



PRINCIPLES OF RESTORATION OF FERTILITY IN YOUNG AGE WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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Abstract:

Polycystic ovary syndrome (PCOS) is a multifactorial heterogeneous pathology characterized by chronic anovulation, menstrual irregularities, infertility, ovarian cystic changes, and hyperandrogenism. The frequency of PCOS is approximately 11% among women of childbearing age, and in the structure of endocrine infertility it reaches 70%. The purpose of this study is to develop modern methods of treating infertility in women with polycystic ovary syndrome based on the study of clinical, anamnestic and laboratory parameters, some genotypic variants of gene polymorphisms, and folate metabolism. The results of the studies showed that the cause of chronic anovulation and, as a result, infertility in patients with PCOS can be hormonal abnormalities, which were detected in 82% of patients. The most typical for PCOS was an increase in total testosterone - it occurred in 63.3% of patients, an increase in the LH / FSH ratio of more than 2.5 was observed in 51.3% of patients. With rational treatment of infertility, it is possible to restore fertility in 40% of cases.

Keywords: Polycystic ovary syndrome (POS), normalization of body weight, correction of metabolic disorders, stimulation of ovulation, gonadotropin releasing factor antagonists, combined oral contraceptives (COCs), in vitro fertilization (IVF).

RELEVANCE. The high incidence of endocrine infertility is a hallmark of the modern problem of infertile marriages [1, 2, 3, 15, 26]. Polycystic ovary syndrome (PCOS) is one of the most common causes of menstrual and reproductive dysfunction. According to various data, PCOS occurs in the population from 10% to 16.6% [4,6,7,8]. Nearly 70% of women who seek help for infertility have PCOS. At the same time, 60% of patients with PCOS are fertile [4, 5, 7, 8, 11]. In 2003, the European Society for Human Fertility and the American Society for Reproductive Medicine proposed the diagnosis of PCOS based on the mandatory presence of two of the three proposed criteria: hyperandrogenism, chronic anovulation, echographic signs of polycystic ovaries [18, 23, 24]. In recent years, information has appeared in the scientific literature on the role of hyperhomocysteinemia in the development of reproductive failure [6, 9, 12, 17, 19]. It has been established that a high risk of developing vascular and metabolic disorders that occur in PCOS may be associated with hyperhomocysteinemia. However, information about an individual approach to restoring the reproductive function of patients with PCOS, taking into account the form of the syndrome - ovarian, adrenal, mixed - the level of homocysteine, age and

form of infertility is not indicated in the available literature.

PURPOSE OF THE STUDY. Development of modern methods of infertility treatment in women with polycystic ovary syndrome based on the study of clinical, anamnestic, laboratory parameters, some genotypic variants of gene polymorphisms and folate metabolism. The studies included the study of clinical and anamnestic data, analysis of laboratory parameters. The treatment of infertility patients with polycystic ovary syndrome was carried out sequentially with the help of normalization of body weight, correction of metabolic disorders, various protocols for ovulation stimulation, a combination of natural restoration of fertility with a surgical method, and the use of assisted reproductive technologies.

MATERIALS AND RESEARCH METHODS. In order to find out the effectiveness of various methods of restoring fertility in PCOS, 150 patients with suspected PCOS with ovarian infertility were examined at the clinic of the Samarkand Medical Institute No. 1 and the Regional Perinatal Center for the period 2018-2020. When fertility was restored, the observation of pregnant women lasted up to 20 weeks.



The research methods were:

- General medical and general clinical research methods (analysis of complaints, anamnesis of life and illness, body type, BMI, degree of hirsutism, examination of the mammary glands and thyroid gland, gynecological examination)

- Biochemical markers of ovarian reserve (anti-Mullerian hormone, levels of gonadotropins - FSH, LH, FSH / LH, prolactin, estradiol, progesterone, 17-OP, DEAS, total testosterone, free androgen index) on the 5-7th day of the cycle and in dynamics.

- Homocysteine in dynamics.

- Study of the role of various genotypic variants of polymorphisms of the MTHFR (C677T, A1298C), MTR (A2756G), MTRR (A66G) metabolism genes.

- Ultrasound of the pelvic organs with a vaginal probe on the 5th-7th day of the cycle and in dynamics.

- Hysteroscopy followed by diagnostic curettage of the endometrium and morphological examination of the endometrium (if indicated).

The methods of treatment were:

- Normalization of body weight by diets and moderate physical activity, correction of metabolic disorders.

- Restoration of the menstrual cycle (COC + folate, dexamethasone + folate).

- Stimulation of ovulation (clomiphene citrate, rFSH, menopur, AGnRH).

- Surgical stimulation of ovulation (laparoscopy - wedge resection, drilling, stromal endocoagulation).

- Preparing for IVF.

RESEARCH RESULTS. To determine the effectiveness of various methods of restoring fertility, depending on the age and type of PCOS, 150 women with suspected PCOS who had infertility, obesity and hirsutism were examined. Of these: 75 women were with ovarian PCOS, 35 women with adrenal PCOS, 40 women with mixed PCOS.

Among 150 examined patients, clinical signs of hyperandrogenism were detected with the following frequency: obvious hirsutism - in 85 (56.6%) patients; oily skin with acne - in 52 (34.6%) patients.

Determination of body mass index (BMI) showed that 72 (48%) patients were overweight. BMI values from 25 to 29.9 ("preobesity" - a low risk of metabolic complications) were determined in 45 (30%) women; BMI values from 30 to 40 ("obesity" of classes I and II - the average degree of risk of metabolic complications) - in 34 (22.6%) women. Visceral distribution of adipose tissue (ratio OT / OB more than 0.83) was observed in 59 (39.3%) women. Nigroid acanthosis was detected in 15 women (10%). All patients with this symptom had a BMI over 30 and a visceral type of adipose tissue distribution.

The majority of patients with PCOS (82%) had hormonal abnormalities, of which the most common were increased testosterone (in 95 - 63.3% of women) and an increase in the LH / FSH index of more than 2.5 (in 77 - 51.3% of women). To this we can add that among 77 patients with LH/FSH values >2.5, an increased LH level was found only in 56 women, while in 21 other patients it remained normal, i.e. in the latter case, the increase in the LH/FSH index was not due to an increase in LH, but due to a relative deficiency of FSH.

It has been proven that menstrual function returns to normal with a loss of 5 to 10% of body weight in 15 patients (10%). For this purpose, complex metabolic therapy is carried out, including the principles of healthy nutrition and medications. With the normalization of body weight and metabolic disorders in other cases, when the menstrual cycle was not normalized, drugs were prescribed to restore the menstrual cycle. As the 1st line of therapy for hyperandrogenism and restoration of menstrual irregularities - combined oral contraceptives (COCs) + folates. At the same time, menstrual function was restored in 47 (31.3%) women. It took 6 months to achieve results of treatment for acne and hirsutism with COCs. Correction of hormonal deviations was carried out under the supervision of specialists - endocrinologists.

At this stage, spontaneous uterine pregnancy occurred in 25 (16.7%) patients. Multiple (twin) pregnancy was in 1 of 25 (4%) patients. Including 27 registered pregnancies, the proportion of ectopic pregnancy was 7.4% (2). Thus, restoration of reproductive function in patients with PCOS with normalization of body weight and restoration of menstrual functions ensured the incidence of uterine pregnancy at the level of 16.7% (25 out of 150).

Ovulation induction was carried out using clomiphene citrate (CC) to patients in three (maximum) cycles for 5 days (from 5 to 9 days of the cycle) at a dose of 100 mg / day. When stimulated with clomiphene citrate, the adequacy of the ovarian response began to be assessed from the 9-10th day of the cycle by determining the size of growing follicles and determining the concentration of E2 in the blood. In the presence of a mature follicle 18 mm in size, concentration E2 = 500-2000 mmol/l, an ovulatory dose of hCG (pregnyl) 5-10 thousand units was administered. 36-48 hours after the introduction of pregnyl, confirmation of ovulation was carried out according to ultrasound. In patients with anovulatory infertility with early detection of resistance to clomiphene citrate, combinations of CC + rFSH were used to stimulate ovulation.

In total, treatment with ovulation inducers was carried out in 125 patients, the first series of controlled



ovulation stimulation, performed before laparoscopy, included the sequential use of folliculogenesis inducers in three cycles, after which spontaneous uterine pregnancy occurred in 28 (18.6%) of 150 patients.

Laparoscopy was prescribed only after correction of hormonal disorders and confirmation of the ineffectiveness of attempts to restore natural fertility with the help of ovulation inducers. For this reason, endoscopic methods were used only in those women in whom the above method failed. When performing laparoscopy, appropriate surgical treatment was performed to induce ovulation - wedge resection, drilling, stromal endocoagulation. All patients underwent chromoperturbation to assess the patency of the fallopian tubes. After endoscopic operations, to prevent infectious complications, broad-spectrum antibacterial drugs were prescribed in the recommended daily and course doses.

In 97 (64.6%) out of 150 patients with persistent infertility, laparoscopy was prescribed to clarify and treat PCOS, as well as concomitant tuboperitoneal factors of infertility. According to the results of laparoscopy, the examined patients had unilateral or bilateral pathological manifestations that required surgical correction. These 97 patients were re-attempted to stimulate ovulation in three consecutive cycles. Folliculogenesis inducers during repeated stimulation of ovulation in patients were started immediately after operative endoscopy, i.e. did not provide for the expectation of the effect of the surgical treatment itself, which implied a 6-month passive expectation of the onset of a "spontaneous" pregnancy. As a result of re-stimulation of ovulation, uterine pregnancy occurred in 7 (4.6%) patients, ectopic pregnancy - in 1 (0.67%) patient.

Assessing the overall effectiveness of the used treatment algorithm in patients with polycystic ovary syndrome, it can be concluded that the consistent use of the methods of ovulation stimulation described above ensured the onset of uterine pregnancy in 60 (40%) of 150 patients. With the ineffectiveness of methods to restore natural fertility, so-called assisted reproductive technologies are used, in particular in vitro fertilization (IVF). The management of pregnancy and childbirth after IVF generally do not differ from the usual ones. The likelihood of complications during pregnancy is often associated not with artificial insemination as such, but with frequent multiple pregnancy among patients in vitro fertilization and with a high average age of women in labor. IVF is costly and time consuming and does not guarantee pregnancy, but it does give couples who were previously unable to have children a chance to have children.

CONCLUSIONS. Based on the results of the study, we made the following conclusions:

1. Young women with polycystic ovary syndrome should examine homocysteine in order to detect hyperhomocysteinemia and select an effective and reasonable method of treatment.

2. In patients with polycystic ovary syndrome, with rational treatment of infertility, fertility can be restored naturally in 40% of cases. For patients with restored menstrual function, uterine pregnancy was achieved in 16.7%. For patients with anovulatory function of the menstrual cycle, the effectiveness of infertility treatment after ovulation stimulation with clomiphene citrate or CC + rFSH was 18.7%, which is determined by the possibility of correcting anovulation before laparoscopy.

3. Patients who did not have a uterine pregnancy at the stage of restoration of natural fertility are recommended assisted reproductive technologies, including IVF.

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