained	6.2 ± 1.6	5.7 ± 2.2	0.19
No. of embryos vitrified	4.3 ± 1.0	4.0 ± 0.6	0.07
Fertilization rate (%)	55.4	64.3	0.16
Sperm parameters			
Count (mill/ml)	12.6 ± 7.7	11.9 ± 7.0	0.62
Progressive motility (%)	15.0 ± 5.8	14.5 ± 6.9	0.72
Normal morphology (%)	15.3 ± 9.8	14.2 ± 7.3	0.51
Cause of embryo freezing n (%)			0.59

Surplus embryos	30 (58.8)	26 (45.1)	
Risk of OHSS	19 (37.3)	21(41.2)	
Endometrial polyp	2 (3.9)	4 (7.8)	

Table 3

Frozen-thawed embryo replacement cycle characteristics

Outcome variable	Progesterone N=51	No progesterone N=51	P value
Endometrial thickness (mm)	8.7 ± 1.3	8.9 ± 1.4	0.64
E2 on hCG day (pg/ml)	208.4 ± 60.2 median: 200	196.9 ± 85.3 median: 170	0.11
Progesterone on hCG day (ng/ml)	0.77 ± 0.09	0.80 ± 0.07	0.08
LH on hCG day (IU/L)	4.9 ± 1.9	4.6 ± 1.7	0.39
No. of days until hCG	14.3 ± 1.8	13.7 ± 1.5	0.07
No. of embryos transferred	1.7 ± 0.5 median: 2	1.9 ± 0.5 median: 2	0.07
Transfers with good quality embryos (%)	54.9	60.8	0.54

Table 4

Pregnancy outcomes

Outcome variable	Progesterone N=51	No progesterone N=51	P value
Chemical pregnancy rate, n (%)	18 (35.3)	16 (31.4)	0.83
Clinical pregnancy rate, n (%)	17 (33.3)	14 (27.5)	0.66
Implantation rate (%)	16.6	15.3	0.93
Clinical abortion rate, n (%)	2 (11.8)	2 (14.3)	0.83

Table of adverse events

First publication date

2013-04-01, 1392/01/12

Abstract of published paper

Abstract Background: The transfer of cryopreserved embryos can be timed with ovulation in a natural cycle or after artificially preparing the endometrium with exogenous hormones. Progesterone is essential for the secretory transformation of the endometrium that permits implantation as well as maintenance of early pregnancy. The purpose of this study is to assess the effect of luteal phase supplementation on pregnancy rates in natural frozen-thawed cycles. Materials and Methods: The study was designed as a prospective randomized clinical trial of 102 women who underwent embryo transfers in natural cycles. The women in the interventional group (n=51) received intra muscular (IM) progesterone 50 mg twice a day starting from 36 hours after hCG administration. The control group (n=51) did not receive any progesterone support. Results: There were no significant differences in demographic characteristics between the groups and no statistically significant differences were observed between study and control groups in clinical pregnancy rate (33.3% vs. 27.5%, p=0.66). There were no differences in implantation rate or spontaneous abortion rate. Conclusion: Our results suggest that luteal phase support does not affect clinical pregnancy rates in natural frozen-thawed embryo transfer cycles (Registration Number: IRCT201108044339N6).