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Effect of transdermal estradiol on endometrial preparation in frozen-thawed embryo transfer

Submission date
18/06/2020

Recruitment status
No longer recruiting

Registration date
02/07/2020

Overall study status
Completed

Last Edited
19/08/2022

Condition category
Pregnancy and Childbirth

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[X] Individual participant data

Plain English summary of protocol

Background and study aims
Frozen Embryo Transfer (FET) is an assisted reproductive technology procedure in which a previously frozen embryo is thawed and transferred into an appropriately prepared uterus (womb) in order to have a baby. In preparation for FET, the lining of the uterus (endometrium) must reach an appropriate thickness. Among various methods for endometrial preparation, the use of estradiol, either through oral (tablet) or transdermal (direct contact on skin), has been shown to be an effective method. However, women usually complain of side effects of using oral estradiol, in some cases leading to them to stop using the medication. The researchers believe that transdermal estradiol can help to reduce these side effects and be a useful way to increase the chance of having a baby. The aim of this study is to compare transdermal estradiol to oral estradiol in terms of effectiveness and acceptability.

Who can participate?
Women aged 18-45 undergoing IVF with FET

What does the study involve?
If the women join the research, they will randomly use either transdermal estradiol or oral estradiol. Beginning at day 3 of the menstrual cycle, they will take one transdermal dosage twice a day or one tablet twice a day for 7 days. The researchers will perform an ultrasound scan at day 10 of the menstrual cycle to evaluate the thickness of the endometrium then gradually increase the dosage. When the thickness of endometrium reaches 8-14 mm, both groups will be prescribed progesterone before transfer and undergo IVF cycles. The researcher will assess the pregnancy outcomes in both groups.

What are the possible benefits and risks of participating?
Participants will be able to contribute to the advancement of the understanding of the effects of transdermal estradiol on endometrial preparation in frozen-thawed embryo transfer cycles. There is minimal risk since estradiol is generally safe and well-known as a hormonal medication for many conditions.

Where is the study run from?
Hung Vuong Hospital (Viet Nam)

When is the study starting and how long is it expected to run for?
January 2020 to March 2022

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Thi Diem Tuyet Hoang
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Contact information

Type(s)
Public

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Additional identifiers

Study information

Scientific Title
Efficiency assessment of transdermal estradiol on endometrial preparation in frozen-thawed embryo transfer cycles: a randomized clinical trial

Study objectives
Is patient usage of transdermal estradiol more effective than oral estradiol on endometrial preparation in frozen-thawed embryo transfer cycles?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/06/2020, Hung Vuong Ethics Committee (128 Hong Bang Street, Ward 12, District 5, Ho Chi Minh City; +84 (0)28 3855 8532; no email provided), no ref provided

Primary study design
Interventional

Study design
Randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Women undergoing IVF

Interventions
Comparison of the effectiveness between transdermal estradiol and oral estradiol on the endometrium of frozen embryo transfer (FET) at Hung Vuong Hospital between January 2020 to August 2021. Patients who indicated frozen-thawed embryo transfer, have at least one excellent /good frozen embryo before thawing, age 18-45 years will be invited to participate in the trial.

A list of randomized groups will be divided using www.random.org software – Appendix 4. The block randomization method (2, 4, 6, 8) and the permutation block size were used. A randomized staff who is outside the study will print the forms with consecutive signs A and B, which are placed into sealed envelopes and randomly assigned following the result table in Appendix 4. Each individual participating in the study has an equal probability (1:1) to be selected for the sample, using drawing method after screening and signing a consent form. Then, the envelopes will be numbered in ascending order from top to bottom. Participants were grouped in turn according to the open of envelope with the form inside and then received drugs as follow:
A: oral estradiol
B: transdermal estradiol

All members including doctors, midwives, staff were blinded to the randomized table. The pharmacists who provide drugs for patients are not blinded to the drug but they do not play any role in this study.

Related interventions:
Study group: Transdermal estradiol regimen
1. Begin at day 3 of the menstrual cycle, daily 5 g dosage during 7 days which is equivalent to 1 transdermal dosage twice a day. 1 ruler dosage equals to 2.5 g
2. Perform an ultrasound scan at day 10 of the menstrual cycle: evaluate the thickness of endometrium then gradually increase the dosage up to a maximum of 20 g/day

Control group: Oral estradiol valerate regimen
1. Begin at day 3 of the menstrual cycle, 4 mg of dosage daily in 7 days which is equivalent to 1 tablet twice a day
2. Perform an ultrasound scan at day 10 of the menstrual cycle: evaluate the thickness of endometrium then gradually increase the dosage up to a maximum of 16 g/day

3. Perform an ultrasound scan to measure the thickness of endometrium 8-14 mm
4. Use 600 microgram progesterone daily during 3 days before day-3 embryo transfer
5. Use 600 microgram progesterone daily during 5 days before day-5 embryo transfer
6. Test the estradiol/blood concentration on progesterone day

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Estradiol gel, oral estradiol

Primary outcome(s)
1. Thickness and shape of endometrium measured using vaginal ultrasound examination at baseline and on progesterone day
2. Serum estradiol concentration measured using immunoassay on progesterone day
3. Mean duration of treatment, recorded at time of procedure

Key secondary outcome(s)
1. Cycle cancellation rate of FET measured from medical records at the time of the patient who is indicated to cancel FET cycle such as insufficient endometrial thickness, loss of embryo viability during thawing, other
2. Implantation rate (number of gestational sacs containing a living embryo implanted in the uterus divided by the number of embryos transferred) measured from medical records 6 weeks after embryo transfer
3. Clinical pregnancy rate as measured by rising beta hCG levels starting at 14 days post embryo transfer, presence of gestational sac at 6-7 weeks post embryo transfer, and presence of fetal heartbeat at 6-7 weeks post embryo transfer

Completion date
31/03/2022

Eligibility

Key inclusion criteria
1. Women aged 18-45
2. No history of uterine intervention: suction or endoscopy
3. Has FET indication
4. Has at least one excellent/good frozen embryo before thawing
5. No pathological background: diabetes, high prolactin level, thyroid disorders, adrenal gland disorders.
6. Agree with FET indication
7. Volunteer to the study and has full contact information

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Female

Key exclusion criteria
1. BMI > 30
2. Egg or embryo donor/receiver
3. Estradiol contraindication
4. Estradiol usage > 27 days
5. Not qualified for FET
6. Abnormal uterine, fallopian tube related to implantation
7. Endocrine disorders (kidney, liver or cardiac disease)
8. Patient does not agree to participate in the study
9. Patient does not adhere to the study
10. Does not follow drug prescription:
10.1. Patient forgot to consume drug for more than 2 consecutive or non-consecutive days
10.2. Patient stops using drug due to personal reasons
11. Late follow-up examination
12. Cannot read or write Vietnamese

Date of first enrolment
04/05/2020

Date of final enrolment
31/12/2021

Locations

Countries of recruitment
Viet Nam

Study participating centre
Hung Vuong Hospital
128 Hong Bang Street
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Ho Chi Minh city
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749099

Sponsor information

Organisation

Hung Vuong Hospital

ROR
https://ror.org/04qrwnv94

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Hung Vuong Hospital

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			29/03/2022	No	No
Dataset	Text in Vietnamese	19/08/2022	19/08/2022	No	No
Protocol file	in Vietnamese version 4	01/04/2020	19/08/2022	No	No