

## TREATMENT OF WOMEN WITH ACNE AND ADRENAL HYPERANDROGENISM

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### Annotation:

The study included 303 women aged of 20 to 40 years with acne. Advanced survey included evaluation of endocrine profile and steroid profile of urine. A group of 31 women was allocated; this group was characterized by early-onset acne and hirsutism, android-type obesity, the prevalence of noninflammatory elements, seborrhea, disorders of endocrine profile and steroid profile of urine, metabolic disorders, increased adrenal glands, and lack of effectiveness of oral contraceptives. At the same time, specific clinical and laboratory signs were revealed that allows to assign them to the diagnostic criteria of adrenal hyperandrogenism in women with acne. It's made it possible to select the rational effective treatment for these patients in the future.

**Keywords:** acne, hirsutism, women, adrenal hyperandrogenism, glucocorticoids, methylprednisolone.

### Introduction

Acne is the most common strange disease sebaceous glands. Begins it usually occurs in adolescence and occurs in approximately 80% of the population. Representatives of all are affected races and both sexes. Physiological acne lasts for 4–5 years, but reduction of other variants of the disease can last up to 10–12, and other where 40–50 years [1, 2]. Despite the lack of statistical data, dermatologists, gynecologists and endocrinologists note an increase in the number women over 20 years old with problematic skin (acne, seborrhea, hypertrichosis and hirsutism). Thus, the problem adult acne (acne adultorum) becomes as relevant as ever teenage acne. And the reason this phenomenon in most cases is hyperandrogenism [3, 4].

The purpose of our work was to study of clinical and laboratory signs adrenal hyperandrogenism (NGA) in women with acne.



Material and methods 303 women with acne from 20 to 40 years. Clinical research methods included anamnesis, testing to determine quality of life, dermatological, gynecological osmo- three with hair growth rating scale Ferriman-Gallwey, anthropometry medical and general clinical examination vaniya. Laboratory methods included hormonal test enzyme immunoassay method, Steroid urine profile method fast gas chromatography, metapain status of patients with assistance Glucose tolerance test; define division of cholesterol levels and tri- glycerides enzymatic colormetric test, biochemical blood test. From instrumental methods we used ultrasound examination of the pelvic organs, sebometry.

### Research results

As a result of studying hormonal background blood and steroid pro- 31 (10%) women had urine files NGA with varying degrees was identified severity of acne. Patient age in this group ranged from 20 to 30 years. The majority (28 people) are was aged between 20 and 25 years (90.32%). The median age was la 19.2 years old. Before starting treatment, patients a detailed history was collected diseases. At the same time, it was revealed but early onset of acne and signs of hirsutism: average age age of first clinical manifestations was  $10.5 \pm 1.2$  years. Average age age of onset of menarche in this group ne was  $12.8 \pm 1.8$  years. Exacerbation arose under the influence of personal factors: menstruation – 5 (16.12%) patients (before menstruation) , climate change – 4 (12.91%), food products and alcoholic drinks – 2 (6.45%), stress – 19 (61.29%), medicinal and cosmetics chemical agents – 1 (3.23%) patient

(Fig. 1). Given the early onset of acne in this group did not include women with long the duration of the disease is less than 5 years.

Duration of the disease ranged from 6 to 11 years and on average it was  $8.97 \pm 1.1$  years. Moreover, Most patients had acne for 7 to 10 years.

From the anamnesis it became known that patients repeatedly received treatment in an outpatient setting, where they standard therapy was prescribed:

external retinoids, azelaic acid, systemic and external anti- biotics, benzoyl peroxide gel, etc. In this case, adapalene gel/cream was obtained 27 (87.10%) people, systemic anti- biotics – 31 (100%), external anti- biotics – 5 (16.13%), azelaic acid – 13 (41.94%), benzoylperox- LED gel – 31 (100%), combined nal oral contraceptives (COCs) – 7 (22.58%), other drugs – 24 (77.42%). All 7 women used called a COC containing cypro- theron acetate, while patients noted the absence of pronounced effect. Previous hormonal examination



was carried out on only 11 women, with no reliable evidence was found for this signs of NGA. During a detailed collection of family history of acne in parents noted in all patients in this group, and hirsutism – in mothers 17 (54.84%) women, which indicated obvious genetic predisposition susceptibility to acne in patients entok with NGA. The father noted the presence of acne or 11 (35.48%) women, the mother had 15 (48.39%), both parents – 5 (16.13%). In this case it is necessary note that among mothers there are complicated for women the course of pregnancy and childbirth had place in 16 (51.61%) cases, possibly the age of mothers over 30 years of age at birth Denia girls were found in 10 (32.26%), and maternal hirsutism or immediate relatives - in 23 (74.19%). When examined by a gynecologist in the city, monoproducing tumors, gyne- cological diseases identified did not have. Sexual development of patients did not differ from normal displays tel. Of the 31 women, 3 gave birth shikh, 11 – suffered from infertility. The menstrual cycle was regular nom in 31 (100%) patients, of whom 8 (25.81%) had elongated cycles (from 32 to 35 days). Average duration of menstrual period cycles in the group was  $31.2 \pm 4.1$  days, menstrual bleeding  $-4.2 \pm 1.5$ . Clinical characteristics When registering inflammatory and non-inflammatory elements of the rash localization features were noted of rashes. Comedonal form acne was reported in 14 (45.16%) patients, and the rashes were extremely common. The pain The majority of women with NGA prevailed closed comedones to a large extent quantities that are registered appeared both on the face and on the body more 9 (29.03%) women had elements rashes were located only on the skin faces, and the combined arrangement (face and torso) was recorded in 22 (70.97%). Initial values of dermatological acne index (DIA) in women with acne and NGA ranged from 3 to 9 points, the average DIA was  $4.78 \pm 1.24$ . Moreover, in 19 (61.29%) patients DIA was  $<5$  points (mild) severity), in 12 (38.71%) – it fluctuated ranging from 6 to 10 (average degree severity). Severe cases in this group was not registered. Average DIA values for mild severity of acne in women with NGA were  $4.74 \pm 1.26$ , with an average –  $6.85 \pm 2.18$  points. Multivariate analysis of cor- lations of age and heredity with the value of the index, DIA showed the absence of such a relationship.

During a gynecological examination research in patients with acne is determined hirsute number. Most often the pigment shaped hair in women of this groups were present in the lower third of the face and above the upper lip, on the sternal chest lines, around the nipples areola, linea alba, groin with the transition to the legs, on the back and extension body surface of the upper extremities news Hirsut number in the ring group ranged from 15 to 28 points Ferriman–Gallwey scale, median –



19.68±1.51 (III degree of hirsutism). When examining the mammary glands in pain, majority (25 women – 80.65%) they had a conical shape, small size and poorly formed sore nipple. In 6 (19.35%) patients the mammary glands were round shape, there was swelling of the window salmon mug, increasing its diameter and weakly expressed pigmentation. Anthropometric parameters rated according to age sick women compared to group of healthy people (corresponding age). Body mass index ranged from 17.38 to 29.63 kg/m<sup>2</sup>, on average the composition fork 25.1±8.07 kg/m<sup>2</sup> and reliably distinguish varied from the index in healthy people, corresponding current age (19.04±1.23 kg/m<sup>2</sup>). An increase was noted waist circumference, ratio waist circumference to hip circumference and visceral adipose tissue. Although there was no increase in mass index body, the patients had signs of initial obesity according to andro- id type. Laboratory research When studying hormonal the background was established reliably a significant increase in lutein levels regulating hormone (LH) up to 7.22±1.51 mIU/ml, which determined the level gonadotropic index – 1.44±0.30. Characteristic for this group is there was a significant decrease in the level estradiol up to 144.18±8.41 pmol/l and increasing the concentration of total testosterone up to 4.72±0.21 nmol/l, dehydroepiandrosterone-sulfa- ta (DHEA-S) up to 4.94±0.63 mmol/l and highly reliable increase in level-nya 17-OH-progesterone to 4.83±0.01 nmol/l (p<0.001; see table). To clarify the availability of NGA pro- conducted a study of steroid urine profile.

### Characteristic results

Were called by an increase in the level of andr- sterone up to 19.43±2.11 µmol/24h, etiocholanolone up to 17.4±2.15, digi- droepiandrosterone up to 4.1±0.58, 11-ketoandrosterone up to 2.87±0.02, 11-ketoethiocholanolone up to 2.93±0.04, the total of 17-ketosteroids was 54.01±9.43 µmol/24 h, which reflected increased secretion of hormones over- kidneys (Fig. 2). All patients with acne and NGA pro- biochemical research was carried out blood. However, it was not revealed abnormalities in liver function and protein kovy exchange. When researching lipid profile found that NGA helps to reduce the indicator- total cholesterol up to 3.11±0.02 mmol/l (p<0.05), low lipoproteins density – up to 1.02±0.01 (p<0.05), very low density lipoproteins – up to 0.24±0.003 (p<0.05), triglyce- reads – up to 1.05±0.02 mmol/l (p<0.05) and relative increase in level high density lipoproteins. There were no significant differences in the levels of insulin no lin and glucose were noted, but the decrease in the HOMA-IR index was significant (p<0.05).



Instrumental examination Ultrasound examination of organs new pelvis in women with acne and NGA did not reveal any organ abnormalities opinion, size of the uterus and ovaries corresponded to the indicators of healthy women. During ultrasound examination the adrenal glands are marked by their uniform increase. Tumor no formations were found. Sebum production was significantly increased at all points measurements evenly and exceeded indicators in healthy women over 30 up to 50% (see Fig. 2). The conducted research allowed to identify the following specific clinical and laboratory parameters in women with acne and NHA:

- early onset of acne and signs of hirsutism before the onset menarche;
- connection between exacerbations and stress;
- ineffectiveness of COCs;
- absolute hereditary pre- location;
- absence of menstrual disorders function and prolongation of the period between menstruation;
- predominance in the clinical picture no comedones over inflammatory ones elements;
- androgen-dependent hair growth areas and III degree of hirsutism;
- android type obesity;
- increased values of con- concentrations, LH, DHEA-S, 17-OH-progesterone, free testosterone and decreased levels estradiol;
- deviations in steroid pro- urine file with increasing levels androsterone, etiocholanolone, dihydroepiandrosterone, 17-keto-11-hydroxy-steroids with significant an increase in the amount of 17-ketostero-dov, as well as van de discriminants Calceide;
- metabolic abnormalities, characteristics experiencing declining levels cholesterol, triglycerides, lipo- low and very low proteins density and increased content high density lipoprtheids sti;
- no enlargement of the uterus and testicles;
- nicks and enlarged adrenal glands;
- pronounced and uniform seborrhea.

### Treatment results

All women with acne and laboratory but proven NGA (n=31) was obtained whether a systemic glucocorticosteroid (GCS) – methylprednisolone in a dose 4 mg/day for a year. For lower- reducing the risk of side effects phenomena from the use of GCS in patients. Entrepreneurs of this group were also used



Asparkam 1 tablet 3 times a day after meals and Calcium D3 Nycomed 1 tablet 2 times a day (total 2-3 course per year of therapy for 30 days). All women were counted number of acne rashes and average them DIA values.

Pronounced dynamics of resolution acne was observed in the group within a month from the start of treatment with formation of persistent clinical logical result for the majority (22 patients – 70.96%) women to three-dark month of observation. Wherein the following changes were identified clinical picture: reliable decrease in average values of quantitative properties of closed and open comedones noted only after six months of pro- guided therapy (from  $25.49 \pm 3.16$  to  $4.59 \pm 0.12$  [ $p < 0.05$ ] and from  $57.38 \pm 5.04$  to  $4.26 \pm 0.05$  [ $p < 0.001$ ], respectively). One year after the start of treatment, the average the number of closed comedones is composed of was  $1.59 \pm 0.07$  ( $p < 0.05$ ), open –  $2.05 \pm 0.09$  ( $p < 0.05$ ). Dynamics of the number quality of papules was as follows: through 3 months – from  $14.24 \pm 1.36$  to  $0.34 \pm 0.04$  ( $p < 0.05$ ), after 6 months and after a year papular elements are absent in patients worked. Pustules resolved with this same intensity as papules: with  $12.05 \pm 1.69$  to  $0.14 \pm 0.02$  ( $p < 0.05$ ) after 3 months, and after 9 months until the end observation period for new pustulosis. There were no significant elements of the rash. So Thus, the use of methylpredni- Zolona e for women with acne and NHA has lo rapid clinical effect. Decrease in mean DIA values by the third month of therapy was 78.66% (from  $4.78 \pm 1.24$  to  $1.02 \pm 0.04$  points [ $p < 0.05$ ]), by 6 months – 88.08% (up to  $0.57 \pm 0.05$  points [ $p < 0.05$ ]), by 9 months- patients treated – 97.07% (up to  $0.14 \pm 0.04$  points [ $p < 0.05$ ]), by the end of the period observations were noted to be highly reliable correct reduction in DIA – by 97.49% (up to  $0.12 \pm 0.001$  points [ $p < 0.001$ ]). Results of therapy in this group one year after treatment there were.

Keywords: clinical recovery observed in 27 (87.10%), excellent improvement – in 4 (12.90%), i.e. medicinal the effect was achieved in all patients.

Tolerability of the therapy FDI was good given the low dosage of GCS and parallel taking potassium and calcium supplements. Side effects from taking methyl- no prednisolone was observed.

Dynamic gynecological examination ke while taking GCS showed that the therapy was effective and on the severity of hirsutism: decrease hirsute number in the group with  $19.68 \pm 1.51$  up to  $10.35 \pm 1.74$  points ( $p < 0.05$ ) – by 47.41%. Hormone therapy with GCS methylprednisolone contributes to a decrease in all elevated values changes in blood hormones. Changes in hormonal status in women with acne and NHA under the influence GCS occurred due to reliably th reduction of testosterone levels to  $1.42 \pm 0.68$  nmol/l ( $p < 0.05$ ), concentration of DHEA-S – up to  $1.91 \pm 0.26$



mmol/l ( $p < 0.05$ ) and 17-OH-progesterone – up to  $2.36 \pm 0.22$  nmol/l ( $p < 0.05$ ), as well as increase in CVS to  $75.99 \pm 1.12$  nmol/l ( $p < 0.05$ ). It is necessary to note the influence reduction of therapy to the level estradiol, which after a year of treatment tended to increase. Average urine SP values after treatment reflected the lack of signs of a hyperandrogenic state. As a result of the therapy a decrease in androsterol was noted to up to  $17.26 \pm 0.51$   $\mu$ mol/24 hours ( $p < 0.05$ ), etiocholanolone – up to  $10.47 \pm 1.06$  ( $p < 0.05$ ), dihydroepiandrosterone – up to  $0.53 \pm 0.01$   $\mu$ mol/24 hours ( $p < 0.05$ ), which indicated the elimination

NGA. Under the influence of therapy using with the introduction of GCS, there was a decrease 11-hydroxylase activity of the cortex adrenal glands, which showed significant a true decrease in 11-ketoandrosterol- by up to  $0.39 \pm 0.04$  ( $p < 0.05$ ) and 11-ketoethyl ocholanolone up to  $1.06 \pm 0.001$   $\mu$ mol/24 h ( $p < 0.05$ ). In addition, it was noted significant decrease in the amount of 17-keto- steroids up to  $30.26 \pm 1.53$   $\mu$ mol/24 h ( $p < 0.05$ ). It must be emphasized that normalization of steroid- urine profile was observed in 100% female patients. Biochemical blood test showed that taking GCS is not conditional normalizes metabolic status, and in some cases worsening shakes him. When using methylpredniso- womb in women with acne and NGA occurs there was a significant increase in the level cholesterol in peripheral blood - from  $3.11 \pm 0.02$  to  $5.28 \pm 0.10$  mmol/l ( $p < 0.05$ ) and glucose concentration – from  $3.99 \pm 0.34$  to  $5.49 \pm 0.28$  mmol/l ( $p < 0.05$ ), i.e. long-term systemic use (1 year) of low doses of GCS led to changes in metabolic status towards insignificance lipid and carbohydrate disorders exchanges.

As the results showed trii during dynamic observation - care for patients, decreased intensity sebum production intensity observed at all points: on the skin of the forehead on the right - from  $297.06 \pm 12.32$  up to  $230.28 \pm 5.01$   $\mu$ g/cm<sup>2</sup> ( $p < 0.05$ ), on forehead skin on the left – from  $287.27 \pm 9.42$  to  $228.54 \pm 3.57$   $\mu$ g/cm<sup>2</sup>

( $p < 0.05$ ), in the area size of the right cheek – from  $311.18 \pm 5.29$  up to  $169.38 \pm 3.68$   $\mu$ g/cm<sup>2</sup> ( $p < 0.001$ ), in left cheek area – from  $299.41 \pm 4.69$

up to  $175.06 \pm 10.33$   $\mu$ g/cm<sup>2</sup> ( $p < 0.05$ ), on the skin of the chin – from  $324.08 \pm 2.55$  up to  $237.26 \pm 7.02$   $\mu$ g/cm<sup>2</sup> ( $p < 0.05$ ). It should be noted that normal

skin production lard reached only two points - on the skin of the cheeks, at other points of change rhenia after the end of therapy were signs of seborrhea were registered. On average, sebum production in the group decreased by 50.57%.



### **Conclusions:**

Systemic use of GCS methyl- prednisolone for women with acne and NGA contributed to:

- fast dynamics and resolution clinical manifestations of acne to three dark month of treatment;
- reduction of dermatological acne index by 97.49%;
- achieving a therapeutic effect in 100% of patients;
- good tolerability of therapy;
- reducing the severity of hirsutism; ma by 47.41%;
- reduction in visceral no adipose tissue;
- reducing the concentration of bases ny androgens (testosterone and DHEA-S), increasing the level of dry hormones and depression of 17-kestosteroids in urine;
- tendencies towards minor violations reduction of lipid and carbohydrate exchanges;
- suppression of skin production lard by an average of 50.57%.

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