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OPTIMIZATION OF OVULATION INDUCTION IN INFERTILE WOMEN WITH ENDOCRINE INFERTILITY

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Annotation. Today, the diagnosis of polycystic ovary syndrome is based on the provisions of the Rotterdam Convention (2003) and includes, first of all, the diagnosis of hyperandrogenism and oligo/anovulation, which do not allow reproductive function. Other manifestations of PCOS, associated with insulin resistance and dyslipidemia, continue to be widely discussed in the literature. And since the incidence of infertility in women with hyperandrogenism and anovulation reaches 90%, the issues of treatment of such patients are extremely relevant and require a comprehensive solution. This article is devoted to the treatment of anovulation by administering ovulation inducers. Research in the field of reproductive gynecology served as the basis for the synthesis and clinical use of drugs that stimulate ovulation, and thereby make it possible to realize reproductive function.

Key words: *anovulation, polycystic ovary syndrome, ovulation induction, menopausal gonadotropin.*

Endocrine infertility in women, accompanied by anovulation, is the most common form of endocrine disorders [3,6]. Polycystic ovary syndrome (PCOS), being the most common cause of anovulatory infertility [3,5], invariably attracts the attention of scientists [1,3]. The management tactics for patients with PCOS are primarily aimed at correcting hyperandrogenism, eliminating anovulation, regulating the rhythm of menstruation and restoring fertility [2, 4].

Over the past 45 years, the “drug of choice” for the treatment of infertility for anovulatory infertility has been clomiphene citrate. Clomiphene citrate acts to increase pituitary FSH secretion by reducing the negative response to estrogen. But the presence of clomiphene-resistant forms of anovulation (30-40%, according to various authors) limits the use of this ovulation inducer [2,5].

With the synthesis and use in clinical practice of new ovulation inducers: menopausal gonadotropins (hMG), recombinant gonadotropins (rFSH), it became possible to choose a method of treating infertility for anovulation of various origins [1,6]. At the same time, the criteria for adequate selection of an ovulation inducer in the treatment of endocrine infertility without the use of ART are not fully presented in the literature, and the assessment of the effectiveness and side effects of ovulation inducers is sometimes contradictory. If we evaluate an ovulation inducer from the perspective of “the minimum time spent to obtain an effect - the price of the drug,” then the choice of the most adequate, in each specific case, ovulation induction regimen will be relevant and important for clinical practice. This will reduce treatment time and increase the efficiency of restoration of reproductive function in patients with PCOS.

Purpose of the study: to determine the criteria for prescribing ovulation inducers in the treatment of infertility in women with PCOS.

Materials and methods. The study included 56 patients of reproductive age with infertility. The age range was from 21 to 39 years. The duration of infertility varied from 3 to 12 years. All

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patients were examined clinically and laboratory according to the protocols we developed for examining infertile couples to identify the cause of infertility. Clinical blood test, urine test, flora smears, Pap test, biochemical blood test, serum glucose level - no pathology was found. In these patients, RW, HBsAg ELISA, and HIV ELISA were negative. All patients were examined for viral and bacterial infections. The hormonal status of patients (FSH, LH, prolactin, estradiol, progesterone, 17-OH-progesterone, testosterone, DHEAS, cortisol, TSH, T4, AMH) was determined using the ELISA method.

We also performed an ultrasound of the thyroid gland and mammary glands on days 5-7 of the menstrual cycle, studying the structure and presence of pathological foci. Ultrasound examination of the pelvic organs included determination of the size of the uterus, the condition of the endometrium, ovaries and folliculometry. The length, width, anteroposterior size of the uterus, as well as the length, width and thickness of the ovaries were assessed. Patients and their sexual partners were examined for sexually transmitted infections (STIs). All women were diagnosed with tubal patency. All patients were consulted by a therapist in order to exclude pathologies that are a contraindication for pregnancy. In order to exclude male factor infertility, sexual partners were examined (spermogram) - no pathology was found. All patients underwent a postcoital test - positive.

According to the forms of infertility, the criteria for inclusion in the study were: an established diagnosis of PCOS, absence of ovulation, FSH < 15 IU/L, estradiol < 50 pg/ml; endometrial thickness <5 mm, body mass index 18-35.

Exclusion criteria: the presence of tumor-like formations of any location, inflammatory diseases of the pelvic organs of one or both spouses, the presence of sexually transmitted infections, obstruction of the fallopian tubes, sperm infertility.

Depending on the chosen stimulation method, the patients were divided into two groups:

in group 1 – patients with PCOS (16 women), ovulation induction was carried out with human menopausal gonadotropin containing FSH and LH in a 1:1 ratio;

Group 2 included women with PCOS (40 people), whose ovulation induction was performed with clomiphene citrate (CC).

The Patients were diagnosed with PCOS based on generally accepted criteria characterizing this syndrome. Menstrual irregularities with menarche were observed in 100% of patients, of which 93.9% were of the oligomenorrhea type. Anovulation is confirmed by ultrasound (folliculometry) and an ovulation test. BMI in 36 (64.3%), hirsutism in 29 (51.7%), hyperandrogenism in 54 (96.4%), increased LH/FSH ratio in 85.7%, LH concentration in all patients was 16.7±0.4 IU/l. Ultrasound signs of polycystic ovaries were recorded in the majority of patients: an increase in ovarian volume - in 88%, an increase in the ovarian-uterine index - in 80%, a small cystic structure of the ovaries in 98%, of which 24% had a peripheral location of cystic follicles.

Subsequently, each patient underwent folliculometry in a cycle of controlled ovulation induction. Basal ultrasound was performed on the 3rd day of the menstrual cycle. Folliculometry was carried out 3-5 days from the start of administration of ovulation inducers, and then daily from the 7-8th day of the cycle to adjust the dose of administered drugs and record the growth dynamics of the dominant follicle.

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To diagnose pregnancy, a test for the h-CG content in the blood serum was performed on the 14th day and an ultrasound on the 20-21st after the introduction of the ovulation trigger.

The results of the study showed that in group 1 of patients, human menopausal gonadotropin was administered at a dose of 75 units to induce ovulation. in accordance with the instructions for use. The total amount of the drug was 525 -1025 units. The drug human chorionic gonadotropin was used as an ovulation trigger at a dose of 6000 units.

Group 2 was prescribed Clomiphene citrate from the 3rd to the 7th day of the menstrual cycle in doses of 50-100-150 mg per day per os for 3 months. Pregnil 5000 - 10000 units was used as an ovulation trigger.

At the first stage of the work, 40 women of group 2 were prescribed clomiphene citrate 50 mg, but in the first cycle of ovulation induction it turned out that in 6 women there was no ovarian response to the chosen dosage of the drug. These women did not have follicle growth of more than 10 mm, so these patients were prescribed hMG in the next menstrual cycle and, therefore, were included in group 1. In a further study, 34 women remained in group 2. To support the luteal phase of the cycle, we used dydrogesterone (Duphaston) at a dosage of 10 mg 2 times a day. In all women taking clomiphene citrate, insufficient transformation of the endometrium at the time of ovulation was noted.

At the next stage of work, 1 group of patients underwent ovulation induction using direct ovulation inducers.

The results of ovulation induction with hMG did not differ significantly in many parameters; the results were significantly different from ovulation induction with clomiphene citrate. The size of the leading follicle during the administration of the drug was 19.5±0.8 mm, the thickness of the endometrium was 9.2±0.7 mm. When the dominant follicle reached 18 mm and the endometrial thickness was at least 8 mm, ovulation triggers were prescribed (hCG at a dosage of 6000 IU. Ovulation was diagnosed in 100% of cases after 2±1 days.

After the second stage of the study, a group of patients was identified (9) in whom ovulation induction with direct and indirect inducers turned out to be ineffective for restoring reproductive function: absence of ovulation, insufficiently prepared endometrium for implantation of the fertilized egg, lack of growth of the dominant follicle in the ovaries during ovulation induction with normal ovarian reserve. In addition, endoscopic operations on the ovaries, previously performed in 20 of the patients, and IVF methods in 7 patients turned out to be ineffective. These patients were regarded as the most difficult for rehabilitation of reproductive function.

Thus, the presented results indicate the need for further study of the effectiveness of conservative treatment of infertility in PCOS, subject to comprehensive preliminary preparation before ovulation induction and differentiated use of ovulation inducers, taking into account the clinical and anamnestic characteristics of patients, the results of laboratory examinations and analysis of the ovarian response.

Conclusions. The success of treatment of patients with PCOS depends on complex conservative preparation before stimulation of ovarian function and differentiated administration of ovulation inducers depending on the initial characteristics of the patients and the characteristics of follicles and steroidogenesis in the ovaries.

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According to our study, about a third of patients (24.6%) with PCOS are clomiphene-resistant. Prognostic criteria for clomiphene resistance may include older age of patients (over 30 years), increased body mass index, enlarged ovaries with peripheral cysts, surgical treatment of PCOS, elevated LH levels (>15 IU/l) in combination with serum E2 concentrations blood below 150 pmol/l.

Considering the rather high percentage of women with PCOS who are not sensitive to clomiphene citrate, it is necessary to recommend that this category of patients be prescribed recombinant gonadotropins as the first ovulation inducer.

The preference for using hMG as ovulation inducers in women with PCOS remains controversial and requires further comprehensive study.

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