Informed consent form and informed notice page

Comparison of the effectiveness and safety of the full-down regulation of early ovarian follicle phase and mid-luteal phase for controlled hyperstimulation: a single-center, randomized, controlled trial

Project Number: SAHoWMU-CR2019-07-115
Version number: 01
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Unit responsible for the experiment: Second Affiliated Hospital of Wenzhou Medical University, Yuying Children's Hospital

Test statistics unit: Second Affiliated Hospital of Wenzhou Medical University, Yuying Children's Hospital

Person in charge of clinical researcher: Ying Yingfen

Informed consent form and informed notice page

Dear patient:

The doctor has diagnosed you as an infertility patient. We will invite you to participate in a prospective randomized controlled study. This study compares the effectiveness and safety of a full-scale downregulation superovulation protocol for early follicular phase and mid-luteal phase: a single-center, randomized, controlled trial project, subject number : SAHoWMU-CR2019-07-115. This research protocol has been reviewed by the Medical Ethics Committee of the Second Affiliated Hospital of Wenzhou Medical University and agreed to conduct clinical research.

Before you decide whether to participate in this study, please read the following as carefully as possible. It can help you understand the study and why it was carried out, the procedure and duration of the study, and the benefits, risks, and discomforts that may be brought to you after participating in the study. If you want, you can also discuss with your relatives and friends, or ask the doctor to explain and help you make a decision.

一、 Research background and research purpose

1.1 Disease burden and treatment status

Since the birth of the first test-tube baby in 1978, in vitro fertilization-embryo transfer (IVF-ET) has become an important means for infertility treatment in countries around the world. IVF-ET treatment requires different ovulation induction protocols. At present, the commonly used controlled hyper-ovulation schemes in clinic are divided into GnRH-a down-regulation schemes and non-GnRH-a down-regulation schemes according to whether gonadotropin releasing hormone agonist (GnRH-a) is used. It is a key problem to be solved in clinical work to develop an individualized controlled super ovulation program for patients in order to obtain high-quality eggs and high-quality embryos, improve clinical pregnancy rate and live birth rate, and reduce the occurrence of complications.

The early follicular phase ultra-long program due to the controlled ovarian hyperstimulation (COH) before the full amount of GnRH-a injection, so that the test tube baby patient's ovulation promotion cycle can obtain a more ideal number of eggs, increase the endometrium for embryo transfer Tolerability, suppression of endogenous LH peaks, and reduction of cycle cancellation rate showed obvious advantages. The mid-luteal corpus luteum long-term plan also applies the full amount of GnRH-a in front of COH, and its down-regulated pharmacological mechanism of action is similar. Our previous retrospective studies have shown that the two programs have comparable clinical effects. However, at present, whether the clinical and perinatal outcomes of the early follicular phase ultra-long regimen have the same benefits as the mid-luteal phase ultra-long regimen have not been prospectively reported at home and abroad.

1.2 Purpose of this study

In the early long follicular phase, a full-length long-acting dose of GnRH-a (3.75mg) before COH can greatly reduce the number of injections of patients, thereby increasing the patient's good compliance under the premise of improving the clinical benefit of patients. This modified ultra-long program is a new IVF program following the traditional luteal phase long program. This scheme greatly improves the clinical benefit of patients by improving endometrial receptivity and improving the internal environment for embryo implantation.

1.3 Number of study participants and expected participants

The Second Affiliated Hospital of Wenzhou Medical University, 1150 cases.

2. Who should not participate in the study

According to different research purposes and research drug regulations,

There are also 1) those with a history of adverse pregnancy, including: repeated abortions: three or more spontaneous abortions, missed abortions, biochemical pregnancy, fetal malformation and history of chromosomal abnormalities / intrauterine fetal death; (2) one side of the ovary After resection; (3) Patients with the following uterine abnormalities: uterine malformation (single horn uterus, double horn uterus, double uterus, mediastinal uterus); submucosal uterine fibroids; intrauterine adhesions; (4) one of the husband and wife Abnormal; (5) Patients with contraindications to assisted reproductive technology or contraindications to pregnancy: such as uncontrolled diabetes, undiagnosed liver and kidney dysfunction, history of deep vein thrombosis, history of pulmonary embolism, history of cerebrovascular accident, uncontrolled Hypertension, heart disease, suspicious cervical cancer, endometrial cancer, breast cancer or previous medical history, unclearly diagnosed vaginal bleeding; (6) unable to follow up regularly or complete this study from all aspects; (7) is participating in other clinical trials By;

3. What will I need to do if I participate in the research?

1. Before you are enrolled in the study, the doctor will ask, record your medical history, and perform test tube baby related examinations.

You are a qualified enrollee. You can voluntarily participate in the study and sign an informed consent form.

If you do not want to participate in the research, we will treat it according to your wishes.

2. If you voluntarily participate in the study, you will proceed as follows:

Patients who meet the enrollment criteria complete all trial examinations at menstruation D3, and then obtain a random group number from the random assigner of the project. If it is an early follicular phase plan, then a GnRHa 3.75mg prescription is prescribed directly by the competent physician for weekly entry; if It is a mid-luteal regimen. A prescription of GnRHa 3.75mg medicine is prescribed by a physician, instructing patients to take weekly injections at a specific time point during mid-menstruation.

Regardless of the early follicular phase or the mid-luteal phase, all patients returned to the competent physician about 34 days after the downregulation, according to the hormone level of pituitary suppression and follicular recovery, Gn activation was performed, when the diameter of 2 follicles was ≥18mm or more than 3 Trigger and retrieve eggs with follicles ≥17mm. Selective single blastocyst transplantation on the 4th-6th days after egg retrieval. Blood is drawn 12 days after transplantation to see if pregnancy, such as pregnancy, continue to be followed up for one to two times until 42 days postpartum.

3. Other matters that require your cooperation

You must come to the hospital with the general medical record and personal treatment diary card at the follow-up time agreed by the doctor and you (the doctor may know your situation by telephone or on the way during the follow-up phase). Your follow-up is very important, because the doctor will judge whether the treatment you received is really working and guide you in time.

You must follow the doctor's instructions for medication and ask you to fill in your medication records in a timely and objective manner. Each time you follow up, you must return the unused medicine and its packaging, and bring other medicines you are taking, including medicines that you must continue to take if you have other complications.

You cannot use other medications related to ovulation induction during the study. If you need other treatment, please contact your doctor in advance.

4. Possible benefits of participating in research

The improved super-long program is gradually becoming the mainstream program in many large domestic reproductive centers. It includes the early follicular phase super-long program or the mid-luteal super-long program. It is also the mainstream program of the reproductive center in the past 5 years, with a standard age success rate of 60 %. It is suitable for a wide range of people: blocked fallopian tubes, decreased ovarian reserve, endometriosis, polycystic ovary syndrome, and male infertility. It combines blastocyst culture and transplantation, which greatly improves your pelvic implant environment and reduces the level of inflammatory factors such as IL-2; inhibits the rise of LH / P levels, increases the tolerance of the endometrium to the embryo, and greatly improves the embryo Implant rate, thereby increasing your clinical pregnancy rate and fetal live birth rate of patients, and truly let you get your baby in the shortest possible time.

Although we already have retrospective evidence in the early stage that the early follicular phase ultra-long regimen or mid-luteal phase ultra-long regimen has satisfactory results, this does not guarantee that it will definitely work for you, because each individual's response to different regimens sometimes varies. The early follicular phase ultra-long regimen or mid-luteal phase ultra-long regimen adopted in this study is not the only method of IVF. If one of the above options is not effective for your condition, you can ask your doctor about possible alternative treatments.

V. Possible adverse reactions, risks, discomfort and inconvenience in participating in the study

The modified ultra-long regimen requires a full injection of 3.75mg GnRHa after menstruation or ovulation after evaluating the cause of your infertility, and some patients will experience a little vaginal bleeding within a month or so after the down regulation , This may cause discomfort to individual patients, and may suspect that he had menstrual blood after playing GnRHa. In fact, this kind of vaginal bleeding after GnRHa is the normal reaction of the endometrium to GnRHa down regulation. Do n't worry, if there is a little bleeding, you do n't need to go to the hospital for a review within a week, because this is a transient endometrial reaction. If individual patients have a lot of bleeding and the duration is long, they can return to the hospital for follow-up. We will use vaginal ultrasound to evaluate the endometrium, and if necessary, give symptomatic treatment such as anti-inflammatory drugs.

6. Related expenses

The patient ' s test-tube baby plan will select the appropriate ovulation-promoting plan according to your actual infertility cause. The entire process is carried out in accordance with the test-tube baby treatment process: including the routine test of the male and female related items before the test-tube baby. Test tube baby medication, egg retrieval, transplantation, corpus luteum support, etc. are all implemented in accordance with the routine diagnosis and treatment plan, without adding any additional costs, so your test tube baby costs are still borne by you.

The doctor will do his utmost to prevent and treat injuries that may be caused by this study. If an adverse event occurs in a clinical trial, the Medical Experts Committee will identify it as related to this research trial. The sponsor will provide treatment costs and corresponding economic compensation for the trial-related damages in accordance with the provisions of China's "Quality Management Standards for Drug Clinical Trials."

For other diseases that you are merging at the same time, such as abnormal thyroid function and high blood pressure, you still need to solve the related expenses yourself.

7. Confidentiality of personal information

Your medical records (research medical records / CRFs, test forms, etc.) will be kept intact in the hospital you are visiting. The doctor will record the results of the tests and other tests on your medical record. Researchers, ethics committees, and drug regulatory authorities will be allowed to review your medical records. Any public report on the results of this research will not disclose your personal identity. We will make every effort to protect the privacy of your personal medical information to the extent permitted by law.

According to medical research ethics, in addition to personal privacy information, the test data will be available for public inquiry and sharing. The query and sharing will be limited to network-based electronic databases, ensuring that no personal privacy information will be leaked.

8. How to get more information?

You can ask any questions about this research at any time and get corresponding answers.

If there is any important new information during the study, which may affect your willingness to continue to participate in the study, your doctor will notify you in time.

9. Can voluntarily choose to participate in the study and withdraw from the study

Whether to participate in the study depends entirely on your wishes. You can refuse to participate in this study or withdraw from this study at any time during the study. This will not affect the relationship between you and the doctor, nor will it affect the loss of your medical or other interests.

For your best interests, the doctor or investigator may suspend your participation in the study at any time during the study.

If you withdraw from the study for any reason, you may be asked about your use of the test drug. If the doctor thinks it is necessary, you may also be required to undergo laboratory and physical examinations.

10. What should I do now?

Whether or not to participate in this study is up to you (and your family).

Before you make a decision to participate in the study, please ask your doctor for questions as much as possible.

Thank you for reading the above materials. If you decide to participate in this study, please tell your doctor, he / she will arrange all matters related to the study for you.

Please keep this information.

Informed consent form. Signed consent page

Name of Clinical Research Project: Comparison of the Effectiveness and Safety of Super-ovulation Promoting with Full-scale Downregulation of Early Follicular and Mid-Luteal: A Single Center, Randomized, Controlled Trial

Project Undertaking Unit: Second Affiliated Hospital of Wenzhou Medical University

Project collaboration unit: None

Subject task book number:

Consent statement

I have read the above introduction about the study and have the opportunity to discuss and raise questions with the doctor about the study. All the questions I raised were answered satisfactorily.

I know the risks and benefits that may arise from participating in this study. I know that participation in the study is voluntary, and I confirm that there is sufficient time to consider this, and I understand:

- I can always consult the doctor for more information.
- I can withdraw from this study at any time without discrimination or retaliation, and medical treatment and rights will not be affected.

I also know that if I withdraw from the study halfway, especially if the drug causes me to withdraw from the study, if I tell my doctor about the changes in my condition and complete the corresponding physical examination and physical and chemical examination, it will be very beneficial to the entire study.

If I need to take any other medical treatment due to changes in the condition, I will seek the doctor's advice in advance, or tell the doctor truthfully afterwards.

I agree to the ethics committee of the drug regulatory authority or the sponsor ' s representative to access my research materials.

I will get a signed and dated copy of the informed consent.

In the end, I decided to agree to participate in this study, and I promised to follow the doctor's advice as much as possible.

Patient's signature: _____ year _ month _ day

contact number:

I confirm that I have explained to the patient the details of the trial, including its powers and possible benefits and risks, and given him a copy of the signed informed consent.

Doctor's signature: _____ year _ month _ day

Doctor's work phone: