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Modern approaches to the diagnosis and treatment of polycystic ovary syndrome in adolescence

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The diagnosis of polycystic ovary syndrome (PCOS) in adolescence still raises many questions. The problem is that the characteristics of normal puberty often coincide with the symptoms of PCOS. The article presents the criteria of a normal menstrual cycle, clinical and laboratory hyperandrogenism. In the diagnosis of the latter, the most informative indicators are the determination of the index of free testosterone and androstenedione, and the assessment of free and total testosterone are relatively low sensitivity.
Clinical hyperandrogenism in adolescents includes only severe acne and hirsutism. The level of antimullerian hormone has no independent significance. Irregular menstrual cycles during the first year after menarche represent a normal period of puberty. At the second and third year after menarche , menstrual cycles of less than 21 days and more than 45 days are considered irregular, and from the fourth year – less than 21 days and more than 35 days. From the second year after menarche, menstrual irregularities are considered to be more than 90 days for any cycle.
Primary amenorrhea is indicated by the absence of menarche at 15 years, or 3 years after telarche. Ultrasound is not used as a criterion for PCOS in the first 8 years after menarche due to the high frequency of ovarian multifollicularity in adolescence. Therefore, adolescent girls in the presence of menstrual disorders and hyperandrogenism may be diagnosed with «PCOS. Phenotype B» (ultrasound signs are not taken into account). Adolescents who have signs of PCOS but do not meet the diagnostic criteria are at risk for PCOS.
The most important stage of PCOS therapy is lifestyle modification, normalization of body weight and metabolic processes. Combined oral contraceptives in adolescents are more often prescribed not for direct purposes (contraception), but as off-label therapy not only at diagnosis, but also in the «risk group», which involves the treatment of irregular menstrual cycles and / or clinical hyperandrogenism. In the absence of the effect of lifestyle changes, proper nutrition to correct metabolic disorders in addition to combined oral contraceptives may be prescribed metformin, inositol and etc.
Keywords: *polycystic ovary syndrome, adolescence, diagnosis, hormonal and ultrasound examination, phenotypes, treatment.*

Сучасні підходи до діагностики та лікування синдрому полікістозних яєчників у підлітковому віці

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У статті наведено огляд літератури, який висвітлює проблему діагностики синдрому полікістозних яєчників (СПКЯ) у підлітковому віці. Обговорено проблему, яка полягає у тому, що характеристики нормального статевого дозрівання часто збігаються з симптомами СПКЯ. Представлено критерії нормального менструального циклу, клінічної та лабораторної гіперандрогенії. Наведені дані, які свідчать, що у діагностиці останньої найбільш інформативними показниками є визначення індексу вільного тестостерону та андростендіону, а оцінювання рівнів вільного та загального тестостерону має відносно низьку чутливість.
До клінічної гіперандрогенії у підлітків відносять лише тяжку форму акне та гірсутизм. Рівень антимюллерова гормону не має самостійного значення. Нерегулярні менструальні цикли протягом першого року після менархе представляють нормальний період статевого дозрівання. Наведено дані, що на другому та третьому гінекологічному віці нерегулярними вважають менструальні цикли, менші за 21 день та більші за 45 днів, а з четвертого гінекологічного віку – менші за 21 день та більші за 35 днів. Починаючи з другого року після менархе, порушенням менструального циклу вважається більше 90 днів для будь якого циклу.
Про первинну аменорею свідчить відсутність менархе у 15 років або через 3 роки після телархе. Як свідчить аналіз наукових публікацій, ультразвукове дослідження не використовують у якості критерія СПКЯ перші 8 років після менархе через високу частоту мультифолікулярності яєчників у підлітковому віці. Тому у дівчат-підлітків за наявності порушення менструального циклу та гіперандрогенії можливим буде діагноз «СПКЯ. Фенотип В» (ультразвукові ознаки не враховують). Підлітки, які мають ознаки СПКЯ, але не відповідають діагностичним критеріям, входять до «групи ризику» виникнення СПКЯ.
Наукові джерела свідчать, що найважливішим етапом терапії СПКЯ є модифікація способу життя, нормалізація маси тіла та метаболічних процесів. Описано терапію комбінованими оральними контрацептивами, яку у підлітків частіше призначають не за прямим призначенням (контрацепція), а у якості терапії off-label не тільки при встановленому діагнозі, але й у «групі ризику», що передбачає лікування нерегулярних менструальних циклів та/або клінічної гіперандрогенії. За відсутності ефекту від зміни способу життя, правильного харчування з метою корекції метаболічних порушень додатково до комбінованих оральних контрацептивів можливе призначення метформіну, інозитолів тощо.
Ключові слова: *синдром полікістозних яєчників, підлітковий вік, діагностика, гормони, ультразвукове дослідження, фенотип, лікування.*

Современные подходы к диагностике и лечению синдрома поликистозных яичников в подростковом возрасте

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В статье приведен обзор литературы, освещающий проблему диагностики синдрома поликистозных яичников (СПКЯ) в подростковом возрасте. Обсуждена проблема, которая заключается в том, что характеристики нормального полового созревания часто совпадают с симптомами СПКЯ. Представлены критерии нормального менструального цикла, клинической и лабораторной гиперандрогении. Приведены данные, свидетельствующие, что в диагностике последней наиболее информативными показателями является определение индекса свободного тестостерона и андростендиона, а оценка уровней свободного и общего тестостерона имеет относительно низкую чувствительность.
К клинической гиперандрогении у подростков относят только тяжелую форму акне и гирсутизм. Уровень антимюллерова гормона не имеет самостоятельного значения. Нерегулярные менструальные циклы в течение первого года после менархе представляют обычный период полового созревания. Приведены данные, что на втором и третьем гинекологическом возрасте нерегулярными считают менструальные циклы менее 21 дня и более 45 дней, а с четвертого гинекологического возраста – менее 21 дня и более 35 дней. Начиная со второго года после менархе, нарушением менструального цикла считается более 90 дней для любого цикла.
О первичной аменорее свидетельствует отсутствие менархе в 15 лет или через 3 года после телархе. Как указывает анализ научных публикаций, ультразвуковое исследование не используют в качестве критерия СПКЯ первые 8 лет после менархе из-за высокой частоты мультифолликулярности яичников в подростковом возрасте. Поэтому у девочек-подростков при наличии нарушения менструального цикла и гиперандрогении возможным будет диагноз «СПКЯ. Фенотип В» (ультразвуковые признаки не учитывают). Подростки, у которых имеются признаки СПКЯ, но не отвечают диагностическим критериям, входят в «группу риска» возникновения СПКЯ.
Научные источники свидетельствуют о том, что важнейшим этапом терапии СПКЯ является модификация образа жизни, нормализация массы тела и метаболических процессов. Описана терапия комбинированными оральными контрацептивами, которую у подростков чаще назначают не по прямому назначению (контрацепция), а в качестве терапии off-label не только при установленном диагнозе, но и в «группе риска», что предусматривает лечение нерегулярных менструальных циклов и/или клинической гиперандрогении. При отсутствии эффекта от изменения образа жизни, правильного питания в целях коррекции метаболических нарушений дополнительно к комбинированным оральным контрацептивам возможно назначение метформина, инозитолов и т.д.

Ключевые слова: *синдром поликистозных яичников, подростковый возраст, диагностика, гормоны, ультразвуковое исследование, фенотип, лечение.*

Polycystic ovary syndrome (PCOS) – is the most common endocrine disease, affecting 8% to 13% of women of childbearing age and 6–18% of adolescent girls, depending on the diagnostic criteria used and the population studied [1, 2, 3, 4, 5]. Its prevalence increases to 20-40% in families with PCOS [6]. In the structure of anovulatory infertility, this pathology reaches 80%, and 70% of women have undiagnosed PCOS [7, 8].

The close association of the syndrome with metabolic disorders leads to the development of complications such as obesity, 10 times increases the risk of developing type 2 diabetes, 7 times – hypertension and coronary heart disease, including myocardial infarction, more than 2 times – the risk of developing cancer of the ovaries, endometrium, breast [9].

Approaches to the diagnosis, treatment and improvement of the quality of life of patients with PCOS are constantly being updated and supplemented. According to the 2018 guidelines (International evidence-based guideline for the assessment and management of polycystic ovary syndrome), the basis for diagnosis remains the 2003 Rotterdam criteria. The relevance of determining the phenotypes of the syndrome [10] was also confirmed. The Joint ESHRE / ASRM Symposium in Rotterdam identified the following PCOS criteria: clinical and / or biochemical hyperandrogenism, oligo- or anovulation; polycystic ovarian transformation, which was detected during ultrasound. The diagnosis is made in the presence of two of the three signs, provided that other diseases are manifested, which are manifested by classic clinical signs of hyperandrogenism and menstrual disorders [11, 12].

PCOS is not only a gynecological and reproductive problem. Changes in carbohydrate and lipid metabolism, cardiovascular function, mental health, and increased risk of oncopathology throughout the life of the woman and her offspring are important. Therefore, to assess the level of risk and the profile of possible comorbidities and to develop a rational individual treatment plan for the patient, it is important to determine the phenotypes of the syndrome [8, 10]. 4 clinical variants (phenotypes) of PCOS were identified. Phenotype A (classical), which is characterized by the presence of all three signs of the syndrome: hyperandrogenism (clinical and / or biochemical) + anovulation + polycystic ovary transformation (according to ultrasound). Phenotype B or incomplete classical: hyperandrogenism + anovulation. Phenotype C or ovulatory: hyperandrogenism + polycystic ovary transformation. Phenotype D or non-androgenic: anovulation + polycystic ovary transformation [7, 8, 11].

The formation and clinical manifestations of PCOS often begins in adolescence. According to the World Health Organization, adolescence is the period between 10 and 19 years, when there are significant and decisive changes in growth, development and puberty [2]. Diagnosis and treatment of PCOS in adolescence still raises many questions. The problem is that the characteristics of normal puberty often coincide with the symptoms of PCOS in reproductive age [2, 9]. Therefore, for adolescents, it is important to prevent missed diagnosis, underdiagnosis, or overdiagnosis. Therefore, it is important to identify girls at risk for PCOS, as well as to carry out scientifically treatment of the symptoms of the disease [2].

Early diagnosis of PCOS allows early monitoring of metabolic complications, which are usually secondary to hyperandrogenism and insulin resistance. These include hyperinsulinemia, type 2 diabetes, hypertension, cardiovascular disease, dyslipidemia, non-alcoholic fatty liver disease, endometrial cancer and an increased risk of depression. About 50-80% of young girls with PCOS are obese, and 30-35% suffer from impaired glucose tolerance. Recent data confirm the genetic link between

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PCOS and diabetes, as PCa-related genes are located next to the insulin receptor gene [6].

Hyperandrogenemia (HA) and insulin resistance (IR) play a key role in the pathogenesis of PCOS [8]. The syndrome is a diagnosis of exclusion, so biochemical studies are aimed not only at detecting HA, but also at the differential diagnosis of HA, which can occur in hypothalamic syndrome of pubertal and postpubertal periods, congenital adrenal dysfunction, hypothyroidism, hyperprolactinemia, obesity, acromegaly, Cushing's disease [13]. The level of androgens in the blood should be determined on day 3-5 of the menstrual cycle, assuming that the release of LH occurs in 7-10 days and increases the level of total and free testosterone by 20-30% [11]. In the diagnosis of HA, the determination of free and total testosterone levels is relatively low, the most informative indicators, according to the recommendations of the European Society of Endocrinology (ESE), are the index of free testosterone and androstenedione. It is the increase in androstenedione and free testosterone index found in over 60% of women with acne and PCOS [13, 14]. It is important to remember that the study of androgen levels is an auxiliary method for diagnosis and in no case should be used as the main criterion or substitute for clinical diagnosis of PCOS [7]. Androstenedione and dehydroepiandrosterone sulfate (DHEAS) provide limited additional information in the diagnosis of PCOS, but may be considered if total or free testosterone is not elevated. Androstenedione and DHEAS are more useful in eliminating other causes of hyperandrogenism. Androstenedione is elevated in nonclassical adrenal hyperplasia. DHEAS is predominantly adrenal androgen and a moderate increase can be observed in PCOS, whereas a significant increase and / or virilization can be observed in androgen-secreting adrenal tumors [2].

The Rotterdam criteria also indicate the diagnostic value of the clinical manifestations of androgen overdose in androgen-dependent dermatopathies (AD), which include acne, hirsutism, seborrhea, and alopecia. Manifestation of symptoms of hyperandrogenism in most women occurs during puberty. AD in adolescents is diagnosed mostly after menarche due to pubertal enhancement of the hypothalamic-pituitary system. The term «perimenarcheal debut» of hyperandrogenism syndrome is used in the literature. In the initial stages of its formation, acne and seborrhea predominate, with minimal or no manifestations of hirsutism. From the age of 8, the secretion of sebaceous glands in girls increases sharply, which indicates the beginning of adrenarche. The main hormone involved in the regulation of sebaceous glands is testosterone. This hormone affects the proliferative activity of the sebaceous glands and the processes of lipogenesis - they are especially pronounced at the age of 12 to 25 years. This is due to the determinism of adolescent changes, when the primary importance in the development of the organism belongs to androgens, which determine the peak of growth, maturation of long tubular bones, closure of diaphyso-epiphyseal cartilage, the appearance of female hair [15]. Guideline 2020 suggests that clinical hyperandrogenism in adolescents includes severe acne and hirsutism [2]. Mild comedonal acne is common in adolescent girls, but moderate or severe comedonal acne (10 or more facial lesions) in early puberty or moderate to severe inflammatory elements during menarche is rare (less than 5%) and most likely associated with clinical hyperandrogenism. Hirsutism is a much more significant feature of HA, and is found in approximately 60% of women with PCOS. Hirsutism is often less pronounced in adolescents than in women of reproductive age, in whom due to prolonged exposure to androgens characteristic hair growth becomes more obvious, ie there is an increase in hirsutism with age and time after menarche [9].

The physiology of the first phase of puberty (before menarche) and the first 2 years after menarche is also characterized by IR due to increased production of growth hormone (insulin is needed during this period as an important mitogenic factor for normal physiological development and maturation of reproductive organs and tissues). Therefore, managing adolescent girls with AD is a very difficult task, as it is necessary to distinguish between so-called «physiological» hyperandrogenism and hyperinsulinemia of puberty, which occur 1-2 years after menarche, from pathology caused by endocrine disorders [13]. The ESE guidelines state that the luteinizing hormone (LH) / follicle-stimulating hormone (FSH) ratio is not a diagnostic criterion for PCOS. Almost 70% of women with PCOS have high levels of LH secretion and a LH / FSH ratio of more than 2.5, but a ratio of less than 2 is not a criterion for excluding this pathology. There are several isoforms of LH, which differ in the level of biological activity due to the different structure of the side oligosaccharide chains. Only the level of bioactive forms of LH can be a truly informative marker of PCOS [9]. Antimullerian hormone (AMH) is a substance produced by granulosa cells of preantral and small antral ovarian follicles and plays an important role in the development of follicles and their maturation. Its level does not depend on the time of the menstrual cycle or the use of combined oral contraceptives, in contrast to LH and FSH. AMH secretion is approximately 75 times higher in polycystic ovaries than in normal ones; plasma levels are 2-4 times higher in women with PCOS than in healthy people [6]. Elevated AMH levels (> 4.5 ng / ml) may be useful during the diagnosis of PCOS if it is not possible to perform a qualitative ultrasound assessment of ovarian morphology, but only the level of antimullerian hormone is not independent [2, 8, 10]. Although the measurement of AMH concentrations has prospects, its diagnostic value for the diagnosis of PCOS in adolescents is currently being studied [6, 16, 17, 18].

Weight gain, obesity in women with PCOS, regardless of age – are indications for assessing the lipid profile (cholesterol, low and density lipoproteins, triglycerides) [8, 10]. The frequency of follow-up further depends on the presence of hyperlipidemia and risk factors for cardiovascular disease: obesity, cigarette smoking, dyslipidemia, hypertension, impaired glucose tolerance and hypodynamics. Laboratory markers of IR and lipid metabolism disorders characteristic of PCOS may be absent in adolescents in the early stages of the syndrome. The use of traditional physical methods to determine the body mass index, the ratio of waist and hips, the thickness of the skin folds allows in the early stages to detect the first signs of metabolic disorders [9].

Regarding anovulation and menstrual disorders in adolescents. It should be remembered that variations in the interval of the menstrual cycle according to the time after menarche are normal physiological phenomena in adolescence, as anovulation is a common physiological event in the early years after menarche. Physiological maturation of the hypothalamic-pituitary-ovarian system occurs with age, and ovulation and menstrual cycles in adolescents may not coincide with those in women of childbearing age [2, 8, 9, 10]. During the first years after menarche, anovulation accompanies 80% of menstrual cycles, and the regular nature of menstruation is observed in 75-80% of girls. Delayed menstruation is observed in 20-25% of adolescents with menarche within two years, which is sometimes replaced by bloody

discharge lasting more than 8 days. Regular ovulatory cycles are registered up to 14-16 years in 75% of girls, but the final formation of the peak of LH and luteal phase occurs only at 17-18 years of age [9]. It has now been shown that irregular menstrual cycles during the first year after menarche represent a normal period of puberty [2, 10]. This does not apply to very heavy, prolonged or frequent menstruation, which is considered abnormal uterine bleeding during puberty and should be treated. From the second or third year after menarche, menstrual cycles of less than 21 days and more than 45 days are considered irregular. From the fourth year after menarche it is less than 21 days and more than 35 days. From the second year after menarche, menstrual irregularities are considered to be more than 90 days for any cycle. We speak of primary amenorrhea in the absence of menarche at the age of 15, or 3 years after telarche [2, 8, 10]. The reason for medical vigilance for adolescent girls should be the lack of tendency to form a stable menstrual cycle for 1.5-2 years after menarche or its violation after a «successful start» [9].

Ovarian morphology was adopted as one of the diagnostic criteria for PCOS according to the Rotterdam Consensus: ovarian volume greater than 10 cm3, the presence of multiple (more than 12) follicles up to 10 mm in diameter in one section, mostly located on the periphery. Many ultrasound physicians do not differentiate this picture with multifollicular ovaries characteristic of puberty. Secondly, abdominal ultrasound (AUS) is more often used during the examination of girls, the informativeness of which may be limited by overweight, flatulence. Magnetic resonance imaging is potentially more accurate in assessing ovarian status, but transabdominal ultrasound remains the primary diagnostic tool in adolescents [9]. According to various authors, the probability of error in the diagnosis of PCOS according to the results of ultrasound is 18-47%. Hyper- and hypodiagnostics of ultrasonic signs are equally likely due to the complexity of their interpretation [8, 10].

This controversial problem has been resolved by the International Guidelines in 2018, which provides specific recommendations [10]. The Guide emphasizes the significant development of ultrasound technology and the growing number of follicles recommended for diagnosis even in adult women, which helped to recommend the use of pelvic ultrasound in the diagnosis of PCOS in women less than 8 years after menarche.

Ultrasound is not used as a criterion for PCOS in the first 8 years after menarche due to the high frequency of ovarian multifollicularity in adolescence. Young women at risk require dynamic monitoring, ie re-examination with re-evaluation of the results. Adolescents who do not fully meet the diagnostic criteria may be identified as having an «increased risk» of developing PCOS. Such patients need to be re-evaluated after puberty or 8 years after menarche [8, 10]. Although pelvic ultrasound is not indicated for the diagnosis of PCOS in adolescents, it can be used to examine other possible uterine or ovarian abnormalities in adolescent girls, such as those with primary amenorrhea [2]. From the above it follows that adolescent girls in the presence of menstrual disorders and hyperandrogenism, we can discuss the diagnosis: «PCOS. Phenotype B» (ultrasound signs are not taken into account). For adolescents who have signs of PCOS but do not meet the diagnostic criteria, the risk group for PCOS may be considered, and it is recommended to re-evaluate in full during or until full reproductive maturity. This time is 3 years after menarche due to menstrual irregularities and 8 years after menarche due to the use of pelvic ultrasound to detect morphology of polycystic ovaries. Reassessment is especially important for adolescent girls with persistent signs of PCOS, significant weight gain, and after hormone therapy [2].

It is vital when managing girls with PCOS or «at risk group» to focus on lifestyle interventions to prevent overweight, avoiding obesity, but lifestyle interventions alone are unlikely to help get rid of excess weight and metabolic changes [2]. In girls and young women who are not planning to become pregnant in the near future, PCOS therapy usually has two goals. One is the normalization of the menstrual cycle and the elimination of clinical manifestations of HA, the other is the prevention of often ignored by many clinicians long-term complications of the syndrome, which significantly impairs the quality of life. This is the prevention of hyperplastic processes in target organs and metabolic disorders that often accompany this syndrome [9].

In the first place in the management of patients with PCOS is a modification of lifestyle, which includes a healthy diet and regular physical activity to normalize body weight, hormonal and metabolic parameters. With overweight, weight loss of 5-10% over 6 months may be accompanied by significant clinical improvements. For women over the age of 18, the recommended physical activity of medium intensity is at least 150 minutes / week, energy intensity – 75 minutes / week. For adolescents will be effective at least 60 minutes of moderate and intense physical activity per day, including exercises that strengthen muscles and bones at least three times a week [7, 8, 10, 19, 20, 21, 22].

Timely correction of metabolic disorders achieved by lifestyle changes and a balanced diet, use of hypoglycemic drugs, vitamin and phytotherapy, which leads to normalization of hormonal status and restoration of menstrual rhythm. In the absence of effect in order to normalize the menstrual cycle, it is possible to prescribe progestogens from 16 to 25 days from the beginning of menstruation for 3-6 months. [9]. Progestin therapy is prescribed if the adolescent is unable or unwilling to use estrogen-progestogen drugs [6].

Inositol (in any form) is recommended for the treatment of PCOS, although it should be considered an experimental treatment for PCOS with evidence of efficacy that requires further investigation. The reason for prescribing inositol in case of PCOS is its antiandrogenic effect. Inositol increases the sensitivity of cell receptors to insulin, and thus leads to a decrease in insulin, glucose. It can be used to correct metabolic disorders and obesity [8, 10, 23, 24, 25, 26, 27].

Combined oral contraceptives pills (COCP) are recommended for women of childbearing potential with PCOS for the treatment of androgen-dependent dermatopathies and / or menstrual disorders [7, 23, 28, 29, 30]. The appointment of COCP in adolescents is possible not only at diagnosis, but also in the «risk group» for the treatment of irregular menstrual cycles and / or clinical hyperandrogenism [2, 10, 31, 32]. For this purpose, low-dose and micro-dose drugs are used, taking into account specific risk factors for PCOS, such as high BMI, hyperlipidemia, hypertension, and similar effectiveness of different types of COCP in the treatment of hirsutism [7, 10, 12, 24, 30, 32]. The combination of ethinyl estradiol and cyproterone acetate 35 mcg is not a first-line drug in the case of PCOS due to adverse effects, lack of evidence of greater efficacy and higher risks, including deep vein thrombosis [2, 10, 32]. All COCP are associated with an increased risk of deep vein thrombosis, but the risk is higher with a combination of 30-35 mcg ethinyl estradiol and gestodene, desogestrel, cyproterone acetate or drospirenone compared with 30 mcg ethinyl estradiol with

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levonorgestrel, norethisterone. Low-risk COCP should be recommended as first-line therapy [2, 33].

When developing a treatment regimen for adolescents with PCOS or «at risk group», physicians need to take into account personal characteristics (gynecological age, somatic and gynecological history, experience and effectiveness of previous therapy), patient preferences. More than half of adolescent girls are concerned about menstrual irregularities, one in ten with hirsutism, and 13% with weight gain [6]. It is important to assess the expected outcome, possible risks and side effects of therapy. It should be borne in mind that COCP and metformin are generally not used for their intended purpose in the treatment of PCOS (off-label). This should be discussed with adolescents and their families when considering the benefits of therapy and potential side effects for each drug. Misuse of drugs occurs when drugs are prescribed for indications that are not included in the document with information about the approval of the drug by the relevant regulatory authority. Off-label therapy is permitted in many countries and is very common in pediatric practice [2]. COCP are relatively safe drugs, but there are absolute medical contraindications that should be considered in accordance with the World Health Organization Guidelines: migraine with aura, deep vein thrombosis, history of pulmonary embolism, known thrombogenic mutations, multiple risk factors for cardiovascular disease, breast cancer, neuropathy, severe cirrhosis and malignant liver tumors [34]. Smoking and obesity are also risk factors for deep vein thrombosis, but the absolute risk of these complications in adolescents remains very low [2].

In the treatment of androgen-dependent dermatopathies, COCP should be preferred to antiandrogens. The ineffectiveness of this therapy for at least 6 months gives grounds to consider the appointment of the latter. If COCP are contraindicated or poorly tolerated, in the presence of effective forms of contraception, antiandrogens may be considered for the treatment of hirsutism or androgenic alopecia. The use of effective contraception is extremely important because of their teratogenic potential [2].

In the absence of the effect of lifestyle changes, proper nutrition to correct metabolic disorders in addition to COCP may be prescribed metformin, including adolescents with PCOS and BMI ≥25 kg / m2. This combination can be most useful at high metabolic risk, in particular in the presence of risk factors for diabetes and impaired glucose tolerance [2, 8, 10, 24, 27, 35, 36, 37, 38].

CONCLUSION

Peculiarities of hormonal homeostasis and metabolism in adolescence create the preconditions for overdiagnosis of polycystic ovary syndrome, and modern guidelines for diagnosis allow not only to avoid this, but also to identify the «risk group» of the syndrome. The most important stage in the treatment of polycystic ovary syndrome is lifestyle modification, normalization of body weight and metabolic processes. Combined oral contraceptives in adolescents are more often prescribed not for direct purposes (contraception), but as off-label therapy not only at diagnosis, but also in the «risk group», which involves the treatment of irregular menstrual cycles and / or clinical hyperandrogenism. After all, timely and adequate treatment of young patients with polycystic ovary syndrome solves not only current medical problems, but also improves quality of life and serves to prevent long-term complications of this condition.

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