UROGENITAL DISORDERS IN WOMEN OF REPRODUCTIVE AGE WITH ANDROGEN DEFICIENCY

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Abstract: According to the consensus of An Endocrine Society Clinical Practice in Princeton, USA, worsening well-being and dystrophic mood, permanent weakness and altered sexual function, including libido decline and lack of orgasm, were considered as typical signs of androgen deficiency syndrome. Particular attention is required to study the state of the genitourinary system, which is hormone dependent, so it is obvious that age-associated symptoms of pathological processes of the lower urinary tract are likely to be considered as a "urological mask" of the deficiency of sex hormones.

Aim of the work. Identify and describe the most common urogenital disorders in women of reproductive age with androgen deficiency.

Materials and methods. The study was conducted at the Ukrainian Scientific and Practical Center of Endocrine Surgery, Endocrine organs and tissues transplantation of the Ministry of Health of Ukraine during 2017–2018 years. A survey was conducted on 80 women of reproductive age who had major complaints of sexual disturbances (decreased libido and lack of orgasm, as well as dyspareunia as the main manifestations of androgen deficiency in women) and 30 healthy reproductive women without complaints of sexual dysfunction. General clinical methods were used (questionnaire of patients with a detailed study of socio-economic status, somatic, gynecological, obstetric and sexual history). The condition of external and internal genital organs was evaluated in the study of cervix and vagina in mirrors and gynecological bimanual study. At the same time, batches of analyzes for bacteriological research and colpocytology studies were conducted. The "HAWK 2102 EXL" (Germany) apparatus was used for ultrasound examination of pelvic organs using transabdominal and transvaginal convection sensors with frequencies of 3.5 and 5 MHz, respectively. Consultation of the urologist in order to exclude organic urological pathology and, if necessary, cystoscopy was also done.

In the plasma of venous blood, the following hormonal indices were also determined by solid phase IFA, namely, content: free testosterone, DHEA, androstenedione, prolactin, ACTH, cortisol, FSH, LH, estradiol, progesterone.

Results. It was revealed after exclusion of the urologist of the organic pathology of the urinary tract, in 49 % (39) of the main group, there were disturbances of urination associated with atrophic changes in the distal sections of the urinary tract. The revealed signs of vulvovaginal atrophy: pH 6.1±0.7 in women of the main group and pH 4.3±0.5 in women of the control group, in addition reduction of the karyopyknotic index and increase of the ripening index as signs of atrophic changes in the vaginal mucosa and cervical canal, was detected in 70 % (56) women in the main group and not found in the control group. At the same time, the prolapse of the genitalia of mild degree in women of the main group was detected in 32 % (27), and in the control group, this pathology was not found.

Conclusions. Detection of these changes, which was considered characteristic of women in perimenopause and postmenopausal, makes it important and valid for the continuation of the study of patients with androgen deficiency, the discovery of clinical and laboratory criteria for diagnosis and the development of methods for correcting androgen deficiency in women of all ages.

Keywords: androgen deficiency, women of reproductive age, urogenital disorders, urogenital atrophy, genital prolapse.

1. Introduction

The importance of androgens for the human body is due to the finding of androgen receptors in the cells of most tissues: the mammary gland, the heart, blood vessels, the digestive tract, the lungs, the central nervous system, and the peripheral nerves, the skin, the musculoskeletal system, the bone marrow, the uterus, ovaries, external genital organs, adipose tissue [1]. Therefore, deficiency of androgens in women can be manifested not only by sexual disorders (decreased libido, sexual pleasure and orgasm), but also other pathological symptoms including mood changes (irritability, anxiety, depression), poor health, physical weakness, changes in cognitive function, illness Alzheimer's disease, memory impairment, chronic pain, urinary tract disorder, reproductive disorders [2].

Known effects of androgens on the state of muscle and mucous membranes of the pelvic floor and perineum in women: the level of estrogen in the blood affects the expression of androgen receptors in the woman's vagina. It is shown that the density of androgen receptors with age significantly decreases [3].

The consensus of the An Endocrine Society Clinical Practice on female androgen deficiency in Princeton, USA, was proposed the term «female androgen deficiency,» which was defined as a group of clinical manifestations at normal estrogen levels and lowered testosterone levels. Accordingly, this consensus, the deteriorating state of health and dystrophic mood, permanent weakness and changes in sexual function, in that pure decrease in libido and the absence of orgasm, were considered as typical signs of syndrome of androgen deficiency. From that point on, several double-blind, placebo-controlled studies have been performed on the use of testosterone in women, which demonstrated its efficacy and safety when administered in physiological doses [4].

Particular attention is required to study the state of the genitourinary system, which is hormone dependent, so it is obvious that age-associated symptoms of pathological processes of the lower urinary tract are likely to be considered as a «urological mask» of the deficiency of sex hormones [5]. Research results show that sex hormones are capable of modulating the functions of the neuroreceptor apparatus of the bladder, both in men (androgens) and in women (estradiol, progesterone, androgens). Androgens may have an effect on the vaginal mucus both via estrogen receptors by flavoring in estrogens and directly through androgen receptors, effectively alleviating the symptoms of urovaginal atrophy [6].

According to the literature [7, 8], the effects of the deficit of sex hormones for both sexes are manifested by a decrease in blood supply to the pelvic organs, due to the induction of pelvic atherosclerosis, which leads to hypoxia and ischemia of the genitourinary system; reduction of the diameter of arteries of the bladder, reduction of the number of small vessels and thinness of their walls (decrease in the density of microcirculation). On the other hand, androgens have anabolic effects on muscle tissue, the receptors for androgens are expressed in the muscles of the pelvic floor and the lower sections of the urinary tract, both in animals and in humans. A recent study showed changes in the metabolism of collagen and elastin in the tissues of the external genitalia when they fall out. These changes relate not only to the synthesis of structural proteins, but also to the balance between the action of major proteolytic enzymes, such as metalloproteinases, which impair the synthesis of the protein. Testosterone is a potent inhibitor of metalloproteinases in the tissues of the uterus [9]. A strong reverse correlation between slow collagen collapse in the urogenital tract and levels of total and free blood testosterone was found in the group of patients, which may be due to the inhibition of metalloproteinase with this hormone [10, 11].

Pathogenetic treatment of androgen deficiency is actively studied by many scientists in the world. A number of experimental studies have shown the effectiveness of the use of androgens – DHEA and testosterone in postmenopausal women with sexual and urogenital disorders [12]. Also, many authors consider the vaginal forms of DHA and testosterone (ointments, creams) with a number of advantages, namely, the high concentration of testosterone obtained in the pelvic area when administered through the mucous membrane of the vagina and the absence of pronounced systemic effects [8, 13].

Proceeding from the fact that the overwhelming majority of studies in women with androgen deficiency were carried out in postmenopausal, to date, not all aspects of correction of sexual dysfunction and urogenital disorders of the female population of different age groups have not been resolved. Therefore, we conducted a study of urogenital disorders in women of reproductive age in order to identify the main clinical manifestations of androgen deficiency in this age group of women.

The aim of the study is to identify and describe the most common urogenital disorders in women of reproductive age with androgen deficiency.

2. Methods

The research was conducted in the Ukrainian Scientific and Practical Center of Endocrine Surgery, Transplantation of Endocrine organs and tissues of MOH of Ukraine during 2017–2018 years.

The study included 80 women of reproductive age who had major complaints of sexual disturbances (decreased libido and lack of orgasm, as well as dyspareunia, as the main manifestations of androgen deficiency in women) and 30 healthy women of reproductive age without complaints of sexual health disorders. General clinical methods (questionnaire of patients with detailed study of socio-economic status, somatic, gynecological, obstetric and sexual history) were used. The condition of external and internal genital organs was evaluated in the study of cervix and vagina in mirrors and gynecological bimanual study. At the same time, batches of analyzes for bacteriological research and colpocytology studies were conducted. The "HAWK 2102 EXL" (Germany) apparatus was used for ultrasound examination of pelvic organs using transabdominal and transvaginal convection sensors with frequencies of 3.5 and 5 MHz, respectively. Consultation of the urologist in order to exclude organic urological pathology and, if necessary, cystoscopy were done.

In the plasma of venous blood, the following hormonal indices were also determined by solid phase IFA, namely, content: free testosterone, DHEA, androstenedione, prolactin, ACTH, cortisol, FSH, LH, estradiol, progesterone.

3. Results

Having analyzed the data from the questionnaires and general-clinical and gynecological examinations and excluded patients with somatic and gynecological pathology, we found that the deficiency of androgens in women was manifested in sexual disorders in 100 % (80 patients) of the main group (decreased libido, sexual pleasure and lack of orgasm). Other pathological symptoms, including mood changes (irritability, anxiety, depression), were detected in 80 % (64 patients) of the main group, while in the control group only 20 % (6 women). Poor feeling and physical weakness after the exclusion of somatic and gynecological pathology were found in 67 % (54) of the main group and 20 % (6) of the control group. Memory impairment and cognitive abilities in 56 % (45) of the main group and 17 % (5) of the control group.

In the analysis of urological disorders, including urinary incontinence, after the exclusion of the urologist of the organic pathology of the urinary tract, 49 % (39) of the main and 4 % (1) control group revealed urinary tract disorders associated with atrophic changes in the distal urinary tract. There are also known effects of androgens on pelvic floor muscle and mucous membranes of the external genitalia in women. To diagnose vulvovaginal atrophy, two main objective methods of diagnosis are needed: the determination of the pH of the vaginal discharge and the calculation of the vaginal index of ripening (the advantage of basal and basal cell layers). The study revealed a pH of 6.1±0.7 in women of the main group and a pH of 4.3±0.5 in women in the control group. In addition, the reduction of the karyopyknotic index and the increase of the ripening index, as signs of atrophic changes in the vaginal mucosa and cervical canal, were detected in 70 % (56) women in the main group and not found in the control group. At the same time, the prolapse of the genitalia of mild degree in women of the main group was detected in 32 % (27), and in the control group this pathology was not found.

In studying the state of hormonal homeostasis in women with symptoms of androgen deficiency in reproductive age, a study was conducted into the basal levels of gonadotropic and sex hormones in serum for 2–3 and progesterone – on the 21st day of the menstrual cycle (**Table 1**).

Table 1

Indicators of gonadotropic and sex hormones in serum of examined women before treatment (M±m)

Hormones	Groups of examined women	
	main (n=80)	control (n=30)
LH, mMo/ml	8.97±1.53	7.21±2.14
FSH, mMo/ml	4.67±0.54	5.17±0.72
Prl, ng/ml	19.34±2.03	10.7±2.64
E_2, pg/ml	223.5±11.3	234.1±14.6
P, nmol/l	12.0±2.03	17.3±2.06
DHEA, μmol/l	46.1±8.6*	159.6±12.7
Free T, nmol/l	0.56±0.92*	1.74±0.56
SHBG nmol/l	87±24	56±35
Androstendiol, nmol/l	0.25±0.15*	3.34±0.21
ACTH, pg/ml	19.33±1.4	19.24±2.1
K, mg/dl	16.1±1.36	7.2±1.58

*Note: * – the difference is significant in relation to the indicator of the control group (p<0.05)*

4. Discussion

Despite the fact that there is still no "gold standard" for the detection of androgen deficiency in clinical practice, research in this direction is carried out. The European Endocrinology community believes that these measures are necessary to identify a clinically acceptable diagnosis of androgen deficiency syndrome based on measured parameters of androgens and the specific clinical effects of female androgen deficiency [14].

As a result of a study of women of reproductive age with confirmed low blood androgens (testosterone free 0.56± ±0.92 nmol/l, DHEA 46.1±8.6 μmol/l, androstenedione 0.25± ±0.15 nmol/l) it was found that, as for menopausal women, the clinical manifestations of androgen deficiency are as changes in the CNS, including mood changes (irritability, anxiety, depres-

sion) in 80 % (64 patients) of the main group, poor health and physical weakness after exclusion somatic and gynecological pathology was detected in 67 % (54) of the main group, impaired memory and cognitive abilities in 56 % (45).

In the analysis of urological disorders, including urinary incontinence, after exclusion by the urologist of the organic pathology of the urinary tract, in 49 % (39) of the main group, mucosal dysfunctions were associated with atrophic changes in the distal sections of the urinary tract. In the diagnosis of vulvovaginal atrophy, two main objective criteria were identified: the determination of pH of vaginal discharge in the study revealed a pH of 6.1±0.7 in women of the main group and a pH of 4.3±0.5 in women of the control group. In addition, the reduction of the karyopyknotic index and the increase of the ripening index, as signs of atrophic changes in the vaginal mucosa and cervical canal, were detected in 70 % (56) women in the main group and not found in the control group. Genital prolapse of mild degree in women of the major group were detected in 32 % (27), and in the control group this pathology was not detected

Based on the fact that the use of androgens leads to improved sexual health and urogenital malformations in postmenopausal women, it can be thought that they can have a positive effect on the status of women with low testosterone and decreased sexual function and before menopause [15]. However, in comparison with the large database of postmenopausal studies in the literature, there is a small number of studies in women of the reproductive period. This makes it important and reasonable to continue the study of patients with androgen deficiency, to identify clinical and laboratory criteria for diagnosis and to develop methods for correcting androgen deficiency in women of all ages.

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