New Day in Medicine
Новый День в Медицине
NDM

TIBBIYOTDA YANGI KUN

Ilmiy referativ, marifiy-ma'naviy jurnal

AVICENNA-MED.UZ

ISSN 2181-712X.
EiSSN 2181-2187

7 (69) 2024

ТИББИЁТДА ЯНГИ КУН
НОВЫЙ ДЕНЬ В МЕДИЦИНЕ
NEW DAY IN MEDICINE

Илмий-рефератив, маънавий-маърифий журнал
Научно-реферативный,
духовно-просветительский журнал

УЧРЕДИТЕЛИ:

БУХАРСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ ИНСТИТУТ
ООО «ТИББИЁТДА ЯНГИ КУН»

Национальный медицинский исследовательский центр хирургии имени А.В. Вишневского является генеральным научно-практическим консультантом редакции

Журнал был включен в список журнальных изданий, рецензируемых Высшей Аттестационной Комиссией Республики Узбекистан (Протокол № 201/03 от 30.12.2013 г.)

7 (69)

2024

ИЮЛЬ

www.bsmi.uz
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Received: 20.06.2024, Accepted: 02.07.2024, Published: 10.07.2024

УДК 618.11-006.25-053.2

FEATURES OF DIAGNOSIS AND TREATMENT OF POLYCYSTIC OVARY SYNDROME

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✓ ***Resume***

Polycystic ovary syndrome (PCOS) is a heterogeneous symptom complex accompanied by the development of endocrine and metabolic disorders associated with structural changes in the ovaries, leading to infertility of endocrine genesis. Formation of PCOS occurs during the period of formation of hormonal and menstrual functions, and its individual signs may be transient phenomena. The issues of early diagnosis of PCOS and its predictors in adolescent patients, determination of clinically significant markers of PCOS, identification of risk groups and development of a systemic approach to the correction of various endocrine and metabolic disorders require special attention and detailed study.

Key words: menstrual disorders, polycystic ovary syndrome, anovulation

ОСОБЕННОСТИ ДИАГНОСТИКИ И ЛЕЧЕНИЯ СИНДРОМА ПОЛИКИСТОЗНЫХ ЯИЧНИКОВ

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✓ ***Резюме***

Синдром поликистозных яичников (СПКЯ) – это гетерогенный симптомокомплекс, сопровождающийся развитием эндокринных и метаболических нарушений, связанных со структурными изменениями яичников, приводящих к бесплодию эндокринного генеза. Формирование СПКЯ происходит в периоде становления гормональной и менструальной функций, а отдельные его признаки могут оказаться транзиторными явлениями. Вопросы ранней диагностики СПКЯ и его предикторов у пациенток подросткового возраста, определения клинически значимых маркеров СКПЯ, выявление групп риска и разработка системного подхода к коррекции различных эндокринных и метаболических нарушений требуют особого внимания и подробного изучения.

Ключевые слова: расстройства менструаций, синдром поликистозных яичников, ановуляция

ТУХУМДОН ПОЛИКИСТОЗ СИНДРОМИ ДИАГНОСТИКА ВА ДАВОЛАШ УСУЛЛАРИ

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✓ ***Резюме***

Тухумдон поликистоз синдроми (ТПС)- тухумдонлардаги ўзгаришлар билан боғлиқ бўлган эндокрин ва метаболик касалликларнинг ривожланиши билан бирга эндокрин келиб чиқадиган бепуштликка олиб келадиган симптомлар мажмуасидир. ТПС шаклланиши гормонал ва ҳайз кўриш функцияларининг шаклланиши даврида содир бўлади ва унинг баъзи белгилари вақтинчалик белгилар бўлиши мумкин. Ўсмир беморларда ТПС ва унинг прогнозларини эрта ташхислаш, ТПС нинг клиник аҳамиятли белгиларини аниқлаш, хавф гуруҳларини аниқлаш ва турли эндокрин ва метаболик касалликларни тузатишга тизимли ёндашувни ишлаб чиқиш масалалари алоҳида эътибор ва батафсил ўрганишни талаб қилади.

Калит сўзлар: ҳайз даврининг бузилиши, тухумдон поликистоз синдроми, ановуляция

Relevance

The diversity of clinical manifestations of polycystic ovary syndrome (PCOS) is associated with difficulties in its diagnosis. In recent years, several diagnostic criteria for PCOS have been proposed [1].

According to the consensus symposium of the European Society of Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM) 2010 [2], PCOS affects 6 to 10% of women, provided that the diagnostic criteria of the US National Institute of Health were used; if we rely on the criteria of the 2003 Rotterdam Symposium [3], this figure is 15%.

It is difficult to determine the prevalence of PCOS among adolescent girls at present due to the lack of reliable diagnostic criteria and insufficient attention to the manifestation of endocrine-metabolic manifestations in puberty.

According to the consensus of the European

Association of Endocrinologists (ESHRE) 2012, 45% of women of reproductive age with PCOS suffer from infertility [2]. The frequency of PCOS in the structure of endocrine infertility reaches 62% [2]. The close association of PCOS with metabolic disorders entails the development of such complications as obesity and type 2 diabetes mellitus, which develops later in 10% of women of reproductive age [4–7, 28, 29]. In 2–7% of patients with PCOS, the development of hyperplastic processes of the endometrium and mammary glands is likely [2, 28, 29].

Etiology and pathogenesis of PCOS: key points PCOS is most often not an independent nosological form. It is a symptom complex, a terminal condition of chronic anovulation of various genesis. The links in this process may include a disturbance in the secretion rhythm of gonadotropic releasing hormone (GnRH) and gonadotropins, mainly luteinizing hormone (LH); hyperandrogenism, insulin resistance and hyperinsulinemia, lipid metabolism disorders, and hyperprolactinemia. It is far from always possible to determine which component of this complex process is primary [4, 6, 8, 9]. Risk factors include changes in the metabolism of neurotransmitters and opioids, and, as a consequence, a decrease in their inhibitory effect on GnRH secretion [6].

Peripheral conversion of androgens to estrogens occurs mainly in adipose tissue. Obesity, especially visceral, during the period of adrenarche is considered one of the leading risk factors for the development of PCOS, as well as a condition that greatly complicates the course of the syndrome.

Visceral fat is metabolically active, and as a result of lipolysis, fatty acids are released and a number of cytokines (tumor necrosis factor, interleukin-6, leptin, resistin) are produced, which contribute to the development of insulin resistance [7, 10, 11]. An increased concentration of fatty acids through tumor necrosis factor (TNF) causes phosphorylation of serine in the insulin receptor, and as a consequence, a violation of its activation mechanism and the formation of insulin resistance. Excess freely circulating fatty acids can lead to an increase in androgen levels due to phosphorylation of cytochrome P450c17, which results in activation of 17,70-lyase, and androgen synthesis through increased production of androstenedione, dehydroepiandrostenedione (DHEA) and testosterone (this is important to consider in laboratory diagnostics of PCOS) [6].

Insulin resistance, which develops against the background of hyperinsulinemia, plays an important role in the pathogenesis of PCOS.

Hyperandrogenism in hyperinsulinemia is formed both by increasing ovarian production of androgens and by suppressing the secretion of sex-steroid-binding globulin (SSBG), which reduces the content of biologically active androgens in the blood. LH and insulin are synergists - insulin potentiates the action of LH. Insulin resistance and hyperandrogenemia are directly dependent on each other [12]. Insulin can play the role of an agonist of receptors to insulin-like growth factor (IGF), and, thus, theca cells of the ovary become more sensitive to the effects of insulin. Insulin resistance may be based on a defect in the activation of insulin signaling pathways (instead of tyrosine phosphorylation, serine phosphorylation occurs), mediated by an excess of freely circulating fatty acids. Thus, excess body weight aggravates existing insulin resistance [13].

Elevated prolactin levels can also contribute to pathological conditions - from shortening of the luteal phase of the menstrual cycle to the development of chronic anovulation [14]. The mechanism of the pathological effect of excess prolactin on the normal menstrual cycle is approximately as follows: in response to an increase in prolactin, the dopaminergic system closely associated with it is compensatorily activated and, in parallel, the level of GnRH decreases, inhibiting its secretion. Detection of clinical (galactorrhea) and laboratory increases in prolactin levels is very important in determining

the genesis of anovulation [14]. One of the reasons for the development of chronic anovulation is a violation of the synthesis of thyroid hormones, including because hypothyroidism is closely associated with hyperprolactinemia [15]. During puberty, even with an established menstrual cycle and hormonal status approaching the levels of hormones of the fertile period, the reproductive system has significant lability and is highly sensitive to the effects of any adverse exogenous and endogenous factors. The instability of the circadian rhythm of gonadotropins and the level of insulin in the blood, characteristic of phase I of the puberty period, is an additional factor contributing to the formation of PCOS. In the prepubertal period, a physiological growth spurt is observed due to the activation of the function of the adrenal cortex with increased secretion and metabolism of androgenic steroids (DHEA-S). The action of any non-specific factor can convert physiological androgenism into pathological hyperandrogenism (HA) and, ultimately, lead to the development of polycystic ovary disease [9, 16]. In the period up to 18–20 years, even minor stress factors: hyperinsolation, excessive physical overload, factors of psycho-emotional stress, previous acute respiratory viral infections and other unfavorable effects - can have a pronounced negative effect on the physiology of the reproductive system, gradually causing dysfunction of the hypothalamic-pituitary system [8, 17, 18].

Features of PCOS diagnostics in adolescents The formation of PCOS and the manifestation of its clinical manifestations often begin in adolescence [19, 20].

A number of specialists [8, 20], seeking to avoid overdiagnosis and unjustified therapeutic measures, are inclined to believe that a diagnosis of PCOS is possible only after 18 years of age, and before that it is advisable to use the term "emerging PCOS". However, according to data from the latest ESHRE/ASRM consensus symposium, young patients can be diagnosed with PCOS if all three diagnostic criteria are confirmed, as well as if hirsutism is detected in them [21].

When identifying signs of PCOS in adolescents, specialists face a number of difficulties due to the peculiarities of the functioning of the girl's reproductive system during puberty.

Menstrual disorders

One of the important clinical manifestations of PCOS is oligomenorrhea or amenorrhea. However, in the first years after menarche, anovulation can be detected in 40-50% of girls [8, 20]. The number of ovulatory cycles gradually increases from 20-25% in the first year after menarche to 60-65% by the 5th year, and this situation, reflecting the peculiarities of the formation of the girl's reproductive system, is not a pathology if considered separately from other criteria. At the same time, the number of ovulatory cycles in women diagnosed with PCOS does not exceed 30-32% [4]. The reason for medical caution in relation to adolescent girls should be the absence of a tendency towards the formation of a stable regular menstrual cycle within 1.5–2 years after menarche.

Hyperandrogenemia/hyperandrogenism

The main clinical manifestations of hyperandrogenemia (HA) in PCOS are various types of androgen-dependent dermopathy: hirsutism, acne, and androgenetic alopecia.

Acne is quite common among adolescents and is often a transient phenomenon. Hirsutism is a much more significant sign of HA. Laboratory diagnostics of HA is often difficult.

Determining only total testosterone in the absence of information on such indicators as SBSH and/or free testosterone is uninformative, including due to the fact that testosterone is converted into more biologically active DHT. On the other hand, reliable methods for determining these parameters are under development [6].

A multisteroid analysis in 20% of girls with PCOS revealed an increase in androstenedione [16]. Possibly, one of the links of hyperandrostenedionemia is excess body weight and an increase in the level of free fatty acids with cholesterol and, as a consequence, the acceleration of its transformation into pregnenolone, 17-progesterone, DHEA-S and then into androstenedione and testosterone. Traditionally, one of the most important diagnostic criteria for PCOS in adolescents is a change in the LH/FSH ratio [4], while the data of the Rotterdam Consensus and the American National Institute of Health do not include it. There are several isoforms of LH, differing in the structure of the side oligosaccharide chains and, as a consequence, in the level of biological activity. A truly informative marker of PCOS may be the level of bioactive forms of LH, and not its ratio to FSH [3, 6].

Ultrasound diagnostics

Ultrasound picture of PCOS - ovarian volume more than 10 cm3, presence of multiple (more than 12) equal-sized cystic atretic follicles with a diameter up to 10 mm, located along the periphery. It is important to differentiate this picture from multifollicular ovaries (MFO), typical for puberty. MFO are characterized by a small number of follicles with a diameter 4-10 mm, located throughout the ovary and, most importantly, an age-appropriate ovarian volume [4, 22, 23]. MFO are a common phenomenon and a normal variant for girls in puberty and are not a sign of PCOS.

Metabolic disorders

Patients demonstrating certain manifestations of metabolic syndrome may represent a risk group for the development of polycystic ovaries [4, 10, 11]. Traditional physical methods with determination of body mass index, assessment of waist-to-hip ratio, determination of skin fold thickness allow to identify the first signs of metabolic disorders.

A direct relationship has been established between the type of menstrual disorder and body mass index of patients with PCOS, as well as between IR and GA. Markers of insulin resistance in PCOS are the F. Caro index (less than 0.33), HOMA-IR (insulin resistance index – Homeostasis Model Assessment of Insulin Resistance) -more than 2.86 and hyperinsulinemia - more than 12.8 μU/ml). Disorders of lipid metabolism are manifested by an increase in the level of cholesterol and triglycerides and a decrease in the level of HDL [3, 6, 24].

Possibilities of PCOS therapy in girls. A pressing issue is the choice of effective and safe treatment

measures aimed at correcting PCOS. The need for therapy in this group of patients is obvious, and medical tactics directly affects the reproductive prognosis of the girl [2]. In patients of reproductive age, the leading reason for seeing a doctor is infertility. Therefore, the basis of the treatment strategy for them is the restoration of reproductive function by stimulating ovulation, correcting concomitant hormonal and metabolic disorders. In some cases, in the absence of the effect of ovulation stimulation, surgical treatment is used - laparoscopic cauterization (drilling) of the ovaries to reduce the excess number of large cystic follicles, reduce hyperandrogenism. The effectiveness of treatment is mainly determined by achieving the desired pregnancy. Combined oral contraceptives (COCs) are also used to treat patients with polycystic ovaries.

Particular attention is required for girls who have manifestations of PCOS, metabolic disorders due to pronounced decompensation of existing endocrine-metabolic disorders [25]. It is at them that therapeutic measures should be primarily aimed. Timely correction of metabolic disorders, achieved by changing lifestyle and a balanced diet, a reduction diet, and the use of hypoglycemic drugs, leads to normalization of the hormonal status and restoration of the menstrual rhythm [7, 10, 11, 27].

In the absence of the desired effect, the second stage of therapy may be the use of COCs. All the mechanisms that ensure control of ovarian functions have not yet been studied, but it is known that they suppress the secretion of LH, which, in turn, leads to a decrease in the level of androgens. The estrogenic component of COCs leads to an increase in the level of SHBG and, consequently, a decrease in the concentration of freely circulating testosterone. At present, there are a number of COCs containing a progestogenic component with antiandrogenic activity (cyptoteron acetate, chlormadinone, drosperinone), positioned as recommended for use in girls and women with clinically pronounced hyperandrogenism [2, 16, 21, 27]. Their action is based on a number of mechanisms: inhibition of ovarian androgen synthesis by the feedforward mechanism, blocking of peripheral androgen receptors, and a decrease in DHT formation as a result of suppression of 5-alpha-reductase. The progestogenic drug with drosperinone has a hypoglycemic effect. It is possible to prescribe COCs according to the standard scheme (21/7) and 3–6 menstrual cycles and according to the prolonged scheme (63/7) [24, 25, 28, 29].

However, the effectiveness of these drugs remains the subject of many discussions and is questioned, possibly due to the lack of reliable data on the effectiveness and limitations of their use in adolescents. For the treatment of hyperandrogenic conditions, it is possible to use antiandrogenic drugs (cyproterone acetate) in combination with COCs, estradiol valerate or separately [6].

After a course of treatment with COCs (in combination with antiandrogenic drugs or without), it is possible to decide on ovulation induction [28].

Conclusion

The manifestation of PCOS in puberty is the result of the impact on the reproductive function of various pathogenetic factors, as a result of their action (which) the maturation and growth of follicles are disrupted, anovulation and menstrual disorders are detected.

Manifest signs of PCOS can be observed during the physiological period of puberty, and some of its signs may be transient phenomena. The issues of early diagnostics, determination of clinically significant markers of PCOS and its predictors in adolescent patients require in-depth study to optimize approaches to screening studies, identify risk groups and develop a systemic approach to correcting various endocrine and metabolic disorders.

LIST OF REFERENCES:

1. Адамян Л.В., Богданова Е.А. Оперативная гинекология детей и подростков. – М.: ЭликсКом, 2004; 208-211 с.
2. Fauser B.C. Consensus on women’s health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group //Fertil. Steril. – 2012; P. 28–38.

3. The Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome //Ibid. 2003;81:19-25.
4. Манухин И.Б., Геворкян М.А., Кушлинский Н.Е. Синдром поликистозных яичников. – М.: МИА, 2004; 192-196 с.
5. Шилин Д.Е. Синдром поликистозных яичников //Междунар. диагност. консенсус и соврем. идеология тер. 2004;9:27-36.
6. Fritz M.A., Speroff L. Clinical Gynecologic Endocrinology and Infertility. – Lippincott Williams & Wilkins, 2011; P. 495-533.
7. Bloomgarden Z.T. American Association of Clinical Endocrinologists (AACE) consensus conference on the insulin resistance syndrome //Diabet Care. 2003;26: 1297-1303.
8. Богданова Е.А. Гинекология детей и подростков. /М.: МИА, 2010; 332-348 с.
9. Тумилович Л.Г., Геворкян М.А. Гинекологическая эндокринология. /М.: ГЭОТАР-Медиа, 2013; 131-138 с.
10. Moran L.J., Noakes M., Clifton P.M. et al. Dietary composition in restoring reproductive and metabolic physiology in overweight women with polycystic ovary syndrome //J. Clin. Endocrinol. Metab. 2003;88:812-819.
11. Solomon C.G., Hu F.B., Dunaif A. et al. Long or highly irregular menstrual cycles as a marker for risk of type 2 diabetes mellitus // JAMA. 2001;286:24-21.
12. Palomba S., Materazzo C., Falbo A. Metformin, oral contraceptives or both to manage oligo-amenorrhea in adolescents with polycystic ovary syndrome? A clinical review //Gynecol. Endocrinol. 2014;79:12-19.
13. Dunaif A.R., Bart C.J.M. Renaming PCOS – A two-state solution //J. Clin. Endocrinol. Metab. 2013;98:4325-4328.
14. The Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group Consensus on infertility treatment related to polycystic ovary syndrome //Fertil. Steril. 2008;89:505-522.
15. Azziz R. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report //Fertil. Steril. 2011;9:456-488.
16. Кулаков В.И., Долженко И.С. Основные тенденции изменения репродуктивного здоровья девочек в современных условиях //Репродукт. здоровье детей и подростков. 2005;1:22-28.
17. Гарден А.С. Детская и подростковая гинекология. /М: Медицина, 2001; 234-242 с.
18. Коколина В.Ф. Гинекологическая эндокринология детей и подростков: Руководство для врачей. 2-е изд. /М: МИА, 2001; – С. 287-293.
19. Уварова Е.В. Современные способы коррекции гиперандрогении у девочек-подростков //Эффективная фармакотерапия в акушерстве и гинекологии. 2008; С. 4-12.
20. Гуркин Ю.А. Гинекология подростков: Руководство для врачей. – СПб.: Фолиант, 2000; С. 574-592.
21. Богданова Е.А., Телунц А.В. Гирсутизм у девочек и молодых женщин. /М: Медпресс-информ, 2002; С. 128-134.
22. Мазитова Л.П. Асламазян Л.К. Патогенетическое обоснование местной терапии акне в подростковом возрасте //Педиатр. фармакология. 2008;5:68-71.
23. Гус А.И., Серов В.Н., Назаренко Т.А. и др. Современные принципы ультразвуковой, клинической и лабораторной диагностики синдрома поликистозных яичников //Гинекология. 2002;4:21-30.
24. Шилин Д.Е. Коррекция метаболических и эндокринных нарушений при лечении гиперандрогении у девочек и девушек //Фарматека. 2003;16:8-12.
25. Уварова Е.В. Возможности применения комбинированных оральных контрацептивов в пролонгированном режиме при лечении СПКЯ //Пробл. репродукции. 2006;4:73-75.
26. Уварова Е.В. Гормональные препараты в практике детского гинеколога // Леч. врач. – 2002. – № 3. – С. 38–45.
27. Dunaif A.R., Chang J. Polycystic Ovary Syndrome: Current Controversies, from the Ovary to the Pancreas //Hum. Press, 2010: 51-122 p.
28. Уварова Е.В. Детская и подростковая гинекология. /М: Медицина, 2009; С. 249–268.
29. Сметник В.П. Неоперативная гинекология: Руководство для врачей. – СПб.: СОТИС, 1995; 224 с.
30. Руководство по эндокринной гинекологии / Под ред. Е.М. Вихляевой. /М.: МИА, 2006; 784 с.

Entered 20.06.2024