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OPTIMIZATION OF A FERTILITY RESTORATION METHOD IN OVARIAN RESISTANCE

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Abstract:
Polycystic ovary syndrome (PCOS) is one of the leading causes of endocrine infertility. This study evaluates the effectiveness of conservative, surgical, and combined treatment methods for PCOS. Objective: To evaluate the effectiveness of various fertility restoration methods in patients with PCOS. **Material and Methods:** This prospective study included 70 women with infertility due to PCOS and 20 women in a control group. Clinical, hormonal, metabolic, and ultrasound parameters were analyzed. Conclusions: A combined approach, including conservative therapy followed by surgical intervention, provides more sustainable restoration of reproductive function.

Keywords: Polycystic ovary syndrome, infertility, fertility, laparoscopy, ovulation stimulation.

Introduction

Among patients with endocrine infertility, the proportion of women with PCOS amounts to 73% [1, 2], and in the structure of infertile marriages, this pathology is detected in 20-22% of cases, occupying 5th-6th place. The high relevance of the problem is due to the significant prevalence of the syndrome and its adverse effect on reproductive function. The feasibility of using endoscopic methods in

patients with suspected PCOS has been confirmed by a number of studies [3, 4]. Laparoscopy allows not only to visually assess the condition of the ovaries, but also to perform their biopsy, which helps to clarify the diagnosis and select the optimal treatment tactics. The advantages of the laparoscopic approach compared to laparotomy include minimal surgical trauma, high diagnostic yield, a reduced risk of adhesions in the pelvis and a reduction in the duration of hospitalization [5, 6]. It should be emphasized that the effectiveness of treatment of patients with PCOS is determined not so much by the elimination of morphological changes in the ovaries, but by the restoration of ovulatory function and the achievement of pregnancy. Surgical methods are considered as a second line of therapy for PCOS.

The aim of the study was to evaluate the efficacy of various fertility restoration methods in patients with PCOS. Ninety women were examined. The prospective study included 70 women with infertility and PCOS; the control group consisted of 20 women of reproductive age with regular ovulatory cycles. Therefore, the women included in the main group were divided into three subgroups depending on the treatment methods used. The first subgroup (A) (n=25) included patients in whom the antiandrogen effect was achieved by using combined oral contraceptives (COCs) for at least 3 months, followed by ovulation induction. The second subgroup (B) (n=20) included patients who, after using COCs for 3–6 months, underwent laparoscopic ovarian drilling surgery. The third subgroup (C) (n=25) included patients who underwent laparoscopic drilling surgery without any preliminary preparation. We observed 70 patients with PCOS aged 22 to 37 years (mean age 31.9±1.4 years) suffering from infertility lasting from 1 to 10 years (mean 5.3±1.2 years). In all cases, tubal, cervical, immunological and male factors of infertility were excluded. Research methods For examination of women, generally accepted methods are used, including collection of anamnesis,

complaints, examination and laboratory tests; on the 2nd–5th day of menstruation – follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, free androgen index (DHEA-S, testosterone) and anti-Müllerian hormone, transvaginal ultrasound examination. Impaired glucose metabolism was assessed using a glucose tolerance test (GTT). In addition, fasting plasma insulin concentrations were determined.

Ultrasound examination (US): to determine the condition of the pelvic organs, an ultrasound scan was performed on days 5-7 of the menstrual cycle using the SonoScape 40 (China) apparatus with transvaginal control. At the same time, the morphology of the ovaries was assessed: the number of antral follicles (on days 2-3 of the menstrual cycle), capsule thickness, stromal echogenicity and ovarian volume. The size of the uterus and the thickness of the endometrium were also assessed. Treatment principles: in case of infertility due to PCOS, basic therapy is carried out in two stages: • 1st preparatory stage – normalization of the main regulations of the reproductive system; • 2nd stage – stimulation of ovulation. During the preparatory stage, metabolic normalization, including obesity treatment, was achieved through a hypocaloric diet, physical activity, and orlistat, a gastrointestinal lipase inhibitor, 3 capsules of 120 mg during or after meals (this drug was used due to the lack of incretin drugs in sufficient supply). In cases of hyperinsulinemia or impaired glucose tolerance, metformin was prescribed at 1000 mg twice daily after meals for 6 months. To normalize the menstrual cycle, combined oral contraceptives (COCs) (ethinyl estradiol/drosperenone 20–30 mcg/3 mg) were prescribed for at least 3–6 months. Ovulation was induced using clomiphene citrate or letrozole; if necessary, human chorionic gonadotropin was used under ultrasound guidance. The main group consisted of patients with PCOS, which was divided into 3 subgroups. Depending on this, the effectiveness of conservative therapy and surgical treatment was compared.

Study results. Taking into account the polymorphism of the causes of PCOS development, we analyzed the social risk factors for the development of the disease in the selected groups of women. A comparative analysis of lifestyle factors between the main and control groups revealed statistically significant differences in the frequency of chronic stress ($p=0.0005$) and dietary disorders ($p=0.0011$). Differences in the level of physical activity between the groups were not statistically significant ($p=0.53$); Table 1. It should also be noted that in women engaged in heavy physical labor, PCOS was more pronounced. This may be associated with a relatively increased secretion of steroid hormones of the adrenal cortex under conditions of physical overexertion. Most women in the main group had a history of severe psychoemotional stress in adolescence and over the past 3-5 years, accompanied by a state of chronic stress. It is known that stress increases the secretion of adrenal steroid hormones, which, in turn, could contribute to the secondary development of PCOS. Women with PCOS have been reported to have infertility, which in itself leads to psychoemotional instability and thus aggravates the disease. From a diagnostic perspective, the clinical manifestations of PCOS are of particular interest. Clinical manifestations of PCOS in the examined women can be roughly divided into three main groups: neuropsychiatric changes, including sleep disturbances, irritability, fatigue, and decreased libido; autonomic disturbances, such as unstable blood pressure, edema, and sweating; and metabolic changes, including hirsutism, acne, and decreased ability to lose weight.

An analysis of the selected groups of women showed that the differences in neuropsychiatric disorders between the main and control groups were statistically insignificant. Thus, excitability was observed in 28.6% of women in the main group and 25% of women in the control group ($\chi^2=0.001$; $p=0.975$), sleep disorders were observed in 21.4 and 15%, respectively ($\chi^2=0.10$; $p=0.751$), and

rapid fatigue was noted in 24.3% of women in the main group and in 40% of the control group (χ^2=1.21; p=0.271). Thus, neuropsychiatric symptoms were comparable between the groups, but there was a tendency towards greater fatigue in the control group. Autonomic disorders were significantly more pronounced in women in the main group.

Thus, a comprehensive analysis of clinical manifestations shows that in women of the main group, neuropsychiatric changes did not differ statistically from those in the control group; however, autonomic and metabolic disorders were significantly more pronounced. It is known that body mass index (BMI) characterizes metabolic changes characteristic of PCOS. In the study, participants in the main group (n=70) and the control group (n=20) were distributed according to BMI categories. In women of the main group, normal body weight (BMI 18.5–25) was observed in 24 (34.3%) patients, while in the control group this category predominated – 17 (85%) women. Overweight (BMI 25–30) was observed in 21 (30%) women of the main group and 2 (10%) women of the control group. The first degree of obesity (BMI 30–35) was had by 15 (21.4%) women of the main group and 1 (5%) woman of the control group. The second degree of obesity (BMI 35–40) was observed in 6 (8.6%) women of the main group, the third degree (BMI> 40) – in 4 women (5.7%), in the control group these categories were not observed. Statistical analysis showed that the differences between the main and control groups were statistically significant for the normal body weight category (χ^2=14.15; p=0.00017), which indicates a significant predominance of normal body weight in the control group. Differences in other categories (overweight, I–III degree of obesity) were not statistically significant (p>0.05), although the tendency towards a higher prevalence of obesity in women of the main group is obvious. Thus, in women with PCOS, there is a tendency towards an increasing proportion of overweight and obesity, which emphasizes the importance of

weight control and metabolic factors in the complex therapy of this syndrome. A survey of 70 PCOS patients revealed that most of them experienced various menstrual cycle irregularities from the onset of menstruation. Normal menstruation was observed in 30% of women in the study group and in all women in the control group, a statistically significant difference.

The presented analysis of the hormonal profile revealed the presence of reliable differences between the main and control groups in a number of key parameters. In particular, the level of LH in the main group was statistically significantly higher compared to the control group (16.4 ± 1.3 IU / L versus 5.1 ± 1.2 IU / L), indicating pronounced disorders of the hypothalamic-pituitary regulation of the reproductive system. The concentration of prolactin in patients of the main group was also significantly higher than in the control group (499.6 ± 22.1 mIU / L and 321.2 ± 26.4 mIU / L, respectively). This indicates the presence of hyperprolactinemia and its possible impact on reproductive function. A similar trend was noted in relation to the level of dehydroepiandrosterone sulfate (DHEA-S), which in the main group exceeded the control group by more than 1.8 times.

The ovaries varied in size, from slightly enlarged (4.5×2.5×4.5 cm) to significantly enlarged (11.4×5.7×8.6 cm). The ovaries were enlarged in 82.1% of patients, and within the normal range in 17.9% (the upper limit of normal ovarian size is 4×1.5×3 cm). Unilateral enlargement was observed only in 19 patients, while the rest had bilateral enlargement. The ovaries were spherical in 30 (66.7%) patients, and oval in 15 (31.2%) patients. All 45 cases had 5 or more characteristic features of PCOS, including enlarged ovaries, a smooth, shiny surface with a vascular pattern on the membrane, a stretched surface, subcapsular cysts, and the presence of small cysts on section. In 42 patients (93.3%), no free fluid was found in the posterior fornix of the uterus in the abdominal cavity. Similar data on the

laparoscopic image indicate the absence of ovulation. It should be noted that with different nature of the menstrual cycle disorders, the endoscopic image of the ovaries in patients with PCOS did not differ. After treatment, hormonal parameters were re-examined only in subgroups A and B of the main group. The reason is that group C and the control group did not receive any drug therapy. Subgroups A and B were re-examined after a six-month course of treatment for the levels of LH, FSH and glucose in the blood (Table 5). In women with hyperinsulinemia, the blood glucose level completely normalized. After treatment, in patients with PCOS, the LH parameters and the LH/FSH ratio changed depending on the method of therapy used. Subgroup A, which received only COCs, showed a moderate decrease in LH and LH/FSH (2.3±0.3).

In the observed groups, restoration of reproductive function depending on the duration of infertility was distributed as follows: in group A, infertility lasting up to 1-3 years was observed in 48% of women, after treatment, pregnancy occurred in 20% of them; with a duration of infertility of 3-5 years, detected in 44% of patients, restoration of fertility was noted in 12% of women; with infertility lasting more than 5 years, registered in 8% of women, pregnancy occurred in 4% of patients. In group B, infertility lasting 1-3 years was observed in 25% of women, of which fertility was restored in 20% of cases; with infertility lasting 3-5 years, detected in 40% of patients, pregnancy occurred in 25% of women; with infertility lasting more than 5 years, registered in 35% of patients, restoration of reproductive function was noted in 10% of patients. In women in group C, who underwent exclusively laparoscopic intervention, the pregnancy rate was lower compared to other groups. In women in subgroup A, 9 (45%) pregnancies were registered within 1 year after the treatment, however, only 3 (12%) of them ended in term delivery, and 2 (8%) cases in premature delivery. In 2 women (8%), a non-viable pregnancy was detected, and in another 2 patients (8%), spontaneous

termination of pregnancy in the early stages was noted. Soon after the loss of pregnancy, 2 women became pregnant again. In 3 patients who had a successful delivery, a repeat pregnancy occurred: in one - 40 days after delivery, in the second - after 3.5 months, in the third - after 6 months. Despite the short interpregnancy interval, the pregnancy was prolonged in 2 women. In one case, given a history of cesarean section and the onset of pregnancy within 40 days after birth, the pregnancy was terminated for medical reasons in order to prevent obstetric complications.

Thus, the best rates of reproductive function restoration were observed in Group B, which had the highest rates of pregnancy and term delivery. In Group A, reproductive outcomes were less stable, with a higher rate of complicated and terminated pregnancies. Fertility rates remained the lowest in Group C, while the control group had the highest rate of favorable pregnancy outcomes. Conclusion: In women with PCOS, the effectiveness of surgical treatment without prior endocrine correction was low. The choice of treatment strategy based on the duration of infertility demonstrated high efficacy. A combined approach to PCOS treatment, including conservative therapy followed by surgery, ensured more stable and long-term fertility restoration compared to surgical treatment alone.

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