PATHOGENESIS OF GENITAL PROLAPSE IN PERI- AND POSTMENOPAUSE (LITERATURE REVIEW)

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Annotation. Despite the widespread prevalence of pelvic organ prolapse, the pathophysiology and natural process of development of this disease are poorly understood. Extensive epidemiological studies have shown that vaginal delivery and aging associated with hypoestrogenism are the main factors in the development of genital prolapse. Genital prolapse is mainly an oestrogen-dependent disease.

Keywords: prolapse, estrogen, estriol, estradiol, perimenopause, menopause, microflora, lactobacillus, pelvic floor muscles, dyspareunia, anorgasmia.

Introduction. Estrogen deficiency is accompanied by decreased blood circulation in the pelvic organs, which leads to ischaemia of the tissues of the urogenital system. The diameter of the vaginal arteries decreases, the number of small vessels decreases and their walls thin out, leading to decreased transudation. Similar changes are observed in the veins and venous plexuses of the vagina located subepithelially. An active dilator affecting the state of vascular plexuses is considered to be vasoactive interstitial polypeptide, the synthesis of which in the vaginal wall is also estrogen-dependent. A very important factor is the dependence of the state of collagen, blood supply and trophics of the pelvic floor detrusor muscles to a certain extent on the level of estrogen [9]. The use of estrogens helps to restore the vaginal microbiota, prevents the recurrence of vaginal and urinary infection and plays an important role in the treatment of urinary incontinence, especially stress urinary incontinence associated with detrusor instability. Estrogens not only help to maintain optimal pressure in the urethra, but also prevent ascending urinary infection by creating a high-pressure zone in the midurethra that acts as a mechanical barrier and by stimulating the secretion of immunoglobulins by the paraurethral glands and mucus by the urethral epithelium [1].

Purpose of the work. To analyse modern sources of domestic and foreign literature devoted to the current issues of pathogenesis of genital prolapse development in perimenopause.

Materials and Methods. We conducted a literature review of scientific papers for the last 6 years, using the resources of Cyberleninka, Cophrane, and PubMed search engines. We also used articles containing evidence base on the issues related to the relationship between estrogen saturation of the genitals and the occurrence of pelvic organ prolapse (POP). And we analysed the most effective method of preparation for vaginal plastic surgery.

When it comes to the estrogen saturation of the vaginal tissue, this fact is important in postoperative recovery just like the microbial flora. The vaginal pH in women is approximately 4.0-5.0, which is maintained by the production of lactic acid by lactobacilli. During vaginal surgery, the number of lactobacilli can decrease, which leads to a decrease in the amount of glycogen and thinning of the vaginal epithelium, and if a woman has a lack of estrogen, the situation begins to worsen. The bulk of women who undergo surgery for PCOS are women in the pre-, peri-menopausal and post-menopausal periods. During this period, due to the reduced concentration of estrogen, the vaginal pH is alkaline to 6.0-8.0. This can be a favourable pathogenic factor for the growth of yeast fungi and bacteria, including Escherichia coli. In this regard, the vagina may be at risk of infections and inflammation during the postoperative recovery period. The health of the urinary tract is also closely linked to the health of the vagina, especially in the case of estrogen deficiency. Surgery for cystocele may be successful, but postoperative recovery and recurrence of cystocele is not impossible and is dependent on estrogen saturation. In addition, an atypical vaginal pH of 6.0-8.0 and infectious agents may affect the lower urinary tract, thereby increasing the risk of acute and recurrent urethritis and cystitis. Estrogen deficiency causes atrophy of the pelvic floor muscles, reduces the elasticity of the muscles and connective structure of the urogenital diaphragm, impairs collagen metabolism and reduces the activity of the adrenergic system, which innervates the bladder neck and the sphincter of the urethra. On this basis, it can be said that estrogens can contribute to the treatment of urinary disorders and incontinence, as well as give a full recovery after anterior colporrhaphy surgery.

The structure of disorders of the urinary system in women traditionally includes diseases and pathological conditions that develop in the genital system and lower urinary system. This is explained by the well-known fact of common embryonic origin, the closest topographic-anatomical links and relationships of the lower

urinary tract (urethra, bladder) and organs of the female genital system, and, most importantly, by common mechanisms of hormonal regulation based on the key role of sex steroid hormones in ensuring their normal anatomical-functional state, since the expression of receptors to sex hormones (estrogens, progesterone and androgens) in women is widely represented not only in the organs of the genital system, but also in all structures of the lower urinary tract, including the ligamentous muscle apparatus of the pelvic floor, as well as in the neurothelium and endothelium of these anatomical areas [2]. Until recently, the pathogenesis of urogenital disorders in peri- and postmenopausal women was considered more from the perspective of age-related estrogen deficiency [3]. Accordingly, the "estrogen" concept of the pathogenesis of genitourinary rather than urogenital disorders in women largely shaped the trends of their hormonal pharmacological correction with emphasis on the predominant local application of estrogen preparations (estriol).

Changes in female sexuality in postmenopause are associated with a variety of different exogenous and endogenous factors. The main trigger for the decrease in sexual activity in postmenopause is the involutional processes of the hypothalamic-pituitary-ovarian system, which is based on the depletion of the follicular apparatus of the ovaries, followed by a gradual decrease in the level of sex steroids [10].

The main forms of sexual dysfunction in postmenopause according to various authors are: lack of sexual desire or hypoactive libido disorder, aversion to sexual activity with the subsequent formation of sexual aversion, sexual arousal disorder, anorgasmia, dyspareunia, vaginismus, decreased lubrication during sexual intercourse, changes in the vaginal microbiome and recurrent cervico-vaginal infections, atrophy of the labia, clitoris, and introital stenosis [6]. The resulting dyspareunia, progressing without treatment, eventually makes sexual life impossible. Thus, a vicious circle is formed, in which dyspareunia limits sexual contacts, and their cessation aggravates atrophy, reducing the intensity of blood circulation in the vaginal walls. The thinning and weakening of the vaginal wall becomes an addition to other factors in the development of another pathological condition associated with estrogen deficiency - genital prolapse [12].

Postmenopausal patients with persistent decrease in estrogen levels are often concerned about genitourinary disorders (dryness, itching and burning in the vagina, urinary disorders, recurrent urogenital infections), which may manifest already in the perimenopause [4]. Menopausal symptoms are due to the fact that the vulva, vagina and pelvic floor tissues contain a large number of estrogen receptors type α and β (ER-α, ER-β). The receptors are localised at the level of basal and parabasal cell

elements of the vaginal epithelium, in the skin and transverse striated muscles of the perineum, and in the endothelium of vaginal vessels. They are also located in the urothelium, in the wall of the bladder and urethra. When estrogen levels decrease, there is a deterioration of trophicity and slowing of microcirculation in all tissues that have ER-α and ER-β. Due to estrogen insufficiency, mitotic activity of cells of basal and parabasal layers of vaginal epithelium is sharply slowed down, which affects the rate of proliferative processes. The latter potentiates the disappearance of glycogen, which leads to a weakening of the protective properties of the vaginal mucosa [13]. The presence of hypoestrogenism in women with severe genital prolapse worsens the prognosis of postoperative course for several reasons. Firstly, there is a high probability of infectious complications. Secondly, these symptoms indicate a possible reduced regenerative capacity of tissues. Thirdly, the juxtaposition of initially thinned mucosa may lead to incomplete epithelialisation in the area of the suture. Consequently, preoperative preparation for surgical treatment of pelvic organ prolapse is justified in postmenopausal patients with genital prolapse before planned surgical treatment, aimed at restoring the functional state of hormone-dependent tissues of the urogenital system and stimulating the mechanisms of natural biological defence of mucous membranes [5].

The pathogenesis of hypoestrogenism, as mentioned above, is related to the common embryonic origin of the genital and urinary tracts, formed from the urogenital sinus and ectoderm and retaining sensitivity to the action of female sex hormones throughout life. Steroid hormone receptors have been identified in the vagina, on cells of the transitional vulvovaginal epithelium, in the urethra, bladder and pelvic floor muscles. Estrogens are the main regulators of physiological processes in the vagina and lower urinary tract. Estrogen receptor density is highest in the vagina and decreases as it approaches the skin and several specific enzymes, including aromatase, which converts testosterone to estradiol, and type 1 and type 2 5a-reductase, which convert testosterone to dihydrotestosterone, are present in all parts of the urogenital tract. The density of androgen receptors is reversed: lower expression is noted in the vagina and higher in the external genitalia. Against the background of hypoestrogenism there is a progressive decrease in the proliferative activity of the vaginal and urethral epithelium, a decrease in the volume of the vascular network and blood supply with the development of ischaemia and atrophy of the epithelium of the vagina, urethra and bladder. Atrophic changes are accompanied by a decrease in paracellular permeability and production of vaginal transudate, this causes vaginal dryness, decreased acidity and, as a consequence,

colonisation of the urogenital tract by opportunistic microflora [11]. The presence of these symptoms worsens the prognosis of the postoperative course of the disease. The first reason is the high probability of infectious complications. The second reason is that these symptoms indicate a possible sluggish regenerative capacity of tissues. That is why patients with genital prolapse caused by estrogen deficiency, before planned surgical treatment it is necessary to restore the functional state of hormone-dependent tissues of the urogenital system, and in its lower parts - to stimulate the mechanisms of natural biological defence.

Many studies have confirmed the impact of estrogen deficiency on the incidence of pelvic organ prolapse and urogenital disorders, as evidenced by the study of S.N. Buyanova (2017), which shows the importance of sex hormones in the development of pelvic floor muscle insufficiency [7]. But, the opposite to these studies there is information obtained from Women Health Initiative with the participation of 270 women, in which there is no statistically significant difference between those who took hormones (for 6 years) and those who took a placebo. Also, studies conducted by Yu.A. Shelygin et al. (2018) [8] found no evidence of the effect of estrogens and other hormonal factors on the development of perineal prolapse syndrome, which developed against the background of unchanged hormonal status. The authors assure that the implementation of hormonal therapy in this category of patients has no influence.

Conclusion. Thus, given the numerous studies indicating the pathogenetic relationship between steroid hormone deficiency and pelvic organ prolapse, the mechanism of this influence on the clinical course and its development remains unclear, which requires further study of this problem.

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