

THE INFLUENCE OF HORMONE REPLACEMENT THERAPY IN PREPARATION FOR EMBRYO TRANSFER IN ASSISTED REPRODUCTIVE TECHNOLOGIES

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Abstract. Among hormonal drugs used in assisted reproductive technology (ART) programs, estrogens occupy a special place. If the prescription of progesterone drugs to support implantation and early pregnancy is quite clearly defined and legitimate, the advisability of using estrogens is far from obvious and needs clarification. It refers to the use of estrogens with a “poor response” of the ovaries to stimulation, thin endometrium, in programs with donor oocytes and embryos, in treatment cycles using cryopreserved/thawed embryos, with support for the post-transfer period and in the early stages of pregnancy.

Keywords: embryo, ART (assisted reproductive technologies), ECO, ICSI, infertility.

INTRODUCTION. ART (assisted reproductive technologies) are modern methods of treating infertility, which include influencing a woman’s body to stimulate the functions of the ovaries, various manipulations with eggs, sperm and embryos, as well as creating optimal conditions for implantation and development of the embryo. ART makes it possible to achieve pregnancy even in very difficult cases. In addition, IVF with PGT (preimplantation abortion of embryos) allows you to achieve the birth of a healthy child if the risk of genetic pathologies in the fetus is high. ART includes various methods, including:

-ECO. In vitro fertilization is widely used to treat various types of infertility and prevent the birth of a child with genetic pathology;

-ICSI (intracytoplasmic sperm injection). The technology is used to treat severe forms of male infertility (up to the complete absence of germ cells in the seminal fluid);

-IVI. Intrauterine insemination, which involves the introduction of pre-treated sperm into the uterine cavity, is closest to the process of natural conception;

-donation of germ cells and embryos. This method is used if patients do not have their own gametes or they are not suitable for fertilization due to low quality;

-surrogacy. The technique gives the opportunity to become mothers for those women who, due to serious health problems, cannot carry a pregnancy to term and give birth on their own;

-cryopreservation of gametes and embryos, which at ultra-low temperatures can be stored for a very long time without losing their original properties. In the future, they can be thawed and used in an ART cycle.

MATERIALS AND METHODS. ECO-The essence of the method is that fertilization does not occur in the woman’s body, but in laboratory conditions.

As a rule, hormonal stimulation of ovulation is carried out first. The goal of this stage is to obtain not one, as is usually the case, but several mature eggs at once. As a result, the chances of program success increase significantly.

During the puncture, doctors obtain follicular fluid, from which oocytes are then isolated.

The embryological stage involves:

-fertilization itself, the result of which is assessed after 24 hours;

-growing embryos to the blastocyst stage, when the chances of successful implantation after transfer are highest. Embryos are cultivated in multi-gas incubators, where conditions are created that are as close to natural as possible. The process of their development is regularly monitored by making notes in journals.

Then the embryos (no more than two, usually only one) are transferred into the uterine cavity. Some of them (or even all, if transfer in a given cycle is not practical) can be vitrified and used in future ART cycles. Possible complications of IVF include primarily ovarian hyperstimulation syndrome, caused by the introduction of hormonal drugs at the initial stage of the program. OHSS develops in less than 2% of cases. To prevent complications, Nova Clinic uses personalized stimulation based on objective genetic analysis data.

ICSI. The technology assumes:

-sperm selection, including both visual assessment of gamete quality and the use of additional techniques (for example, PIXI);

-introduction of each male germ cell with the best characteristics inside one of the oocytes. For this, the embryologist uses special microinstruments.

The resulting embryos, as in the previous case, are cultivated in incubators and then transferred to the uterine cavity. In other words, IVF and IVF/ICSI programs fundamentally differ only in the method of fertilization.

ICSI is effective for severe forms of male infertility.

To obtain sperm, if they are not in the seminal fluid, surgical methods are used to extract cells from the tissue of the testicle or its epididymis.

Intrauterine insemination. The essence of the method is that sperm is introduced into the patient's uterine cavity using a catheter. IUI is fundamentally different from IVF in that fertilization occurs in the woman's body. Most often the method is used:

-with minor disorders of spermatogenesis;

-if a woman does not have a sexual partner (donor ejaculate is used).

Treatment of female infertility can be carried out using different methods. Thus, conservative therapy and surgery are often used to restore fertility. If such methods did not give or initially could not give a positive result, assisted reproductive technologies come to the rescue. Indications for the use of ART include:

-impaired patency and/or function of the fallopian tubes;

-cervical factor, when, due to the properties of cervical mucus, sperm cannot move through the woman's genital tract;

-involuntary spasm of the pelvic floor muscles, preventing sexual intercourse (vaginismus);

-the woman does not have a sexual partner;

-disruption of the activity of the endocrine glands (for example, the thyroid gland), if the use of other methods did not lead to pregnancy;

-late age, when both the quantity and quality of oocytes begin to decline sharply;

-a decrease in the supply of follicles in the ovaries, not associated with age;

-endometriosis (if other methods did not allow pregnancy);

-infertility, the causes of which could not be identified during the examination;

-various pathologies in which pregnancy and childbirth are contraindicated (for example, absence or severe deformation of the uterus, renal or liver failure, severe forms of diabetes).

THE ROLE AND DISCUSSIONS.

DONATION OF OOCYTES AND EMBRYOS. Order 107n* defines the following indications for the program "oocyte donation":

-absence of oocytes due to natural menopause, premature ovarian failure syndrome, syndrome resistant ovaries, condition after oophorectomy, radiotherapy or chemotherapy, genetic diseases;

-unsuccessful repeated attempts at the IVF program

(ICSI) (3 or more) with insufficient ovarian response to stimulation of superovulation, repeated receipt of low-quality embryos, the transfer of which does not lead to pregnancy, decreased ovarian reserve. Indications for IVF using donor embryos are:

- a) the partners lack their own germ cells;
- b) high risk of developing hereditary diseases;
- c) repeated receipt of low-quality embryos, transfer which does not lead to pregnancy (with 3 or more IVF attempts).

Order 107n states: "Embryos for donation can be obtained as a result of fertilization of donor oocytes with donor sperm. For the purpose of donation, embryos left after IVF patients can be used, subject to their mutual written consent. It is allowed to use fresh and cryopreserved donor embryos. When using donor embryos, recipients must be provided information about external data, as well as medical results, medical genetic examination of donors, their race and nationality."

Hormonal support in an IVF cycle using donor oocytes and embryos in women with ovarian failure (testimony see above: order 107n, paragraph "a"). Estrogens are prescribed from the 1st day of artificial menstruation cycle, usually at a dose of 2-4 mg when using transdermal forms, which corresponds to 4-8 mg in relation to drugs used orally. During the embryo transfer cycle, the condition of the endometrium is assessed for Day 7. If the thickness is less than 7 mm or its structure indicating estrogen deficiency, estrogen dose can be increased by 2 mg when administered transdermally, which corresponds to 4 mg oral reception. Support of the luteal phase of the menstrual cycle with gestagens begins on the day of follicle puncture or the next day. For this Vaginal and oral forms of progesterone preparations can be used for purposes. When pregnancy is confirmed by biochemical indicators, and then, according to ultrasound data, estrogen therapy is continued with a gradual dose reduction and canceled by the end of the first trimester (by the 12th obstetric week, 10 weeks after embryo transfer). Hormone therapy with progesterone drugs is usually continued until the due date 12-16 weeks.

ART PROGRAMS WITH TRANSFER OF CRYOPRESERVED EMBRYOS. Technological advances, including the development of vitrification techniques, have made embryo cryopreservation one of the main methods for increasing the chances of pregnancy in the calculation for a stimulated cycle. Indications for cryopreservation of embryos can be divided into 3 groups: the presence of normally developing tissues remaining after the transfer embryos

-presence of contraindications for embryo transfer in this cycle (threat of developing severe forms of OHSS, patient's illness, etc.)

-impossibility of performing embryo transfer due to the occurrence of non-medical problems (urgent need departure, etc.).

There are two options for transferring thawed embryos:

-in the natural menstrual cycle, when one's own ovulation is monitored without adding any hormonal drugs, the transfer is carried out depending on stage of embryo development (3-5 days after ovulation).

-against the background of hormone replacement therapy, which is aimed at ensuring proper preparation of the endometrium for transfer embryo. Estrogens are prescribed either from 1-2 days to suppress ovulation, or from the 7th day of the menstrual cycle under ultrasound control for endometrial proliferation in a dose of 2 - 4 mg / day with transdermal administration, which corresponds to 4-8 mg orally.

Hormonal support for the luteal phase of the stimulated cycle and early pregnancy is carried out similarly to that described in section "Hormonal support in an IVF cycle using donor oocytes and embryos":

CONCLUSION. Estrogens have been used in obstetric practice for more than half a century. The identified connection between cases of vaginal cancer in girls, born to mothers who took diethylstilbestrol during pregnancy prompted manufacturers of estrogen drugs include pregnancy in the list of contraindications for their use. This contributed to the formation of a cautious attitude among both doctors and patients towards the use of estrogens, even to the point of abandoning them to stop bleeding when there is a threat of termination of a spontaneous pregnancy. At the same time, there is no information in the literature about experimental studies or clinical observations proving the presence of a teratogenic effect in modern estrogen preparations, in particularly estradiol. Just as there is no data on studies that meet the requirements of evidence-based medicine that would indicate developmental disorders of the reproductive organs and psychosexual development of children whose mothers received steroid hormones during pregnancy. Clinical practice shows that abrupt withdrawal of estrogens, prescribed to the patient as part of hormonal support, may because of termination of pregnancy, as it inevitably leads to decline in concentration and deficiency of sex hormones. Rational The tactic is the gradual abolition of estrogens and their cessation use during the period from 8 to 12 weeks of pregnancy (start time formation and hormonal activity of the placenta).

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