ASSESSMENT OF THE ROLE OF DROSPIRENONE-CONTAINING DRUGS IN ANTIANDROGEN THERAPY

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Objective of the study. To assess the effectiveness of drugs containing drospirenone in treating reproductive function disorders in hyperandrogenism.

Materials and methods. For the study, 126 women of reproductive age with hyperandrogenism syndrome and reproductive disorders were selected from those who sought treatment at the reproductive center department of the Bukhara regional branch of the Republican Specialized Scientific and Practical Center for Mother and Child. Additionally, 32 healthy women of the same age without reproductive diseases were chosen as a control group. The study employed anamnestic-clinical, laboratory, and statistical research methods.

Results: After the complex treatment phase, normalization of the menstrual cycle was observed in 29% to 81% of cases. Following treatment, clinical skin changes characteristic of hyperandrogenism were not detected in 90.6% of patients.

Keywords: Hyperandrogenism, drosperinone, infertility, menstrual cycle disorders.

ОЦЕНКА РОЛИ ПРЕПАРАТОВ, СОДЕРЖАЩИХ ДРОСПИРЕНОН, В АНДРОГЕННОЙ ТЕРАПИИ

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Цель исследования. Оценить эффективность препаратов, содержащих дроспиренон, в лечении нарушений репродуктивной функции при гиперандрогенизме. **Материалы и методы.** Для исследования были отобраны 126 женщин репродуктивного возраста с синдромом гиперандрогенизма и нарушениями репродуктивной функции, обратившихся за лечением в отделение репродуктивного центра Бухарского регионального филиала Республиканского специализированного научно-практического центра матери и ребёнка. В качестве контрольной группы были выбраны 32 здоровые женщины того же возраста без репродуктивных нарушений. В исследовании использовались анамнестико-клинические, лабораторные и статистические методы.

Результаты. После проведения комплексного лечения нормализация менструального цикла наблюдалась в 29–81% случаев. После терапии клинические кожные проявления, характерные для гиперандрогенизма, не выявлялись у 90,6% пациенток.

Ключевые слова: гиперандрогенизм, дроспиренон, бесплодие, нарушения менструального цикла.

Relevance of the research. It is well-known that hyperandrogenism in women not only hinders the full realization of reproductive potential but also manifests in various forms of menstrual cycle disorders, diminishing women's quality of life indicators. In our experience, a decrease in work capacity in complicated cases is not uncommon. Furthermore, dermatological and cosmetological issues caused by hyperandrogenism evoke a sense of dissatisfaction with body and skin structure in women, leading to feelings of shame. Therefore, the treatment of this pathology is of paramount importance, stemming not only from medical necessities but also from social, cosmetological, and psychological needs [1,2].

Late complications of hyperandrogenism pose a high risk of developing endometrial cancer due to increased proliferative activity, and also create conditions for the development of type II diabetes mellitus and cardiovascular diseases [3,7].

One of the most frequent causes of hyperandrogenemia development in women of fertile age is polycystic ovary syndrome (PCOS) and a non-classical type of congenital adrenal hyperplasia. While the frequency of PCOS in women of this age is 10-15%, the development of adrenal hyperplasia occurs in 1:1000, 1:100 people, respectively, across different ethnic groups [4,6]. The identification of clinical signs in both cases creates a number of difficulties in differential diagnosis. In the diagnosis of hyperandrogenism, the correct determination of the genesis of its development allows for justified pathogenetic therapy[1].

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Results and discussion: According to the anamnestic data, the number of patients under 20 years of age in the main group was 9 (7.1%), the number of patients aged 21-26 years was 52 (41.3%), the number of patients aged 27-34 years was 41 (32.5%), and the number of patients aged 35 years and older was 24 (19%). Also, according to the data obtained from the objective examination of the subjects of the main and control groups, women with abdominal obesity were identified using body mass index (BMI) using height and body weight, as well as waist circumference and hip circumference. In particular, during the study, in the main group of patients, patients with BMI up to 18.5 were 5.6%, patients with normal BMI were 27%, patients with excess weight were 38%, patients with obesity of the first degree were 25.4%, and patients with obesity of the second degree were 4%. (Table 1).

Table 1

Distribution of subjects of the main and control groups by BMI indicator

Parameters	<18,5		18,5-24,9		25-29,9		30-34,9		35-39,9	
	n	%	n	%	n	%	n	%	n	%
Main group	7	5,6	34	27	48	38	32	25,4	5	4
Control group	4	12,5	10	31,2	12	37,5	5	15,6	1	3

During the study, the lumbar/thigh index was calculated in all examined women, according to which abdominal obesity was noted in 58.5% of women in the main group, and the lumbar/thigh index was higher than 0.85.

Also, according to the collected anamnesis of reproductive potential in patients of the main group, primary infertility was detected in 25.4% (n=32) of patients, and secondary infertility in 37.3% (n=47) of patients (in the control group, these signs were not detected).

Among the clinical signs identified during the study, in particular, changes in the menstrual cycle, secondary amenorrhea was detected in 13% (n=16) of patients, opsomenorrhea in 28% (n=35), oligomenorrhea in 28% (n=35), polymenorrhea in 0.80% (n=1), hypermenorrhea in 1.6% (n=2), and algodysmenorrhea in 4% (n=5), while signs of primary amenorrhea and proomenorrhea were not found in patients of the main group. Also, menstrual cycle disorders were not detected in 29% (n=36) of patients (Fig. 1).

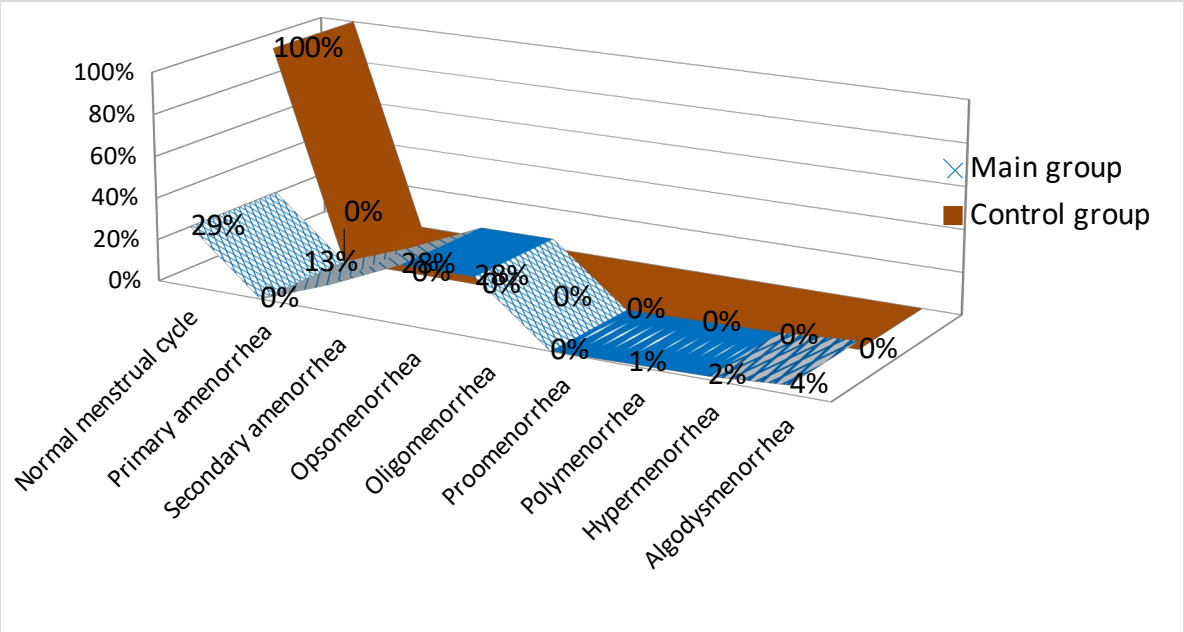

Figure 1. Manifestations of menstrual cycle disorders in patients of the main group.

Also, among skin changes in patients with hyperandrogenism (n=126), acne was detected in 17.5% (n=22), acanthosis nigra in 21.4% (n=27), seborrhea in 16.7% (n=21), alopecia in 1.6% (n=2), while in 42.8% (n=54) of the remaining patients, no such changes were found. Also, in the control group, acne was detected in 12.5% (n=3; $p<0.05$ (the significance of the distribution of symptoms in different groups was calculated according to the chi-square indicator)), sobereia - in 3.1% (n=1; $p<0.05$) of the examined, on the other hand, in 84.4% (n=28; $p<0.05$) of the examined, no skin changes were observed. Accordingly, among the skin changes in hyperandrogenism in women, acne and acanthosis nigra were the most common symptoms, while patients with alopecia were very rare.

In women with hyperandrogenism, methods for its correction have been developed depending on their complaints, i.e., what type of disorders they have. In this case, mixed oral contraceptives containing drospirenone were selected for antiandrogen therapy in women with menstrual cycle disorders and administered for a period of 3 to 6 months, depending on changes in clinical and laboratory signs. At the same time, taking into account the fact that weight gain exacerbates the state of hyperandrogenism, women were recommended a modified lifestyle. It is known that mixed oral contraceptives, combining the properties of estrogen + progesterone, reduce the release of gonadotropins from the pituitary gland by having a progesterone-like effect; inhibit the process of steroidogenesis in both the ovaries and the adrenal glands, but do not affect the synthesis of glucocorticoids and mineralocorticoids. Also, their antiandrogenic effect not only reduces androgen synthesis but also inhibits the synthesis of dihydrotestosterone in the skin, which has a stronger androgenic effect than testosterone [8,9,10]. At the same time, it reduces the sensitivity of androgen receptors. In addition, ethinyl estradiol in mixed oral contraceptives also reduces the level of free testosterone, since it has a positive effect on the expression and production of sex hormone-binding globulin

(SHBG) from the liver. In the treatment of infertility, which is one of the most common complications of hyperandrogenism, antiandrogen therapy was carried out in the first stage to normalize the level of hormones in the blood serum. In this case, tablets containing drospirenone, produced in a complex with a mixed oral contraceptive + metapholin, were selected. Metapholin prepares the body for pregnancy and reduces possible defects in the fetal nerve tube. It is biologically active against folic acid and is well absorbed by the body. After treatment, induction of ovulation was performed in patients with anovulation. Considering that 25- (OH) D deficiency is an important risk factor for the development of hyperandrogenism, patients with vitamin D deficiency were given vitamin D lamira at a dose of 5000 IU once a day for 2 months, and in case of insufficiency - at the same dose for one month. A prophylactic dose of Akvodetrim was recommended at 4 drops daily.

Analysis of the effectiveness of treatment practice depending on clinical indicators revealed a statistically significant decrease in the frequency of such clinical signs as secondary amenorrhea, opsomenorrhea, oligomenorrhea, in particular, according to menstrual cycle changes (from 13% to 0% ($p<0.05$); 28% to 3.2% ($p<0.05$); 28% to 11% ($p<0.05$)). Thus, after treatment of patients in the main group, the normal menstrual cycle was restored in 81% (before treatment, this indicator was 29% ($p<0.05$)) (Fig. 2).

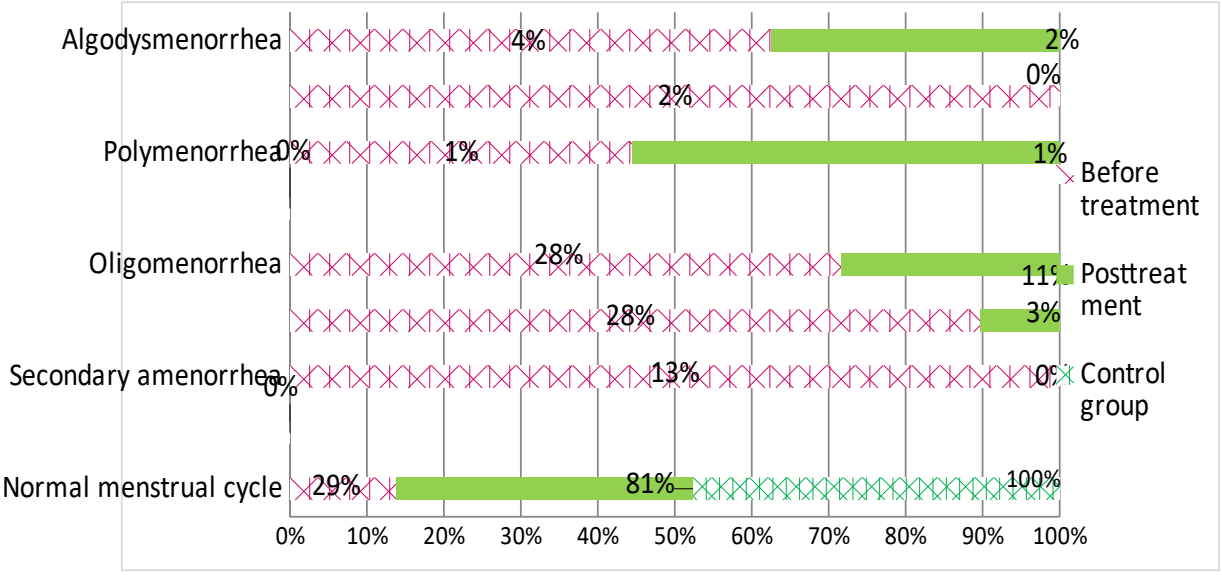

Figure 2. Frequency of detection of menstrual cycle disorders after treatment in patients of the main group.

When examining skin changes characteristic of hyperandrogenism after treatment, a significant change was observed in almost all clinical signs (acne symptom from 17.5% to 3.2% ($p<0.05$); acanthosis nigra symptom - from 21.4% to 4% ($p<0.05$); sobereia - from 17% to 2.2% ($p<0.05$)). As a result, clinical changes in the skin characteristic of hyperandrogenism were not detected in 90.6% of patients after treatment (this indicator was 42.8% before treatment ($p<0.05$)) (Fig. 3).

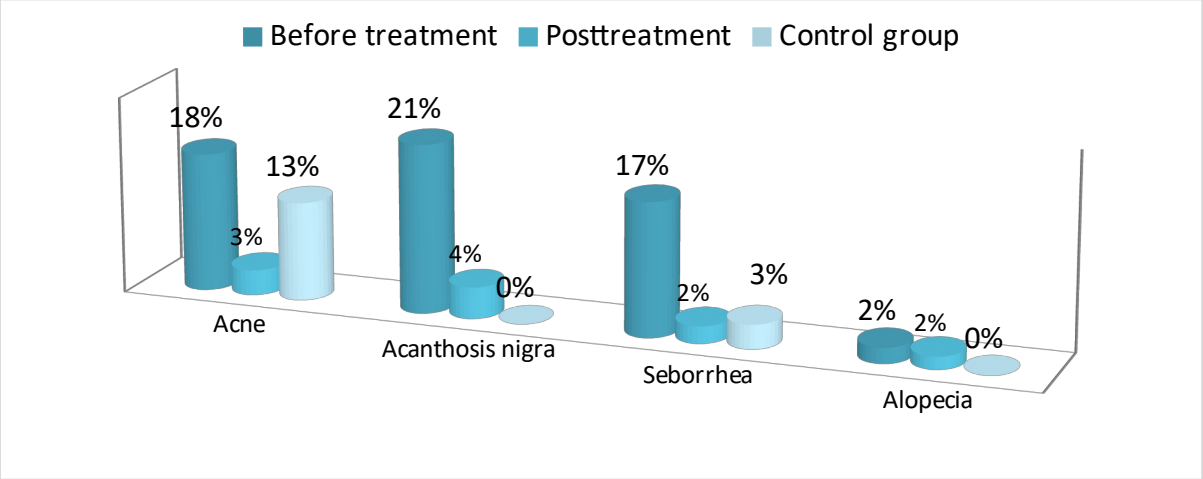

Figure 3. Frequency of detection of skin clinical signs characteristic of hyperandrogenism in patients of the main group after treatment.

Also, when analyzing the frequency of various degrees of hirsutism in patients of the main group, the initial degree of hirsutism was 11.9% (before treatment, this indicator was 35% ($p<0.05$)), and the frequency of mild and

pronounced hirsutism in patients was 99.2% ($p<0.05$) (Fig. 4).

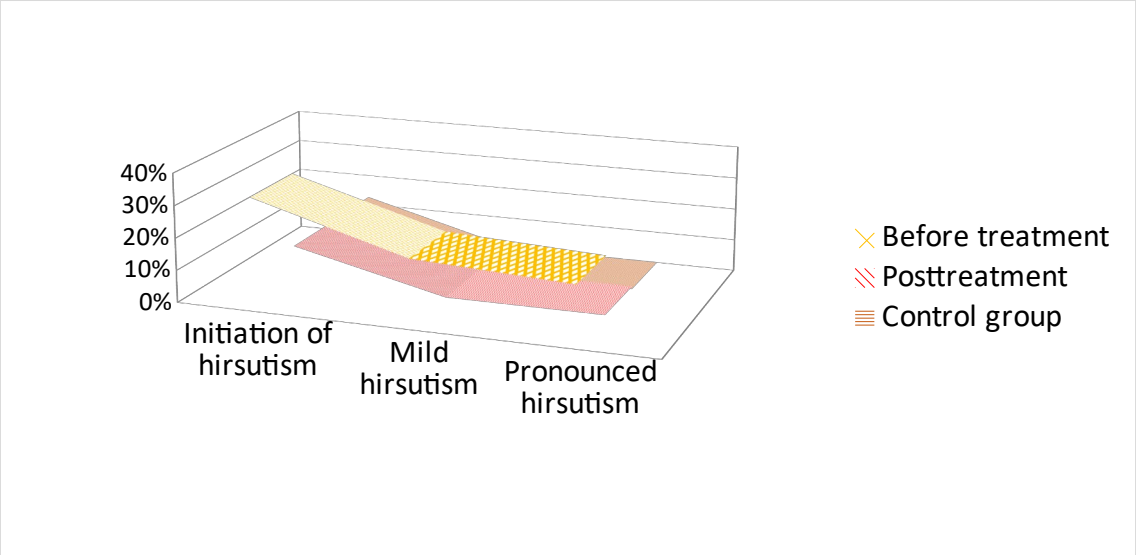

Figure 4. Frequency of detection of clinical signs and severity of hirsutism after treatment in patients of the main group.

Mutual analysis of the frequency of occurrence of clinical signs characteristic of hyperandrogenism before and after treatment showed that as a result of treatment practice, a reliable disappearance or reduction in the degree of these clinical signs was achieved in most patients.

Conclusion. The results of our study also confirmed the effectiveness of combined oral contraceptives containing drosperinone, selected in a complex, as antiandrogen therapy to eliminate dermatopathies and menstrual cycle disorders observed in hyperandrogenism syndrome. In particular, the inclusion of a modified lifestyle and vitamin D in the treatment complex increased the effectiveness of treatment. In particular, a statistically significant decrease in the frequency of such clinical signs as secondary amenorrhea, opsomenorrhea, oligomenorrhea in menstrual cycle disorders was revealed.

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