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ANOVULATORY INFERTILITY ASSOCIATED WITH THE INSOLVENCY OF THE ENDOMETRIUM

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Abstract:

Female infertility is a very important problem of modern gynecology and reproductive science (the prevalence of female infertility in different countries of the world is 1.5-12%) and is an important interdisciplinary problem. The overall frequency of female infertility as a result of gynecological and extragenital diseases does not decrease below 21%. Objective of the study: to estimate the percentage of infertile women and to conduct a study of the causes of female infertility. Analysis of the obtained data showed that the most common causes of female infertility are: polycystic ovary disease - 25%, anovulatory cycle - 21%; hormonal disorders - 18%; obstruction of the fallopian tubes - 12%; anomalies in the development of the genitourinary system (vaginal atresia, complete or incomplete septum in the uterine cavity, uterine atresia) - 9%; change in the viscosity of cervical mucus - 7%; premature menopause — 2–3%. Conclusions: early diagnosis and timely treatment of gynecological and extragenital diseases can play a significant role in maintaining a woman's health, but the initial manifestations of these diseases are mostly latent and can only be detected by targeted screening.

Keywords: endometrium, female infertility, anovulatory infertility, ultrasound examination

According to the expert council of the country committee, more than 3 million married couples in Russia need assisted reproductive technologies [1], the effectiveness of which does not exceed 30% [3], which requires further study and optimization of treatment tactics in this category of patients. The state of the endometrium is one of the main factors determining the onset of pregnancy. Despite this, a comprehensive study of the parameters of the endometrium during the so-called "implantation window" still remains one of the unsolved problems of modern reproductive science [6]. Adequate preparation of the endometrium for the period of possible implantation can increase the percentage of successful ART attempts.

THE PURPOSE OF THE STUDY: was to study the clinical aspects of endometrial preparation in patients with infertility.

MATERIALS AND METHODS OF THE STUDY: An analysis of the results of a comprehensive clinical diagnostic and histological study of 36 patients was carried out. The patients had predominantly endocrine infertility. At the stage of preparation for infertility treatment, patients of all groups underwent an examination of the endometrium. Indications for hysteroscopy with morphological and immunohistochemical examination of the endometrium were discrepancy between the echographic picture and the cycle phase, lack of structure, and unclear contours. Hysteroscopy with endometrial biopsy or separate diagnostic curettage of the cervical canal and the walls of the uterine cavity was performed in the private clinic Sarvinoz med clinic. Before the procedure, patients signed voluntary informed consent. Before inserting the hysteroscope, a bacteriological culture for flora and sensitivity to antibiotics was taken from the uterine cavity.

Hysteroscopy was performed according to the standard technique using hysteroscopic equipment. Hysteroscopy was performed without dilation of the cervical canal, or with minimal dilation sufficient for insertion of the hysteroscope. During hysteroscopy, the following were assessed: the condition of the cervical canal mucosa; the shape and size of the uterine cavity; the presence or absence of deformation of the cavity; height, uniformity and color of the endometrium, presence or absence of focal pathology of the endometrium; visualization of the mouths of the fallopian tubes and their condition; in some cases it was possible to visualize the presence of endometrioid passages. Endometrial biopsy or separate diagnostic curettage was performed according to the standard generally accepted technique. Scrapings were placed in 10% formalin solution and sent for histological examination.

During stimulation, ultrasound and hormonal monitoring of folliculogenesis was carried out according

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to the standard technique, which was also the control of the study. Ultrasound monitoring of folliculogenesis was carried out on ultrasound scanners.The condition of the endometrium was assessed on the 2nd-3rd day of the stimulated cycle, and then once every three days during ovulation induction. The following were assessed: M-ECHO thickness, the dynamics of its change during ovulation induction; the appearance of a three-layer structure characteristic of the "mature" endometrium of the late follicular phase, as well as the response of the endometrium to the use of estrogen preparations (Divigel, Progynova) in case of an echographic picture inadequate to the day of the cycle. Ovulation triggers (Decapeptyl 0.3; 10,000 IU Human chorionic gonadotropin) were administered when three leading follicles reached a diameter of ≥ 18-20 mm, an Estradiol level of 300 pmol/l (per follicle), and an endometrial thickness of ≥ 9-10 mm. After confirmation of ovulation by ultrasound, the luteal phase was maintained with progesterone at 200 mcg twice daily for 14 days.

RESULTS OF THE STUDY. In all observation groups, most patients were aged 23 to 36 years; the average age of all examined patients was 26±0.7 years. No significant differences in age were found in the groups of patients: the average age of women with primary infertility was 24.0±0.8 years, with secondary infertility - 26±4.1 years, with an endocrine factor of infertility. The main complaint of all patients was the absence of pregnancy for more than 1 year (from 1 to 16 years, 5.8±0.4 years on average) before seeking help with regular sexual activity without the use of contraception. Most patients were observed for infertility for 1 to 5 years (more than half in the groups with primary and secondary infertility and endometriosis). The average duration of infertility (6.9±0.9 years) in patients with an endocrine factor was slightly higher than in other groups. 41.2% of them had been observed for infertility for 6 to 10 years. From the anamnesis it was found that before contacting us 24 (66.7%) patients had previously failed attempts at treatment with intrauterine insemination with sperm - 10 (27.8%), in different clinics.

The study of the generative function showed that among the examined patients 34 (47.2%) patients had a history of pregnancy, more than half of them (55.9%) - only one. The average number of pregnancies of all the examined women was 0.9 ± 0.1, and a greater number of pregnancies were had by patients with tubal-peritoneal factor of infertility: the average number of pregnancies in this group (1.1 ± 0.2) was significantly higher than in others. The most frequent outcome (38.3%) of all pregnancies was induced abortion, and the average number of induced abortions in the groups of patients with tubal-peritoneal factor of infertility and endometriosis was significantly higher than in the group with endocrine factor of infertility. Other pregnancy outcomes were childbirth, spontaneous abortions; in the group with endocrine factor of infertility, the average number of spontaneous abortions was significantly lower than in other groups, and patients with endometriosis did not have a history of childbirth.

Among the past and concomitant gynecological pathology revealed by the anamnesis, examination and transvaginal ultrasound of the pelvic organs, the most common in the examined patients were inflammatory diseases of the uterine appendages and sexually transmitted infections (in 55.6% and 50.0% of patients, respectively). Benign diseases of the cervix were detected in 30.6% of women, uterine myoma in 22.2%, tumors and tumor-like diseases of the ovaries in 26.4% of women, endometriosis in 38.9%, polycystic ovary disease in 12.5%, hyperprolactinemia in 6.9%, and ovarian reserve depletion syndrome in 4.2% of those examined. A third of patients had indications of one or another pathology of the endometrium.

When comparing the structure of gynecological diseases in the examined patients by groups, some features were revealed. It is natural that endometriosis and endocrine diseases were significantly more common ($p<0.05$) than in others in the groups with the corresponding infertility factor, and inflammatory diseases of the uterine appendages and sexually transmitted infections - in the group with the tubal-peritoneal infertility factor ($p<0.05$). Tumors and tumor-like diseases of the ovaries were significantly less common ($p<0.05$) than in other groups in patients with the endocrine infertility factor. When studying the hormonal profile of patients, it was found that the average values of estradiol (E) and progesterone (P) in the groups did not have reliable differences and were within the reference values of reproductive age. Deviations in estradiol values were detected in 5.6% of patients, progesterone - in 16.7.

Bacteriological culture of material taken from the uterine cavity revealed opportunistic microbes from the streptococcus and enterococcus groups in 22.2% of cases, with a slightly higher frequency in the group with tubal-peritoneal infertility factor. Benign diseases of the cervix were detected in 30.6% of women, uterine myoma in 22.2%, tumors and tumor-like diseases of the ovaries in 26.4% of women, endometriosis in 38.9%, polycystic ovary disease in 12.5%, hyperprolactinemia in 6.9%, and ovarian reserve depletion syndrome in 4.2% of those examined.

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In patients of all three groups, at the beginning of the superovulation stimulation protocol, ultrasound examination revealed poor prognostic factors for adequate endometrial maturation: either linearity of M-ECHO or an increase in endometrial thickness > 5 mm, discrepancy between M-ECHO thickness and the day of the menstrual cycle. All patients of groups I and II required auxiliary therapy with estrogen preparations (Divigel, Proginova) during ovulation induction. Against the background of estrogen therapy, in patients of group II, the M-ECHO parameters examined on the 6th day of the menstrual cycle ranged from 3.5 to 7 mm, on average - 5.64 +/- 1.8 mm. By the time of transvaginal puncture, the endometrial thickness parameters (M-ECHO) ranged from 8.6 to 13 mm, on average - 9.49 +/- 2.2 mm. A distinctive feature of the dynamics of the echo parameters of M-ECHO was the appearance and/or improvement of the M-ECHO structure by the 11th day of the menstrual cycle. In patients of group 1, against the background of estrogen therapy, there was an inexpressible dynamics of the increase in the thickness of the M-echo, often the thickness of the M-echo did not correspond to the day of the menstrual cycle and to the time of transvaginal puncture of the follicles. Indicators of the echographic state of the endometrium Comparative assessment of ovulation induction cycles made it possible to assess the effectiveness of prescribing a short stimulation regimen as the same in all groups. The average total dose of rFSH, stimulation duration, the number of aspirated follicles, oocytes and embryos did not differ from those in the group without the use of HRT. However, the frequency of pregnancy was significantly more often ($p < 0.05$) observed in patients who underwent endometrial preparation with hormone replacement therapy.

CONCLUSIONS.

1. Evaluation of the reproductive system and associated systems is a necessary diagnostic factor for choosing a treatment method in patients with infertility.
2. Preparation of patients for assisted reproductive technology programs taking into account the immunohistochemical characteristics of the expression of receptors to steroid hormones allows not only to individualize the approach to hormone therapy, but also improves the prognosis of the endometrial response to ovulation induction and the use of estrogen drugs.

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