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Management of Patients with Polycystic Ovary Syndrom

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Abstract. Polycystic ovary syndrome (PCOS) is a pathology of the structure and function of the ovaries, the main criteria of which are ovulatory dysfunction and hyperandrogenism. In this abstract is given the general information about PCOS and made literature review about it.

Keywords: Polycystic Ovary Syndrome; PCOS; Hyperandrogenism; Anovulation; Insulin resistance; Reproductive health; Metabolic syndrome; Infertility; Hormonal imbalance; Ovarian dysfunction.

Introduction:

Polycystic ovary syndrome (PCOS) is a pathology of the structure and function of the ovaries, the main criteria of which are ovulatory dysfunction and hyperandrogenism. Polycystic Ovary Syndrome (PCOS) is one of the most prevalent endocrine and metabolic disorders among women of reproductive age, affecting approximately 5–15% of this population worldwide. It is a heterogeneous condition characterized by chronic anovulation, hyperandrogenism, and polycystic ovarian morphology on ultrasonography. The exact etiology of PCOS remains multifactorial and not completely understood, involving a complex interplay between genetic, hormonal, metabolic, and environmental factors. Women with PCOS often present with menstrual irregularities, infertility, hirsutism, acne, and obesity. Furthermore, the syndrome is associated with an increased risk of insulin resistance, type 2 diabetes mellitus, dyslipidemia, and cardiovascular disease. Due to its diverse clinical manifestations and long-term health implications, PCOS represents a major challenge for reproductive endocrinology and women's health worldwide.

The aim of this review is to summarize and critically analyze current research findings (2020–2025) on the pathophysiology, diagnosis, and management of Polycystic Ovary Syndrome (PCOS). The study seeks to highlight emerging evidence on hormonal, metabolic, and environmental factors contributing to PCOS development, as well as to evaluate recent advances in diagnostic biomarkers and therapeutic approaches aimed at improving reproductive and metabolic outcomes in affected women.

Materials and methods

This literature review was conducted using peer-reviewed scientific publications retrieved from major electronic databases, including PubMed, Scopus, ScienceDirect, and Google Scholar. The search covered the period from January 2020 to June 2025 and used combinations of the following keywords: *"Polycystic Ovary Syndrome," "PCOS," "metabolic dysfunction," "insulin resistance," "reproductive health,"* and *"treatment strategies."*
Only English-language articles published in indexed journals were included. Studies were selected based on relevance to the review objectives, focusing on human subjects, experimental models, and meta-analyses discussing etiology, clinical manifestations, diagnostic methods, and therapeutic interventions. The selection process excluded articles lacking full-text access or those unrelated to reproductive and

metabolic outcomes. Data were extracted and synthesized thematically, emphasizing pathophysiological mechanisms, diagnostic innovations, and evidence-based management strategies.

Results:

The main symptoms of PCOS (which determine the diagnosis) are:

- hyperandrogenism,
- ovulatory dysfunction,
- Polycystic ovarian morphology.

Diagnosis of PCOS requires differential diagnosis and exclusion of similar conditions. A detailed examination and identification of the main symptoms of PCOS, as well as exclusion of similar conditions, are necessary for diagnosis.

Additional symptoms (which determine long-term risks) are:

- carbohydrate metabolism disorders,
- dyslipidemia,
- fat metabolism disorders,
- metabolic syndrome,
- anxiety -depressive disorders,
- sleep disorders.

A detailed examination and identification of additional symptoms of PCOS is necessary to identify and prevent long-term risks.

Clinical picture and diagnostics of the main clinical manifestations of pcos

Next, we will consider the clinical picture and diagnosis of the main clinical manifestations of PCOS and the differential diagnosis of the syndrome.

1. Hyperandrogenia. In PCOS, clinical and biochemical hyperandrogenism are distinguished.

1.1 Clinical hyperandrogenism includes skin manifestations such as:

- hirsutism,
- acne,
- Alopecia.

We will look at them in more detail below.

Hirsutism. The most reliable clinical sign of hyperandrogenism in PCOS is hirsutism, the prevalence of which in PCOS is 65-75% [2]. Hirsutism is assessed using visual scales. The most widely used is the modified Ferriman - Gallwey scale according to Hatch. et all (Appendix 1.1). Each of the 9 body areas sensitive to the effects of androgens is scored from 0 (no guard hair) to 4 (significant growth) and summed to estimate the hormonal hirsutism number. The discriminant value is ≥ 6 points. The presence of acne and androgenetic alopecia is taken into account, but is not considered a reliable sign of hyperandrogenism. women with PCOS [2] and is an auxiliary

Acne. Acne affects approximately 15-25% of women with PCOS [2] and is an ancillary clinical sign of hyperandrogenism in PCOS. It is not included in the diagnostic criteria for the syndrome, but is considered when combined with OD or PCOS. Acne is also assessed by severity using visual scales, which distinguish between grades III and IV, and by the type of rash (comedones, papules, pustules, cysts) (Appendix 1.2).

Alopecia. Androgenetic alopecia has been poorly studied in PCOS. Its prevalence in this disease ranges from 5% to 50% [2]. It is also an auxiliary clinical sign of PCOS and is not included in the diagnostic criteria, but is considered when combined with OD or PCOS. Clinically, hair loss in women with androgenetic alopecia begins at the parting and spreads in all directions. There is no single,

generally accepted classification of androgenetic alopecia. It is assessed using visual scales – Ludwig (Appendix 1.3) – and by stages:

Stage 1. Hair thinning frontoparietal region may be accompanied by others manifestations of hyperandrogenism).

Stage 2. Moderate thinning and hair loss in the same area

Stage 3. Severe thinning of hair in the frontal and parietal areas. In the border areas, hair is preserved but thinned.

The activity of the hair loss process and the assessment of the area of its distribution are carried out using a hair tension test (pool test) (Appendix 1.3). The course of androgenetic alopecia is accompanied by remissions and exacerbations, so the Pool test can be either positive or negative depending on the period.

1.2 Biochemical hyperandrogenism. Hyperandrogenism is manifested by an increase in serum Androgen levels: testosterone, DHEAS, and androstenedione. Androgens and 17-OH progesterone are measured from days 1 to 10 of the menstrual cycle at 8:00 a.m.

Serum testosterone is the most important androgen in women. Approximately 70% [2] of women with classical PCOS have elevated free testosterone levels. According to the ABS consensus and the Rotterdam criteria, it is recommended to calculate the free testosterone index (FTI) using the formula [1]

IST = total T (nmol /l) x 100/SSG (nmol /l).

Therefore, it is necessary to determine the level of SSBG in clinical practice.

Limitations/Disadvantages

Free testosterone measurement is considered more informative than total testosterone measurement. However, direct radioimmunoassay (common in clinical practice) for free testosterone measurement is uninformative and is not recommended by AES experts. Quantitative physicochemical methods using gas chromatography/mass spectrometry are highly sensitive and specific, but are currently used primarily in scientific research. The study requires a large amount of material, and a plasma T extraction step is necessary. Such methods are rarely used in widespread clinical laboratory practice due to their extreme labor intensity and low productivity. The use of automated immunochemical analyzers for determining androgen levels in women (Architect, Immulite) is uninformative, as their readings are highly variable, and the analyzers themselves have low sensitivity. It should also be taken into account that population, ethnic, and age- specific androgen level norms in most clinical laboratories are not defined or are defined inadequately. Therefore, at present, high-quality determination of androgen levels in women is practically unavailable in the clinic [2].

DHEAS. Reflects the secretion of adrenal androgens. Approximately 20-30% of women with PCOS demonstrate elevated DHEAS, but only 10% of them experience isolated elevation [2]. DHEAS measurement is recommended in patients with PCOS [2], although it only slightly increases the detection rate of the syndrome.

Limitations/Disadvantages

DHEAS levels decline with age. Age-specific norms for this indicator need to be determined for each laboratory.

Androstenedione. It is synthesized in both the ovaries and adrenal glands. Its elevated levels are observed in 18% of patients with PCOS. It can be used to diagnose PCOS in women.

Limitations/Disadvantages

Little studied in PCOS.

2. Ovulatory dysfunction in PCOS belongs to class II according to the WHO classification (normogonadotropic normoprolactinemic hypogonadism). Approximately 75-85% of women with PCOS suffer from menstrual and/or ovulatory dysfunction; this is mainly oligomenorrhea/amenorrhea. However, about 1.5% of women suffer from polymenorrhea. The diagnosis of ovulatory dysfunction depends on the length of the menstrual cycle:

- with a menstrual cycle duration ≥ 35, or ≤ 26 days, as well as with < 10 menstrual cycles per year, ovulatory dysfunction is reliable;
- In cases of irregular menstrual cycles, as well as in the presence of hirsutism and regular menstruation, ovulatory status is assessed (the most reliable method is to determine progesterone levels 7 days before expected ovulation) by measuring them in three consecutive cycles. If progesterone levels are anovulatory (basal body temperature chart, ovulation test) in two out of three cycles, ovulatory dysfunction is confirmed.

Limitations/Disadvantages

Although ovulatory dysfunction in PCOS is related to normogonadotropic normoprolactinemic In hypogonadism, it is important to know that 40% of patients with PCOS have relatively elevated LH levels. Also, in some patients, prolactin levels may be at the upper limit of normal or slightly elevated. With severe IR, a slight decrease in FSH levels is observed [2].

It should also be noted that ovulatory dysfunction does not always cause menstrual dysfunction. Research suggests that approximately 20-30% of women with PCOS and regular menstrual cycles have ovulatory dysfunction [2]; also, approximately 40% of patients with hirsutism, normal plasma androgens, and regular menstrual cycles suffer from oligoovulation, which can be detected with a thorough examination.

3. Polycystic ovarian disease is common in more than 80% of patients with polycystic ovarian syndrome and is diagnosed by ultrasound examination [1] using a transvaginal probe. The most common criteria are those of the American and European Societies of Human Reproduction, 2003:

The presence of 12 or more follicles with a diameter of up to 10 mm in each projection and/or an ovarian volume greater than 10 cm*. These changes must be present in one ovary.

Limitations/Disadvantages

This criterion is not applicable to women taking oral contraceptives; if a dominant follicle (>10 ml) or corpus luteum is present, the test should be repeated in the next cycle.

However, more recent studies [8, 9] indicate that normal ovarian volume does not exceed 7-7.5 cm, and that a larger volume may be associated with the development of PCOS. However, these studies have not yet led to changes in the ultrasound criteria for PCOS.

Differential diagnosis of pcos in accordance with the ESHRE\ASRM, AES criteria is carried out with the following diseases.

By Simit hyperandrogenism PCOS must be differentiated:

- with Itsenko-Cushing's syndrome or disease,
- non-classical form of congenital adrenal cortex,
- androgen -secreting tumors,
- HAIRAN syndrome (severe insulin resistance and hyperandrogenism syndrome).

Based on the symptom of ovulatory dysfunction, PCOS must be differentiated

- with hypo- and hypergonadotropic hypogonadism,
- hypothyroidism,
- hyperprolactinemia.

Itsenko-Cushing's syndrome, or disease, is a relatively rare pathology. Differential diagnosis is mainly based on the clinical picture. In addition to hyperandrogenism and carbohydrate metabolism disorders, it is characterized by such clinical signs as hypertension, myopathy, moon-shaped facies, thinning skin, and the appearance of striae. In the presence of such manifestations, it is necessary to study the level of 24-hour urinary free cortisol. Dexamethasone suppression tests can be used. However, it should be remembered that the low-dose dexamethasone suppression test is informative only in 70% of patients with Itsenko-Cushing's syndrome and disease [10].

Non-classical congenital adrenal cortex dysfunction occurs in 1-10% of patients with the clinical picture of PCOS, the prevalence depends on the ethnic group. The risk group includes the population of Ashkenazi Jews, residents of Latin America, representatives of the Armenian diaspora, Yugoslavs and a number of others. According to modern concepts, PCOS and the non-classical form of congenital adrenal cortex dysfunction are clinically indistinguishable [2]. The most common form of congenital adrenal cortex dysfunction is 21-hydroxylase deficiency. Deficiency of 3ß-HSD and 11ß-hydroxylase is extremely rare. Screening for the non-classical form of congenital adrenal cortex dysfunction is performed by determining the level of 17-hydroxyprogesterone in the first phase of the menstrual cycle at 8:00 am. If the basal level of 17-OH progesterone increases to more than 2 ng /ml, an ACTH stimulation test is performed with a bolus intravenous injection of ACTH (Cortrosyn, Synacten). The diagnosis is then localized using PCR diagnostics [2]. Typically, approximately 10-12 mutations are investigated, covering the most frequently affected alleles. The disease is inherited in an autosomal recessive manner. The type of mutation and the associated clinical picture are given in Appendix 3.

Limitations/Disadvantages

A. Basal 17-OH progesterone levels should be measured no later than 8:00 a.m. (after the nocturnal ACTH peak), as they decline thereafter. Patients often fail to follow this rule, which can be quite difficult to detect. It should also be noted that 17-OH progesterone levels are elevated in only 80-90% of patients with the non-classical form of congenital adrenal hyperplasia; in the rest, they are normal. Therefore, some centers in the United States and Western Europe perform ACTH stimulation on all patients with hyperandrogenism at risk (Ashkenazi Jews, etc.), without relying on basal 17-OH progesterone levels.

B. Neither intravenous nor subcutaneous ACTH is currently registered in Russia, so performing an ACTH stimulation test is not possible. Therefore, standard diagnostics of CAH are impossible. PCR testing can only be performed on all patients at risk (those with elevated basal 17-OH progesterone and/or a high incidence of the disease in a given ethnic group).

4.3 Androgen-secreting tumors (ASO) are rare, occurring in 1/300-1/1000 patients with hyperandrogenism [2]. They are generally excluded based on the clinical presentation of rapidly progressing hyperandrogenism symptoms, as well as the presence of a tumor in the pelvis, in the adrenal region. It should be noted that, contrary to popular belief, only 50% of patients with ASO experience elevated androgen levels [11, 12, 13, 14].

4.4 HAIRAN syndrome occurs in approximately 3% of patients with hyperandrogenism and is an independent nosology [I5]. Differential diagnosis is carried out based on the clinical picture (the presence of pronounced nigroid acanthosis, signs of hyperandrogenism) in combination with laboratory tests: fasting insulin more than 60 mU /ml or during a glucose tolerance test with a parallel study of insulin more than 300 mU /ml.

4.5 Hypo / hypergonadotropic Hypogonadism is quite rare and is excluded based on clinical examination and the levels of the gonadotropins FSH and LH on days 2-4 of the menstrual cycle (decreased or increased, respectively). To verify the diagnosis, two tests of these hormones are necessary.

4.6 Hypothyroidism has a significant impact on a woman's reproductive function and negatively affects the development of fetal intelligence. The incidence of clinical and subclinical hypothyroidism in patients with PCOS is low (0.32-7.3%); however, due to its high significance for reproductive function, TSH level testing is recommended for all patients with suspected PCOS [1, 2].

4.7 True hyperprolactinemia occurs in less than 1% of patients with hyperandrogenism. It is diagnosed by clinical presentation (galactorrhea) and/or a twofold increase in PRL levels during the first phase of the menstrual cycle. If prolactin levels are elevated, macroprolactinemia (macroprolactin test) and pituitary adenoma (sellar MRI) must be excluded [2].

Clinical picture and diagnostics of auxiliary clinical manifestations of pcos

Next, we will look at the diagnosis of additional symptoms of PCOS, as well as the risk groups for cardiovascular disease in this syndrome.

Cardiovascular disease risk groups in pcos. According to the 2010 AES and American Cardiovascular Association guidelines, several risk groups for developing karyovascular pathology in PCOS are identified. These groups are subdivided as follows:

- optimal risk;
- high risk;
- Very high risk.

group of women with PCOS is the presence of one of the following risk factors:

- obesity ;
- cigarette smoking ;
- hypertension ;
- dyslipidemia ;
- subclinical atherosclerosis;
- Impaired glucose tolerance;
- Family history of early CVD (less than 55 years in men, less than 65 years in women) [16].

A group of women with very high risk PCOS

- metabolic syndrome;
- Type 2 diabetes ;
- Clinical atherosclerosis and/or kidney pathology [17].

The optimal risk is determined for all other patients [7].

Let's consider the auxiliary criteria of PCOS and their diagnosis.

1. **Carbohydrate metabolism disorders** in PCOS include insulin resistance, impaired glucose tolerance, and type II diabetes. Insulin resistance occurs in 60-80% of women with PCOS [36], and by the fourth decade of life, 40% of women develop impaired glucose tolerance and type 1I diabetes [18, 19]. Diagnosis of carbohydrate metabolism disorders includes a glucose tolerance test with 75 g of dry glucose.

Indications: BMI over 30 kg/m*, age over 40 years, family history of diabetes, history of gestational diabetes. Rescreening is performed every two years if normal, annually if abnormal or if additional risk factors are identified [7].

It should be noted that a two-hour glucose tolerance test (GTT) with insulin and glucose measurements is considered more informative. Fasting and exercise glucose levels are assessed according to WHO recommendations (Appendix 5.3); the presence and severity of IR is assessed based on the peak insulin level during the GTT:

- women with normal body weight in the absence of IR: <60 µl /ml;

- obese women without IR: <100 µl /ml;
- mild degree of IR: 100-150 µl /ml;
- moderate IR: 151-300 µl /ml;
- severe IR: >300 µl /ml.

2. Dyslipidemiia is observed in 70% of patients with PCOS [7]. They are characterized by:

Hypercholesterolemia, hypertriglyceridemia, decreased HDL levels. Dyslipidemia in patients with PCOS is mainly due to the effects of IR and hyperandrogenism in combination with environmental and genetic factors [20, 21]. It is determined by examining the lipid spectrum. Examination is mandatory for all women with PCOS. Optimally, every two years if normal, annually - if abnormal or in case of weight gain [7]. In the presence of dyslipidemia, ultrasound examination of the intima-media thickness of the carotid artery wall is indicated to detect atherosclerosis.

3. Disorder of fat metabolism is assessed by the body mass index and waist circumference: BMI (kg/m²) = body weight (kg)/height (m²). Underweight is defined as BMI <20, normal weight is 20-24.9, overweight is 25-29.9, obesity is 30-39.9, and severe obesity is >40. Waist circumference should be measured between the hypochondrium and the pelvic bone along the midaxillary line. In Caucasian women, it should not exceed 88 cm (according to ATP III criteria).

4. Hypertension detection. Blood pressure is measured at every visit. If systolic pressure rises above 130 mmHg and diastolic pressure rises above 85 mmHg, daily blood pressure monitoring with a diary is recommended.

5. Metabolic syndrome in PCOS occurs in 8-25% of cases of the classical course of the syndrome in Europe [27, 28] and in 33-47% of cases in the USA [22-26], which is three times higher than in the general population [29, 25, 26, 30]. METABOLIC SYNDROME in PCOS is diagnosed using the ATP III criteria, 2001

The criteria for metabolic syndrome are given in Appendix 5.1.

- abdominal obesity (waist circumference over 88 cm);
- TG level > 1.7 mmol/l;
- HDL-C level < 1.29 for women;
- BP level > 130/85 mm. rt. Art.;
- Fasting plasma glucose level > 6.1 mmol/L.

6. Anxiety-depressive disorders and sleep disorders are more common in patients with PCOS than in the general population [31-34]. Current data indicate that these disorders are independent risk factors for CVD [31, 32]. Diagnosis and treatment of this pathology is an interdisciplinary problem, the solution of which involves doctors of different specialties: obstetricians-gynecologists, psychotherapists, psychiatrists and neurologists. For the initial screening of this group of patients for the presence of anxiety-depressive disorders and sleep disorders, the questionnaires provided in Appendices 4.1 and 4.2 can be used.

Treatment of PCOS outside of pregnancy planning

Since the etiology of the syndrome is unknown, treatment is symptomatic. Treatment options for PCOS manifestations differ in patients planning and not planning pregnancy. Below, we will discuss the treatment of cutaneous manifestations of hyperandrogenism in PCOS and metabolic disorders.

It should be noted that in modern medicine, treatment (diagnostic) methods are typically categorized by the degree of evidence. The evidence system described below is generally accepted.

Classification of levels of evidence

1a - Meta-analysis/systematic review

1b - Randomized placebo-controlled trial

2a - Well-designed controlled trial without randomization.

2b - Quasi-experimental study of good design.

3 - Comparative studies, correlational studies and case reports.

4 - The opinion of a committee of experts or a conclusion drawn from the clinical experience of respected authoritative doctors.

The objectives of PCOS treatment outside of pregnancy planning are: correction of skin manifestations of hyperandrogenism (hirsutism, acne, alopecia), regulation of the menstrual cycle, prevention of mortality from cardiovascular diseases - treatment of metabolic disorders.

Correction of skin manifestations of hyperandrogenism

TREATMENT OF HIRSUTISM [3]

Combined oral contraceptives. Combined oral contraceptives are first-line treatment for hirsutism (Ib). COCs are more effective than placebo. COC monotherapy is the first-line treatment for hirsutism. The efficacy of COCs is comparable (Ib) to antiandrogens (finasteride), GnRH agonists, and insulin synthesizers. The optimal types of COCs have not been determined. Theoretical assumptions limit the use of COCs with residual androgenic effect (IV). It has been shown that COCs containing drospirenone are as effective in treating hirsutism as COCs containing cyproterone (Ib) acetate. There are no RCTs comparing the efficacy of low-dose and high-dose COCs based on ethinyl estradiol content. Observational studies indicate that these types of COCs are comparable (III). Thus, COCs are the first line of treatment for hirsutism. Effect evaluation should be performed no earlier than after 6 months. The following medications are recommended: Diane-35, Yarina, Jess, and Janine. Drospirenone -containing medications also promote weight loss of 1.2-1.5 kg per year, not only due to their diuretic effect but also by normalizing appetite in women with hyperandrogenism. Questionnaires for determining acceptability of COC therapy are provided in Appendix 4.3.

Antiandrogens. If COC monotherapy is ineffective for 6 months, a combination with direct antiandrogens (Ib), such as cyproterone acetate, spironolactone, and finasteride, is possible. Flutamide is not recommended due to hepatotoxicity.

Medications: Androcur 0.01 from day 1 to day 15 of the cycle, in combination with Diane-35. Other antiandrogens may be used: Veroshpiron 50-100 mg daily, Finasteride 5 mg daily. However, these medications are not licensed for use by women and may cause hypogonadism in a male fetus if they cause pregnancy. Some experts believe that finasteride should be avoided by women who are not yet of reproductive age.

Permanent hair destruction methods. For enhanced results, they can be combined with permanent hair destruction methods. The optimal method is photoepilation (II a).

Acne treatment. This is carried out in consultation with a dermatocosmetologist. For patients with PCOS, acne therapy should be comprehensive and include topical and systemic medications.

Local preparations are selected by a dermatocosmetologist.

Drugs with proven effectiveness according to the American Dermatology Association guidelines (4) include:

- Topical retinoids (I a) are teratogens and require double contraception when used;
- local antibiotics (I a);
- azelaic acid (I b);
- Benzoyl peroxide and its combination with topical antibiotics (I a).

Systemic medications for patients with PCOS include (4) hormones/antihormones, systemic antibiotics, retinoids.

Hormones/antihormones:

- COC (Ia). First-line treatment for acne in women with hyperandrogenism. Indications (special instructions) for the treatment of acne are registered for the drugs " Yarina " and " Jess." The minimum period for evaluating effectiveness is 3 months.

- Antiandrogens (II b). The drugs studied include cyproterone acetate and spironolactone. See the dosage regimen above. Contraception is mandatory.

- Oral corticosteroids (II b). In patients with adrenal hyperandrogenism, short-term use of low doses of dexamethasone is possible in some cases (optimal duration and doses have not been determined).

Systemic antibiotics (Ia). Tetracyclines and macrolides are effective for acne. The optimal course of treatment is also three weeks. Doxycycline 0.1 is used twice daily for three weeks.

Oral retinoids (Ia). The drug "Roaccutane" 0.5-1.0 mg/kg for 16-30 weeks. Cumulative dose: 100-150 mg/kg, should not exceed the dose of 1.0 mg/kg. The drug has a pronounced teratogenic effect on the fetus, a double method of contraception is required when using it [4].

Treatment of androgenic alopecia. Treatment is long-term, with results observed within 6-8 months. When treating androgenetic alopecia, it should be noted that in the early stages of the disease, differential diagnosis between androgenetic alopecia and telogen effluvium is virtually impossible. However, the therapeutic approaches at this stage are virtually identical.

Conservative treatment methods [35]

- Minoxidil - "Regaine", 2% (Ia) - is the only drug whose effectiveness has been reliably confirmed by clinical studies [36, 37]. Structural analogs of minoxidil "Aminopyrimidone", "Vontersil", "Dixidox", "Pinacidil", "Alerana", "Aminexil" are cosmetic products, concentration is unknown, RPCTs have not been conducted.
- Systemic antiandrogens (finasteride, cyproterone acetate, veroshpiron). A systematic review (Ga) in PubMed and MEDLINE 2010 showed that finasteride has limited efficacy in women. Its use is possible if minoxidil is ineffective and contraception is available [38]. Spironolactone and cyproterone Acetate is ineffective in approximately 88% of women, with the stage of alopecia affecting its effectiveness. The effect is primarily based on a reduction in the rate of hair loss [39].
- Topical antiandrogens – eucapil (2 ml of 2% fluridil solution in isopropyl alcohol, 50 mg of grape seed oil) Antiandrogen: 5-alpha reluctase receptor blocker. Applied topically. Its effectiveness has been poorly studied.
- COCs should be used by women as a contraceptive when using minoxidil or androgens (cyproterone, finasteride, spironolactone). So ide Pain is contraindicated with them. The effectiveness of COC monotherapy for alopecia has not been studied.

Laser therapy (Naï -Max comb) (1b). Effectiveness is indicated, approved for use by the FDA, USA. Biostimulation of hair follicles restores the normal hair growth cycle [40].

Surgical treatment.

- Follicular unit transplantation. This method recreates the maximum density of transplanted hair and the natural hairline.
- Micrograft transplantation. Less aesthetic than follicular transplantation.
- Alternative methods. Non-surgical replacement of lost hair (hair integration, contact hair, contact volume). These methods do not address the cause of alopecia, but only create a cosmetic effect.

Regulation of the menstrual cycle. Combined oral contraceptives (see above) are the drugs of choice. Progestogens may be used during the second phase of the cycle. Preferred progestogens are those

similar to natural progesterone: Duphaston, 1 tablet twice daily from days 16 to 25 of the menstrual cycle, or Utrozhestan, using the same regimen.

Prevention of cvd and dm 2 - treatment of metabolic disorders [7].

Therapeutic lifestyle modification (Ib). A hypocaloric diet (a reduction of 500-1000 kcal from the usual diet) with limited fat intake and increased monounsaturated and polyunsaturated fatty acids is recommended. At least 30 minutes of moderate-intensity physical activity per day is recommended. Compliance with these recommendations has been shown to significantly reduce BMI and improve insulin sensitivity and lipid profile. The target weight loss for women with stage I and higher GI obesity should be at least 10-20% of baseline weight. To optimize weight loss efforts, a questionnaire identifying eating behavior patterns and a food diary can be used (Appendices 4.4 and 7). Patients with elevated cholesterol levels should consume foods that promote cholesterol reduction (Appendix 6).

Insulin synthesizers. Prescribed in conjunction with an endocrinologist. Currently, the use of metformin (Glucophage) for ovulation induction is limited, as RCTs [53] have shown that the rate of early pregnancy terminations is higher with its use than with other ovulation inducers. With regard to metabolic disorders in PCOS, its use causes minor weight loss (2-3%), improves the lipid profile (increased HDL, decreased triglycerides), but does not reduce LDL and should not be used by women who have elevated these parameters [4].

The use of metformin, according to the AES consensus [4], is recommended:

- women with diabetes II;
- in case of impaired carbohydrate tolerance, only if lifestyle modification does not produce the expected effect;
- in metabolic syndrome;
- for subclinical atherosclerosis.

Not recommended for women with isolated hypertriglyceridemia or isolated low HDL unless they are at moderate or high risk for metabolic syndrome (see above).

Lipid-lowering agents. Prescribed by a physician. Women with PCOS should use lipid-lowering agents according to the ATP III recommendations (Appendix 5.2). It should be noted that despite a wide range of lipid-lowering drugs, only statins have been studied in PCOS. Some studies have confirmed that statins not only normalize lipid profiles but also reduce total and free testosterone levels and improve endothelial dysfunction in these patients. In a group of women resistant to lifestyle modification in combination with monotherapy statins, a combination of drugs is necessary. It has been shown that in such patients, the addition of metformin does not provide additional benefits [41]. Combination with fibrates is necessary in the presence of hypertriglyceridemia and low HDL levels. Fenofibrate is the most preferable due to the lower risk of negative drug interactions. The use of nicotinic acid preparations (Niacin) is possible, but with caution, since they worsen the glycemic profile. Omega-3 fatty acids should be taken 4 g per day in the form of medications; their use is approved by the FDA for hypertriglyceridemia.

Antihypertensive drugs. Prescribed by a therapist. Pharmacotherapy is indicated for blood pressure exceeding 140/90 mmHg. The target blood pressure value for the prevention of CVD is 120/80. The AES expert group recommends (IV) a combination of antihypertensive therapy with lifestyle modification. It should be remembered that the majority of antihypertensive drugs (ACE inhibitors, β-blockers, diuretics) are contraindicated for use during pregnancy and require contraception [4].

Pharmacotherapy of obesity. According to the AES guidelines [4], pharmacotherapy is not recommended for PCOS. Orlistat induces only minor weight loss. Sibutramine in combination with a hypocaloric diet improves weight loss, insulin resistance, and reduces triglyceride and testosterone levels

[42, 43]. However, it can cause undesirable side effects for patients with PCOS: an increase in diastolic blood pressure and heart rate [44]. It is also not approved for use during pregnancy. Due to the limited clinical experience in PCOS and the risk of side effects, the AES does not recommend the use of sibutramine in PCOS. Bariatric surgery induces weight loss of up to 60% [45], significantly improves the course of diabetes, hypertension, dyslipidemia, reduces mortality from cardiovascular diseases and cancer. For women with PCOS, bariatric surgery The surgery has proven its effectiveness. Mortality and complications from this surgery are 0.1-1.1%. The ineffectiveness of conservative methods of weight loss with a BMI of more than 40 kg/m or 35 kg/m in the presence of complications associated with obesity has been proven [4] (see Appendix 5.4).

Depression. If subclinical (clinical) depression and/or anxiety are detected in patients with PCOS, they should be referred to a psychotherapist (psychiatrist) for treatment. Selective serotonin reuptake inhibitors (SSRIs) are typically the first line of treatment for these conditions.

Sleep disorders. If sleep disorders (insomnia, dyssomnia) are detected during the questionnaire, patients with PCOS should be referred to a neurologist and/or a sleep laboratory. It is important to remember that patients with PCOS are more likely than others to suffer from sleep apnea, which can significantly reduce their life expectancy if left untreated.

Treatment of PCOS when planning a pregnancy

Approximately 70-80% of patients with PCOS experience ovulatory dysfunction, subfertility, and infertility. Therefore, several options are available when planning a pregnancy.

Waiting for pregnancy is acceptable for women with PCOS under 35 years of age for a year if they ovulate spontaneously, even irregularly. Recommendations regarding the estimated time of conception and the optimal frequency of intercourse (at least twice a week, ideally every other day) are necessary.

Anovulation is the main cause of infertility in PCOS. Treatment is aimed at restoring ovulatory menstrual cycles in patients. When evaluating infertile women with PCOS, other conditions and causes of infertility in the couple must be excluded. Even a singleton pregnancy in PCOS is associated with a high risk to the health of both mother and fetus.

Treatment methods for infertility in patients with PCOS are systematized in the working document “Consensus on the treatment of infertility in patients with PCOS” [5].

pre-gestational counseling is mandatory, including recommendations for lifestyle modifications (diet, exercise to normalize weight) [46, 47]. Alcohol and smoking cessation are recommended, and folic acid is prescribed.

1. First-line therapy for ovulation induction is clomiphene citrate.

1.1. The drug is prescribed at 50-100 mg/day, from days 5 to 9 of the menstrual cycle. The maximum daily dose is 150 mg.

The effectiveness of clomiphene citrate is that ovulation is achieved in 70-80% of patients (48, 49). The conception rate is up to 22% per cycle [50, 51, 521]. The cumulative pregnancy rate is 50-60% for 6 months

Approximately 30% of patients with PCOS are resistant to CC.

Criteria for clomiphene resistance [58]:

- Age>30 years;
- BMI>25 kg/m2;
- Increased ovarian volume (> 10 cm*);
- LH level>15 IU/l;
- Estradiol level<150 pmol/l.

Treatment with clomiphene citrate should be limited to 6 ovulatory cycles.

1.2. Combination therapy

The addition of metformin or dexamethasone to clomiphecitrate does not improve infertility treatment outcomes in patients with PCOS [53–55].

Metformin is used in PCOS only in cases of impaired glucose tolerance. Routine use of this drug for ovulation induction is not recommended.

2. The second line of therapy - if clomiphene citrate is ineffective - is ovarian stimulation with gonadotropins or laparoscopy.

2.1. Gonadotropins

Two modes of ovulation stimulation with gonadotropins are used.

- Step- up regimen. FSH is prescribed at a dose of 37.5-50 IU per day. If follicle growth is absent after one week of stimulation, the FSH dose is increased by 50%. If follicle growth is adequate, the FSH dose remains unchanged. This is known as a chronic low-dose regimen.
- Step- down regimen. Use of high initial doses of FSH—100-150 IU per day—followed by a gradual reduction.

Ultrasound monitoring is mandatory before the start of each treatment cycle and to monitor follicular growth in response to stimulation (risk of multiple pregnancy). Strict criteria for cycle cancellation must be agreed upon with the patient before treatment. Cycle cancellation or transfer to IVF is recommended if three or more follicles measuring 14 mm or larger are present. HCG is not administered:

- with more than two follicles with a diameter greater than or equal to 16 mm,
- with one follicle greater than or equal to 16 mm and an additional two follicles greater than or equal to 14 mm in women with PCOS up to 38 years of age in the absence of other infertility factors.

The effectiveness of gonadotropins: monofollicular ovulation with low doses of gonadotropins is achieved in 70% of cases, pregnancy rate is 20%, multiple pregnancies are 5.7%. Ovarian hyperstimulation is less than 1%.

Combination therapy - routine use of GnRH agonists in ovulation induction in patients with PCOS is not recommended (high risk of hyperstimulation and multiple pregnancy, high cost of treatment) [5].

The duration of treatment with gonadotropins should not exceed 6 ovulatory cycles.

2.2 Laparoscopic surgery

Indications.

- Clomiphene resistance in PCOS patients.
- LH hypersecretion.
- The need for laparoscopic surgery in patients with PCOS (endometriosis, other causes).

Remote residence of patients from the hospital - the impossibility of monitoring during use of gonadotropins (5).

Laparoscopy should not be used in the absence of infertility.

Monopolar therapy is used with equal effectiveness. Electrocautery and laser. Most researchers recommend using 4 to 10 punctures, as a higher number of punctures is associated with premature ovarian failure.

Efficacy. Laparoscopy is effective in only 50% of patients; the remainder require ovulation induction. If ovulation is absent 12 weeks after laparoscopy, clomiphene citrate should be used. The addition of gonadotropins should be considered after 6 months.

3. The third line of therapy - if ovulation stimulation and laparoscopy are ineffective - is ART methods.

IVF is also indicated for patients with PCOS in the case of concomitant pathology - tubal factor, severe endometriosis, the need for PGD, age over 35 years, male factor [5].

Protocols. The most widely accepted stimulation protocol is the long protocol with recombinant FSH (the antagonist protocol).

Efficiency. The clinical pregnancy rate per treatment cycle is 35%.

Complications. A high incidence of ovarian hyperstimulation is observed in patients with PCOS.

Conclusion: Recent literature underscores that PCOS is a multifactorial disorder involving complex interactions between genetic predisposition, hormonal imbalance, insulin resistance, and environmental influences. The review highlights that lifestyle modification, weight management, and personalized pharmacological interventions remain the cornerstone of therapy. Moreover, the integration of novel biomarkers and individualized treatment protocols shows promise for improving both reproductive and metabolic outcomes. Continued research is essential to better understand the molecular pathways of PCOS and to develop preventive strategies that address its long-term cardiovascular and metabolic risks.

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