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Modern view on the etiology and pathogenesis of hyperandrogenic conditions in women of reproductive age against the background of normal levels of male steroid hormones

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Abstract: the article presents current literature data on the etiology and pathogenesis of hyperandrogenic conditions in women of reproductive age against the background of normal levels of male sex hormones. Most often, hyperandrogenic conditions occur due to excessive production of androgens by the ovaries or adrenal glands with increased sensitivity of sebaceous and hair follicle receptors to androgens. One of the main tools for clinical confirmation of hyperandrogenic conditions is the Ferriman-Gallway scale. Activation of androgen receptors, which are localized in the basal and glandular cells of the sebaceous glands, leads to the development of acne and other hirsute manifestations. These processes are most often realized by increasing the activity of 5 α -reductase, an enzyme that converts testosterone to dihydrotestosterone and is a direct stimulator of sebum synthesis. Treatment of hyperandrogenic conditions is carried out jointly by obstetricians and Gynecologists and dermatologists. Today, the leading link in therapy is combined oral contraceptives, which block the production of 5 α -reductase. One of the most effective agents is ciproterone acetate, which is a synthetic hydroxyprogesterone with antiandrogenic and antigonadotropic activity. Flutamide, which is a nonsteroidal selective androgen receptor blocker, is also widely used in the treatment of hyperandrogenic conditions. Thus, the review indicates the absence of a single view on the etiology and pathogenesis of hyperandrogenic conditions against the background of normal levels of sex hormones, and also indicates the absence of a single algorithm for correcting clinical manifestations.

Key words: [Acne](#), [Hyperandrogenism](#), [Hormones](#), [Hirsutism](#), [Polycystic Ovary Syndrome](#), [Flutamide](#), drosperinone, ciproterone acetate.

Introduction

Hyperandrogenic conditions are one of the most common endocrinopathies in women of reproductive age. This condition is observed in approximately 10–20% of women, while approximately

80% of cases are polycystic ovary syndrome and are associated with impaired reproductive function, pregnancy complications, metabolic disorders, risk of endometrial cancer, and other conditions (Azziz et al., 2016; Inoue et al., 2014; Tan et al., 2021).

Aim

To investigate the main links of the pathogenesis of hyperandrogenic conditions in women of reproductive age against the background of normal levels of male sex hormones.

Materials and methods

Analysis of modern literary sources indexed in Scopus, Web of Science.

Review and discussion

Hyperandrogenism is an endocrine disease associated with increased synthesis or activity of male sex hormones in a woman's body. Direct manifestations of hyperandrogenism include dermatopathies and polycystic ovaries. The main dermatological manifestations of hyperandrogenism include acne, hirsutism, androgenic alopecia and seborrhea (Inoue et al., 2014; Sung, Oh, Chung and Lee, 2014; Azziz et al., 2016; Tan et al., 2021). Hirsutism is defined as excessive hair growth in women in androgen-dependent areas (according to the male type) – the inner surface of the thighs, abdomen, around the nipples, neck, upper lip, chin, temples. In addition to an increase in the levels of male sex hormones, a possible reason for the development of this condition may be the increased sensitivity of receptors of sebaceous glands and hair follicles to androgens, as well as increased conversion of testosterone into more active forms (Inoue et al., 2014; Azziz et al., Bissonnette et al., 2015; 2016; Liu et al., 2015; Tan et al., 2021). In the vast majority of cases, an increase in the level of male sex hormones or adrenal hormones can be determined in the laboratory, but very often in the clinical practice of an obstetrician-gynecologist, there are cases when the clinical manifestation of hyperandrogenism is present, but the increase in androgen levels is not confirmed in the laboratory (Inoue et al., 2014; Azziz et al., 2016; Kim et al., 2017).

The ability to visually confirm the presence of an increased amount of hair is often used as a clinical diagnostic criterion for hyperandrogenic conditions. The degree of hirsutism, its expressiveness and coverage of body areas in modern clinical practice is determined using the modified Ferriman-Gallway scale. To determine the hirsut number, hair growth is evaluated on 9 androgen-sensitive areas of the woman's body, each of them is evaluated on a point scale. If the total number of

points exceeds 8, the clinician has the right to diagnose "hirsutism" (Inoue et al., 2014; Liu et al., 2015; Soares-Jr, Sá and Baracat, 2019).

Acne and alopecia are other common androgenic skin changes that may occur without hirsutism in some women with hyperandrogenism. Hyperandrogenism can manifest itself as an isolated clinical symptom (for example, acne or hirsutism), but a combination of symptoms in various combinations is more often observed (Yildizhan, Gokce, Yildizhan and Cim, 2015; Azziz et al., 2016; Ceruti et al., 2018;).

Today, polycystic ovary syndrome (PCOS) is a common endocrine disorder among the female population starting from puberty to late reproductive age. Classic manifestations of PCOS are menstrual cycle disorders (anovulation), hyperandrogenism, and polycystic ovarian changes. There are four phenotypes of PCOS: phenotype A, B, C and D. Phenotype A, or classical, is characterized by the presence of hyperandrogenism, anovulation and polycystic ovarian changes. Phenotype B or incomplete classic is diagnosed with hyperandrogenism and anovulation. Hyperandrogenism and polycystic ovaries are characteristic of the C or ovulatory phenotype. Phenotype D or non-androgenic – anovulation and polycystic ovarian changes. In patients with PCOS, hyperandrogenism is a frequent finding, which is diagnosed with the help of clinical and laboratory studies (Камінський, Татарчук, Дубоссарська, Ю.О. і Дубоссарська З. М., 2016; Azziz et al., 2016; Резниченко Н. Ю. і Резниченко Г. И., 2017).

There are many reasons for the development of acne in PCOS against the background of normal androgen levels. A number of modern researchers had many opinions regarding the mechanisms of development of this condition. Separate studies confirm the increased activity of enzymes in sebaceous gland cells. Others are inclined to the opinion that the development of this condition is influenced by increased transcriptional activity of the androgen receptor (AR), which is caused by coregulators of the androgen receptor, polymorphisms in the androgen receptor gene (Bissonnette et al., 2015; Azziz et al., 2016; Demirkan, Sayın and Gündüz, 2019).

That is why, in order to understand the mechanisms of the development of hyperandrogenic con-

ditions against the background of a normal level of sex steroids in the blood serum, it is first necessary to consider the structure of the androgen receptor, its localization and possible factors that can lead to the occurrence of this condition (Bissonnette et al., 2015; Clayton et al., 2019; Demirkan et al., 2019).

Today, it is known that the effect of androgens on the skin is mainly mediated through the androgen receptor, a ligand-dependent nuclear transcription factor and a member of the steroid hormone nuclear receptor superfamily. Androgen receptor includes three main functional domains: N-terminal domain of transcription regulation, DNA-binding domain and ligand-binding domain. The N-terminal domain is the most variable, while the DNA-binding domain is the most conserved region among different members of the steroid hormone nuclear receptor family. The DNA-binding domain of all nuclear receptors of steroid hormones consists of two zinc fingers that recognize specific consensus DNA sequences (Kim et al., 2017; Clayton et al., 2019; Demirkan et al., 2019).

Zinc fingers contribute to the direct binding of androgen receptor DNA to the promoter and enhancer regions of androgen-regulated genes. As a result of the activation of the functions of the N-terminal and ligand-binding domains, the transcription of these genes is stimulated or suppressed. Considering the fact that the DNA-binding domain is highly conserved among the family of nuclear receptors of steroid hormones, it has been proven that the binding of selective androgen response elements enables specific activation of AR (Zimmerman, Eijkemans, Coelingh Bennink, Blankenstein and Fauser, 2014).

Thus, for further understanding of the mechanism of acne development in PCOS, it is necessary to get acquainted with the localization of the androgen receptor in human skin. When conducting research, the purpose of which was to find out the localization of the androgen receptor, an immunohistochemical method was used using a polyclonal antibody against the human androgen receptor. According to the results of the study, during which a biopsy of a skin area with and without acne was performed, respectively, it was established that the distribution of the receptor was similar in men and women. Androgen receptor is found in basal and glandular cells of sebaceous glands, in the outer

root layer of hair follicles and in apocrine sweat glands. The presence of the androgen receptor in different types of skin cells reflects the multiple direct effects that androgens can have on these sites (Bergler-Czop, 2014; Buzney, Sheu and Reynolds, 2014; Liu et al., 2015; Azziz et al., 2016; Costa et al., 2018; Clayton et al., 2019; Chappell et al., 2021).

Increased activity of enzymes in the cells of the sebaceous glands can lead to the development of acne in PCOS against the background of normal levels of androgen hormones. In view of this, it is necessary to consider the role of increased activity of 3β -hydroxysteroid dehydrogenase (3β -HSD) and 17β -hydroxysteroid dehydrogenase (17β -HSD) enzymes (Azmahani et al., 2014; Ceruti et al., 2018).

Dehydroepiandrosterone is converted into androstenedione under the action of the 3β -HSD enzyme. This transformation can also occur in the sebaceous gland, where 3β -HSD type I isozyme is detected, the activity of which is greatest in the skin. While the reverse conversion of androstenedione to testosterone is catalyzed by 17β -HSD in human skin. There are 11 isoenzymes of 17β -HSD, which differ depending on the localization in tissues and the ability to reduce or oxidize hormones. At the same time, it is known about the expression of 17β -HSD types 2, 5 and 11 in human sebaceous glands (Azmahani et al., 2014; Ceruti et al., 2018).

Many studies confirm the role of increased 5α -reductase activity in the development of acne in PCOS against the background of normal androgen levels (Azmahani et al., 2014; Yildizhan et al., 2015; Ceruti et al., 2018;). 5α -reductase is a series of enzymes that transform testosterone into dihydrotestosterone, which is a direct stimulator of sebum synthesis. So far, three distinct isoforms of 5α -reductase have been identified. Of interest is the type I isoenzyme, which consists of 259 amino acids, has an optimal pH and is localized in the sebaceous glands. Some researchers also claim that variations in sleep patterns, free testosterone, and 5α -reductase type I activity are associated with changes in sebum secretion in women (Bläuer et al., 1991; Bakry, Samaka, Shoeib, and Maher, 2014; Liu et al., 2015; Ju et al., 2017).

Since specific inhibition of 5α -reductase type I may represent a new therapeutic approach to

acne treatment, it is important to understand the localization of this isoenzyme and its isoforms.

The isoenzyme of 5 α -reductase type I, which catalyzes the conversion of testosterone into dihydrotestosterone in peripheral tissues through a NADPH-dependent reaction, is expressed mainly in the skin (Bläuer et al., 1991; Azmahani et al., 2014; Bakry et al., 2014; Ju et al., 2017).

The expression of 5 α -reductase type I is constantly observed in the brain, liver, and sebaceous glands, while 5 α -reductase type II is mainly found in the urogenital tract, genital skin, and liver. Type III 5 α -reductase has testosterone reductase activity. There are certain publications that talk about its role in the occurrence of hormone-refractory prostate cancer (Soares-Jr et al., 2019). Immunohistochemical studies indicate that the localization of the 5 α -reductase type I enzyme is mainly in nuclear or perinuclear membranes (Soares-Jr et al., 2019; Chappell et al., 2021;). Separate studies have reported that proteins fused to the N-terminus of eGFP indicate that all members of the 5 α -reductase family reside in the endoplasmic reticulum (Soares-Jr et al., 2019).

According to other studies, women with PCOS have significantly higher ratios of 5 α THF/THF (5 α -reduced tetrahydrocortisol to 5 β -reduced tetrahydrocortisol) and An/Et (androsterone/etiocholanolone) levels, which according to group analysis indicates that it is in increased activity of 5 α -reductase was observed in women with PCOS (Yildizhan et al., 2015).

Therefore, as a result of the transformation of testosterone under the action of 5 α -reductase, a more active dihydrotestosterone (DT) is formed, which has a greater affinity for the receptor. The created DT-receptor complex is more stable and, as a result, more stable. This is also because the cells of the sebaceous glands have all the necessary enzymes to convert testosterone. After that, the androgen-receptor complex interacts with DNA in the nuclei of sebaceous cells, regulating genes involved in cell growth and lipid production (Azmahani et al., 2014; Ceruti et al., 2018). It is well known that androgens stimulate the work of sebaceous glands and increase the mitotic rate of sebocytes, including those on the human face (Yildizhan et al., 2015; Hafsi and Badri, 2017; Clayton et al., 2019;).

There is no doubt that the local biosynthesis and metabolism of androgens in human sebaceous glands can play a key role in the synthesis and secretion of sebum. Immunohistochemical analysis of human skin samples proved that various enzymes that produce and metabolize androgens are functionally localized in sebocytes, in turn accumulate lipid droplets, and changes in the expression of 17 β -HSD in immortalized human sebocytes (SZ95) affect the expression of factors related to associated with sebogenesis (Ju et al., 2017; Clayton et al., 2019;).

In addition, sebocyte culture provides new insight into the involvement of DT in the production of inflammatory cytokines in acne. According to the results of the study, during which the possible participation of DT in the production of inflammatory cytokines in cultured sebocytes was tested by immunohistochemistry and PCR methods, an increase in the regulation of IL-6 and TNF- α was observed in the immunohistochemical study and an increase in the amplification of RNA for IL-6 and TNF- α after the addition of DT compared to control. This study shows that DT can participate not only in the production of sebum, but also in the production of pro-inflammatory cytokines in acne (Lakshmi, 2013; Liu et al., 2015; Yildizhan et al., 2015; Piszczatoski and Powell, 2021).

Modern studies prove that PPAR cofactors (receptors activated by peroxisome proliferators) and their ligands are involved in the induction of the full androgenic effect of sebaceous glands. PPARs regulate numerous lipid metabolism genes in mitochondria, peroxisomes, and microsomes in the cytoplasm of sebocytes. Indeed, dihydrotestosterone has previously been demonstrated to interact with PPAR ligands in inducing rat sebocyte-like prepubertal cell differentiation and lipid synthesis. PPAR α is the most important PPAR that regulates lipid synthesis and inflammation (Barrault et al., 2015; Lizneva, Gavrilova-Jordan, Walker and Azziz, 2016).

There is information in separate literary sources that a more active AR can cause a hyperandrogenic phenotype in the absence of markedly increased androgens, since the biological activity of androgens depends not only on their level in blood serum, but also on the activity of AR receptors (Azmahani et al., 2014; Ceruti et al., 2018). To-

day, it is known about one more AR coregulator that modulates the effect of androgens – the androgen-dependent lncRNA CTBP1-AS (C-terminal binding protein 1-antisense), whose expression is inversely correlated with the expression of CTBP1 (Lizneva et al., 2016; Papadakis et al., 2021). It was established that in patients with PCOS there is a significant increase in the expression of CTBP1-AS compared to healthy control women. (Barrault et al., 2015; Lizneva et al., 2016; Papadakis et al., 2021).

The transcriptional activity of AR is affected not only by coregulators, but also by polymorphisms in its gene. The human androgen receptor contains a highly polymorphic polyglutamine tract, which is encoded by CAG repeats in exon 1 of the AR gene. It has been reported that CAG repeats in the range from 11 to 38 are inversely correlated with AR activity (Fu et al., 2014). A recent study found a higher frequency of short CAG alleles in women with PCOS compared to healthy women (Fu et al., 2014).

Functional studies demonstrate an inverse correlation between CAG repeat length and AR activity. It has been established that shorter CAG repeats have a higher sensitivity of receptors to the androgenic response (Fu et al., 2014; Zimmerman et al., 2014; Peng et al., 2016;). Thus, shorter CAG alleles in exon 1 of the AR gene increase susceptibility to PCOS by increasing AR activity (Zimmerman et al., 2014; Fu et al., 2014; Peng et al., 2016;). In addition, clinical studies have also shown that CAG repeat polymorphisms may lead to an increased risk of many diseases due to abnormal androgen sensitivity (Zimmerman et al., 2014; Fu et al., 2014; Peng et al., 2016).

A study of the risk of developing acne, which studied the relationship between the CAG and GGN polymorphisms of the AR genes, included 238 patients and 207 healthy individuals. The length of the AR gene repeats was determined by GeneScan analysis. Males with CAG<23 and females with CAG<24 had a significant risk compared to males with CAG≥23 and females with CAG≥24. In men, GGN repeats considered independently of CAG repeats have no significant effect on acne risk, but when combined with CAG repeats, acne patients showed a significantly higher frequency of CAG<23/GGN≤23 haplotypes com-

pared to controls. The results of the study convincingly demonstrate that shorter CAG repeat length and specific AR haplotypes are associated with the risk of developing acne and thus may serve as a susceptibility marker (Fu et al., 2014; Lizneva et al., 2016; Peng et al., 2016).

Treatment of acne with polycystic ovary syndrome is carried out by obstetrician-gynecologists together with dermatovenerologist doctors. At present, the issue of treatment with the help of modern combined oral contraceptives (COC) and antiandrogen drugs, which are androgen receptor blockers and 5α-reductase inhibitors, is widely discussed (Zimmerman et al., 2014; Barrault et al., 2015; Liu et al., 2015; Luque-Ramirez, Nattero-Chavez, Ortiz Flores, and Escobar-Morreale, 2018).

In order to treat acne, antiandrogen drugs are used, which include pure and non-steroidal ones. Pure antiandrogen drugs are represented by the antiandrogen-progestin series: chlormadinone acetate (XMA), cyproterone acetate (CPA), while nonsteroidal antiandrogens are represented by drugs that lack antigonadotropic progestogenic, estrogenic, and glucocorticoid activity and act mainly at the level of androgen receptors: finasteride, spironolactone, ketoconazole (Legro et al., 2013; Barrault et al., 2015; Vitek, Alur and Hoeger, 2015; Zaenglein et al., 2016).

Currently, CPA is the most widely used antiandrogen, which is a synthetic hydroxyprogesterone with antiandrogenic and antigonadotropic activity. Its antigonadotropic activity is due to the substitutional binding of structures of cell receptors of androgens. In clinical practice, a drug containing 35 μg of ethinyl estradiol (EE) in combination with 2 mg of CPA is widely used (Zhang et al., 2013). It has been proven that the combination of EE/CPA is effective in the treatment of acne against the background of a laboratory-confirmed normal level of androgens (Barrault et al., 2015; Zaenglein et al., 2016).

Drospirenone 3 mg/ethinylestradiol 20 mcg is also effectively used in the treatment of moderate acne. Drospirenone has both antiandrogenic and antimineralocorticoid properties and is a derivative of spironolactone. This drug is indicated for the treatment of moderate acne in women who are not planning pregnancy. Comparative studies have

shown that the combination of EE/CPA has the greatest antiandrogenic effect in the treatment of acne compared to drospirenone and indicates a statistically significant improvement in the treatment of acne in the case of COC use compared to placebo until the end of 3 cycles (Qi et al., 2015). Spironolactone is an aldosterone receptor antagonist and has pronounced potent antiandrogen activity, which is realized by reducing testosterone production and competitive inhibition of testosterone and dihydrotestosterone binding to androgen receptors in the skin. Also, the properties of spironolactone include the ability to inhibit 5-alpha-reductase and increase the level of globulin, which binds steroid hormones (Zimmerman et al., 2014; Barrault et al., 2015).

However, despite its positive effects, spironolactone as an antiandrogen is not FDA approved for the treatment of acne (Qi et al., 2015).

Flutamide is a non-steroidal selective androgen receptor blocker that has been successfully used in the treatment of acne in low doses, but is also not FDA approved for use in this condition (Wu, Wei and Jiang, 2017). In studies, flutamide at a dose of 250 mg twice daily combined with a triphasic COC reduced acne by 80% compared to spironolactone at a dose of 50 mg, which reduced acne by only 50% after 3 months of therapy (Peng et al., 2014; Qi et al., 2015).

It should be noted that the use of flutamide can be associated with idiosyncratic fatal hepatotoxicity, which, most likely, depends on the dose and age. That is why careful monitoring of liver function indicators is necessary during the entire period of use. In view of the above, it was concluded that the use of flutamide for the treatment of acne is still not recommended, except in cases where the benefit justifies the risk (Peng et al., 2014; Qi et al., 2015).

On the other hand, many patients with acne, which is a consequence of PCOS, do not take COCs due to contraindications for use: smoking, migraines, as well as due to personal beliefs. In such a situation, oral treatment with isotretinoin may be the option of choice. The mechanism of action of isotretinoin consists in reducing the secretion of sebum, inhibiting the proliferation of bacteria and cells, and inducing differentiation and apoptosis in various types of cells. It is also able to show anti-inflammatory properties (Acmaaz et al.,

2014; Qi et al., 2015; Davey, Grossmann and M., 2016; Zhang et al., 2021).

There is more and more evidence that the suppression of sebum secretion occurs due to apoptosis of sebocytes. In view of this, the teratogenicity of isotretinoin is also considered as an apoptotic effect of the retinoid on neural crest cells. Isotretinoin has been shown to increase the expression of p53, FoxO1 and FoxO3 and all transcription factors that promote apoptosis. Recent studies indicate that FoxO1 and FoxO3 are p53 target genes for isotretinoin (Acmaaz et al., 2014; Qi et al., 2015; Davey et al., 2016;).

Research in recent years demonstrates the ability of isotretinoin to inhibit the oxidative activity of 3 α -hydroxysteroid dehydrogenase (3 α -HSD) and retinol dehydrogenase-4 (RoDH-4). Since 3 α -hydroxysteroid dehydrogenase is a generally accepted key enzyme in the biosynthesis of androgens, this explains the decrease in testosterone levels when taking this drug (Acmaaz et al., 2014; Qi et al., 2015).

Among the newest drugs for the treatment of acne in men and women, a local androgen receptor inhibitor – clascoterone, is successfully prescribed today, the use of which was approved as a local remedy in August 2020. Clascoterone has a higher affinity for androgen receptors than DT and exhibits greater activity when binding to them (Zhang et al., 2013; Qi et al., 2015; Podfigurna, Meczekalski, Petraglia and Luisi, 2020).

From a clinical point of view, the treatment of hirsutism is a more complex and time-consuming task compared to the treatment of acne, which is largely determined by the physiological cycle of hair growth (Inoue et al., 2014; Vitek et al., 2015; Menshawy et al., 2019). Currently, the treatment of hirsutism is based on a dual approach: pharmacological therapy to reduce androgen secretion and/or androgen action and removal of already existing "extra" hair (Qi et al., 2015). Usually, the clinical effect of the prescribed drugs has to be expected for several months, so the initial evaluation of the therapeutic effect of the prescribed therapy should be carried out no earlier than 6 months after its start (Zhang et al., 2013; Qi et al., 2015).

Today, the drugs of choice for the treatment of hirsutism are low-dose COCs containing a neutral (low androgenic) progestin, such as desogestrel or

gestodene, or an antiandrogen such as cyproterone acetate, chlormadinone acetate, or the spironolactone derivative drospirenone. These drugs are able to ensure adequate normalization of the testosterone level and, as a result, improve the condition of androgen-dependent areas of the skin (Liu et al., 2015; Qi et al., 2015; Zaenglein et al., 2016; Morgante, Cappelli, Troia and De Leo, 2020).

Treatment for PCOS must be tailored to each woman's specific goals, reproductive interests, and specific set of symptoms. That is why a multidisciplinary approach is recommended (Ceruti et al., 2018). COCs containing chlormadinone acetate or drospirenone are recommended as first-line treatment, because this progestin has a more favorable effect on the lipid profile, insulin resistance, and hyperandrogenism (Камінський та ін., 2016; Zaenglein et al., 2016; Резниченко Н. Ю. і Резниченко Г. И., 2017; Morgante et al., 2020).

For women diagnosed with folate cycle gene polymorphisms and clinical manifestations of PCOS, the drug of choice may be a COC with an active form of folates – ethinyl estradiol and drospirenone in combination with calcium levomefolate (Hacivelioglu et al., 2013; Zaenglein et al., 2016; Scaglione et al., 2017). Metformin is recommended for women with PCOS who suffer from type 2 diabetes in case of ineffectiveness of diet or lifestyle correction, or in case of impaired glucose tolerance, including as second-line therapy in case of contraindications to taking COCs (Zhang et al., 2013; Liu et al., 2015; Zhang et al., 2021).

Conclusions

Thus, direct manifestations of hyperandrogenism include dermatopathies (acne, hirsutism, and androgenic alopecia) and polycystic ovary syndrome. Hyperandrogenic conditions in women of

reproductive age can in most cases be determined in the laboratory, as there is an increase in the level of male sex hormones or adrenal hormones. However, quite often in clinical practice there are cases when laboratory indicators remain unchanged, although the manifestation of hyperandrogenism is present. There are several mechanisms that confirm this condition: increased activity of enzymes in cells of sebaceous glands, increased transcriptional activity of the androgen receptor, which is influenced by coregulators of androgen receptors or polymorphisms in the gene of androgen receptors. In women with various manifestations of hyperandrogenism, it is necessary to take an individual approach to the implementation of therapeutic measures, since often the treatment is carried out jointly with a dermatovenerologist in the case of acne or requires a double approach when hirsutism is confirmed.

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Conflict of interest

The authors certify that there is no conflict of interest.

Consent to publication

All authors have read the text of the manuscript and have given their consent for its publication.

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Сучасний погляд на етіологію та патогенез гіперандрогенних станів у жінок репродуктивного віку на фоні нормальних рівнів чоловічих статевих гормонів

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Анотація: в роботі наведено сучасні літературні дані щодо етіології та патогенезу розвитку гіперандрогенних станів у жінок репродуктивного віку на фоні нормальних рівнів чоловічих статевих гормонів. Частіше за все, гіперандрогенні стани виникають внаслідок надмірної продукції андрогенів яєчниками або наднирниками при підвищенні чутливості рецепторів сальних і волосяних фолікулів до андрогенів. Одним з основних інструментів для клінічного підтвердження гіперандрогенних станів є шкала Феррімана-Галлвея. Активація андрогенових рецепторів, які локалізуються у базальних і залозистих клітинах сальних залоз призводить до розвитку акне та інших гірсутних проявів. Дані процеси частіше за все реалізуються за рахунок підвищення активності 5 α -редуктази, ферменту, який перетворює тестостерон у дигідротестостерон і є безпосереднім стимулятором синтезу шкірного сала. Лікування гіперандрогенних станів проводиться сумісно акушерами-гінекологами та дерматологами. На сьогодні, провідною ланкою терапії є комбіновані оральні контрацептиви, які блокують вироблення 5 α -редуктази. Одним з найбільш ефективних засобів є ципротерону ацетат який є синтетичним гідроксипрогестероном з антиандрогенною та антигонадо트로пною активністю. Також в терапії гіперандрогенних станів широко застосовується флутамід, який є нестероїдним селективним блокатором рецепторів андрогенів. Таким чином, проведений огляд свідчить про відсутність єдиного погляду на етіологію та патогенез розвитку гіперандрогенних станів на фоні нормальних рівнів статевих гормонів, а також засвідчує відсутність єдиного алгоритму щодо корекції клінічних проявів.

Ключові слова: акне, гіперандрогенія, гормони, гірсутизм, дросперинон, синдром полікістозних яєчників, флутамід, ципротерону ацетат.



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