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Comparing two routes of administration of progesterone hormone for support in fertilization via intrauterine insemination

Submission date
22/08/2020

Recruitment status
No longer recruiting

Registration date
04/11/2020

Overall study status
Completed

Last Edited
05/11/2020

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Infertility is when a couple cannot get pregnant (conceive) despite having regular unprotected sex. It is estimated that around 1 in 7 couples experience infertility. Fertility treatments can include assisted conception such as intrauterine insemination (IUI). Intrauterine Insemination (IUI) is a treatment that involves inserting sperm inside a woman's uterus. The goal of this treatment is to increase the number of sperm that reach the fallopian tubes and subsequently increase the chance of fertilization.

Alongside IUI, support for the preparation of the lining of the uterus to receive a fertilized egg may also be given. The luteal phase of the menstrual cycle, which occurs after ovulation (when the ovaries release an egg), involves the lining of the uterus becoming thicker to prepare for a possible pregnancy. Progesterone supplementation is the first-line of treatment during IUI if there is a deficiency in the luteal phase. Previous studies suggest that progesterone supplementation improves clinical pregnancy and live birth IUI treatment.

Progesterone can be administered via the mouth (oral), vagina, or injection into a large muscle. Vaginal administration results in higher uterine concentrations, but is often uncomfortable in the presence of vaginal bleeding, or may be washed out if bleeding is severe. The vaginal route also associated with vaginal irritation, discharge, bleeding, and interference with sex. Oral administration requires a higher concentration in order to compensate for the breakdown of the drug in the liver, but is generally the easiest and most acceptable method for the patient. Oral dydrogesterone is a synthetic progesterone with that could overcome these issues.

A previous study has shown that oral dydrogestrone is as effective as vaginal progesterone for luteal phase support in women undergoing IUI cycles and that participants were more satisfied with the oral medication.

The aim of this study is to compare the effect of oral dydrogesterone with vaginal progesterone for the luteal phase support on the pregnancy outcomes of IUI cycles.

Who can participate?
Patients who will be undergoing IUI treatment.

What does the study involve?
Participants will be identified by the researcher from the clinic's census book during IUI treatment and will be assessed for eligibility. The researcher will explain the study to the patients and obtain their informed consent to participate.

Participants will be randomly assigned into 2 groups, A and B. Those in group A will receive Dydrogesterone (a tablet taken by mouth) 10mg twice per day, and those in group B will receive progesterone (also known as Uterogestan, applied in the vagina) 200mg twice per day. This medication will be taken before IUI and for 2 weeks after IUI.

A blood test of a hormone used to diagnose pregnancy, beta human chorionic gonadotropin (BHCG), will be checked two weeks after IUI. If this test is positive then the medication will be continued until 12 weeks of pregnancy. Measuring this hormone is a standard procedure at the study center. A transvaginal ultrasound will be performed at 6 weeks of pregnancy to confirm clinical pregnancy. This is a standard procedure at the study center. If blood tests and ultrasound confirm pregnancy, the patient will be followed up again at 12 weeks of pregnancy.

Participants will be able to report on their satisfaction with the medications and the study in questionnaires provided after 2 weeks on the study medication.

What are the possible benefits and risks of participating?
The chance of possible benefits to the participants is not known. Information obtained from this study will help improve the treatment or management of other patients with the same disease or condition.

This study uses two medications, these may cause some discomfort (vaginal irritation, and excessive vaginal discharge) but no serious adverse effects are expected. These medicines are not recommended for use in patients with a known allergy to Dydrogesterone or micronized vagina progesterone. If a participant develops any complications, the primary doctor will be informed and the participant will be managed accordingly.

Where is the study run from?
Reproductive Clinic of University Malaya Medical Center (Malaysia) and Hospital Tengku Ampuan Rahimah (Malaysia)

When is the study starting and how long is it expected to run for?
From July 2020 to May 2021

Who is funding the study?
University Malaya Medical Center (Malaysia)

Who is the main contact?
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Contact information

Type(s)

Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Comparison of oral dydrogesterone with vaginal progesterone for luteal phase support in intrauterine insemination

Study objectives
Oral dydrogesterone is non-inferior to vaginal progesterone for luteal phase support in woman undergoing IUI cycles

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/07/2020, University of Malaya Medical Center Clinical Research Ethics Committee (University Malaya Medical Center, Lembah Pantai, 59100 Kuala Lumpur, Malaysia; +60 (0)3-79493209/225; iresearch@ummc.edu.my), ref: 202039-8363

Study design
Multicenter randomized controlled trial

Primary study design
Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied
Female infertility

Interventions
This is a randomized controlled trial, carried out in the reproductive unit in University Malaya Medical Centre and in multicenter hospitals that have sufficient and appropriate expertise and experience in intrauterine insemination (IUI). All patients who will be undergoing IUI treatment and who fulfill the inclusion criteria will be recruited to participate in the study. The recruitment procedure will be as follows:
1. The patients will be identified by the researcher from the clinic's census book during IUI treatment and follow up
2. The patients will be assessed for eligibility before recruited into this study using the Eligibility Form
3. The researcher will explain the study protocol to the patients and obtain their informed consent
4. The researcher will obtain socio-demographic data from the patient directly and from their medical records
5. Patients who do not fulfill inclusion criteria will be excluded. Proforma will be filled up once the patients are recruited in the study
6. Randomization will be done once the consent form is signed by the patient
7. Patients will be randomized into 2 groups, A and B. Randomisation will be using a random number generator at Random.org in random one block
8. The random allocation sequence will be placed in sealed numbered opaque envelopes for a strict number order assignment to participants
9. Randomisation will be done by opening the lowest remaining numbered sealed envelope
10. Those in group A will receive oral Dydrogesterone 10mg twice per day and those in group B will receive vaginal micronized progesterone (Uterogestan) 200mg twice per day until IUI
11. The decision to proceed with IUI is made by the usual care provider
12. Luteal phase support will be started after IUI with Dydrogesterone 10mg twice per day in group A, and vaginal micronized progesterone 200mg twice per day in group B for 2 weeks after IUI occurs
13. Serum Beta human chorionic gonadotropin (BHCG) will be checked two weeks after IUI. If serum BHCG is positive (>25) then the medication will be continued until 12 weeks of pregnancy. Measuring serum BHCG is a standard procedure for IUI at the study center. 3 ml of blood for each serum BHCG will be taken and will be sent to the UMMC laboratory.
14. Patient satisfaction will be obtained from patients based on questionnaires after 2 weeks on the study medication
15. A transvaginal ultrasound will be performed at 6 weeks of pregnancy to confirm clinical pregnancy. TVS is a standard procedure for IUI at the study center
16. If serum BHCG is >25 and clinical pregnancy is confirmed, the patient will be followed up again at 12 weeks of pregnancy for a trans abdominal ultrasound scan to confirm the viability of the pregnancy. If serum BHCG is <25, the participants will be counseled if they are keen to continue with another cycle of IUI or to proceed with IVF.
17. The patient will be terminated from the study if they develop an allergic reaction towards the medication or refuse to continue with the study
18. Clinical pregnancy rates, abortion rates, and patient satisfaction in both groups will be compared and will be recorded in case record form

Intervention Type

Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Oral dydrogesterone 10mg BD and vaginal micronized progesterone 200mg BD (Uterogestan)

Primary outcome(s)
1. Clinical pregnancy rate outcome measured using serum BHCG at 2 weeks, transvaginal ultrasound scan at 6 weeks, and follow-up appointment trans abdominal ultrasound scan at 12 weeks
2. Miscarriage rate measured using serum BHCG at 2 weeks, transvaginal ultrasound at 6 weeks, and follow-up appointment trans abdominal ultrasound scan at 12 weeks

Key secondary outcome(s))
1. Patient satisfaction measured using investigator-designed questionnaires at 2 weeks

Completion date
31/05/2021

Eligibility

Key inclusion criteria
1. Infertile women
2. Aged <40 years
3. Undergoing ovarian stimulation with gonadotropins for intrauterine insemination treatment
4. Normal hormonal assay
5. Normal pelvis in transvaginal sonography

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Key exclusion criteria
1. Basal levels of FSH ≥10 mlU/ml
2. Endometriosis stage 3 or 4
3. Severe male factor infertility

Date of first enrolment
01/09/2020

Date of final enrolment
01/03/2021

Locations

Countries of recruitment
Malaysia

Study participating centre
Reproductive Clinic
University Malaya Medical Centre
Lembah Pantai
Kuala Lumpur
Malaysia
59100

Study participating centre
Reproductive Clinic
Hospital Tengku Ampuan Rahimah
Jalan Langat
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41200

Sponsor information

Organisation
University Malaya Medical Centre

ROR
https://ror.org/00vkrxq08

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University Malaya Medical Centre

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version V1.0	09/03/2020	05/11/2020	No	No