



ALGORITHM OF LOCAL THERAPY OF VAGINITIS IN POSTMANOPAUSAL WOMEN.

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Abstract. The problem of atrophic vaginitis (AV) in postmenopause is widespread; it is considered a natural aging process and is currently not solved. To ensure the proliferation of multilayer squamous epithelium for the formation of vaginal resistance to infection in postmenopausal, local estrogen therapy is performed. Before restoring the functions of the vagina with estrogen preparations, preliminary sanitation is advisable. The appearance on the market of combined drugs with antimicrobial and fungicidal action requires the development of schemes for their effective use.

Key words: Ovipol Clio, clindacin B prolong, atrophic vaginitis, postmenopause.

Relevance of the study. The problem of atrophic vaginitis (AV) in postmenopause is widespread, but often changes as a natural process of aging and extinction of the body. The health and quality of a woman during a period of hypersensitivity to sensitivity, one of them is a decrease in the level of estrogens, which causes a violation of the proliferative processes of epithelial inflammation, a decrease in the mitotic activity of the kidneys (primarily the base and parabasal layers), a change in the sensitivity of the receptor apparatus [4]. With the duration of postmenopause and a high probability of estrogen deficiency, the vaginal environment is alkalinized, dysbiotic and atrophic processes are initiated [3, 4].

The results of molecular genetic studies of the regulation of vaginal microecosystems in different age periods show that the endogenous vaginal microflora is a dynamic biosystem that is in equilibrium with the macroorganism and undergoes changes under the influence of endogenous and exogenous factors [6]. The state of a woman's reproductive tract depends on hormonal regulation, an increase in the mass of microflora, the immune system and biologically active substances produced by them.

The representation of microflora in the vagina and cervical canal (lactobacilli, opportunistic microflora) depends on the etiology of the inflammatory process and hormonal background [6].

For the vital activity and growth of lactobacilli, cytolysis of continuously serviced epithelial cells with the release of glycogen is necessary. The colonization of the epithelium by lactobacilli and E. coli depends on the level of estrogens. With estrogen deficiency, the insufficiency of epithelial accumulation leads to anatomical and physiological insufficiency of the multilayered squamous epithelium (MPE) of the vagina, glycogen deficiency, the quantitative amount and elimination of lactobacilli, a shift in the pH of the vagina to the alkaline side. When compiling the estrogen content to account for the differentiation of

desquamous epithelium and keratinization of the vaginal epithelium, adhesion and colonization of E. coli colonization does not occur [6]. Against the background of hypoestrogenism associated with age-related biological changes in a woman's body, the vaginal MPE cells decrease in size.

To form resistance of the vagina to infection, it is necessary to saturate the body with estrogens that stimulate the proliferation of MPE and increase the production of glycogen in inflammatory cells. An important role of the estrogenic background in preventing the proliferation of MPE and glycogen production in cells that cause cell resistance to infection, when examining vaginitis in postmenopause, local therapy with drugs infected with estrogens with a high level of safety, as well as selective activity against mucosal allergy of the urogenital tract is regularly performed [4]. In such a framework, the tactics of therapy causes estriol, a substance that is a synthetic analogue of estrogens. Estriol is subject to a short duration of action and does not cause endometrial proliferation, and therefore no additional prescribing of progestogens is required [3, 4]. Estriol pointed to the person AB. Consumption of therapeutic doses of estriol, colds and safe diseases [3, 4]. Currently, the Russian pharmaceutical market has a drug estriol for topical use in postmenopause – Ovipol Clio (JSC "Akrikhin", Russia). symptoms are detected in 0.5 mg candles, recommendations for AV and other disorders of the urogenital tract [3, 4]. Currently, the Russian pharmaceutical market has a drug estriol for topical use in postmenopause – Ovipol Clio (JSC "Akrikhin", Russia). symptoms are detected in 0.5 mg candles, recommendations for AV and other disorders of the urogenital tract [3, 4]. Currently on the Russian pharmaceutical market For optimal therapeutic results in postmenopausal AV before restoring vaginal function with the help of treatment with estriol, an estimated comprehensive preliminary sanitation of the vagina for the prevention and correction of activation of opportunistic microflora. In the arsenal of doctors there are many combined antibacterial drugs that are used in the treatment of the vagina of mixed etiology with high efficiency. To eliminate an excessive amount of anaerobic drugs, etiotropic drugs of the 5-nitroimidazole group or clindamycin are used. From the point of view of clinical interest, clindamycin is an antibiotic of the lincosamide group. According to the effectiveness of vaginitis therapy, clindamycin is treated with metronidazole (89-93%) with less frequent symptoms [3, 4, 10]. As part of the combined therapy of vaginitis, butoconazole (an imidazole derivative) is used, which has fungicidal activity against fungi and some gram-positive bacteria. With a single application of butoconazole (2% vaginal cream), repeated efficacy occurs with a 7-day course of miconazole (2% vaginal cream) [7]. The combined content of butoconazole (antifungal component) and clindamycin (antibacterial component), presented in the combined topical preparation Clindacin B prolong (vaginal cream), which causes interest in the use of the drug for the treatment of vaginitis. In the instructions for using the drug, pharmacological properties are consumed: the hydrophilic cream base of the dosage form corresponds to a gel-like consistency at a temperature of 35-40 ° C, and therefore, with intravaginal application, the cream does not float and the active substances are on the vaginal mucosa for 1-3 days. These properties of the drug are manifested by high bioadhesiveness and prolonged nature of action in the absence of irritating action, which is important for achieving the effectiveness of treatment of forms of diseases, especially in postmenopausal. Vaginal cream, butoconazole 2%, clindamycin 2%, 1 time a day intravaginally, daily before bedtime, daily for 3-6 days. The recommended dose is 5 g of cream, which corresponds to 100 mg of butoconazole nitrate and 100 mg of clindamycin,

according to the instructions for use. Thus, in postmenopause, against the background of hypoestrogenism, the frequency and severity of AV symptoms increases: dryness, itching and burning in the vagina, recurrent vaginal discharge, contact spotting. As a result of the progression of symptoms, an unsatisfactory and revealed quality of life of a woman arises, which determines the relevance of an early diagnosis and the accuracy of determining the diagnosis. The appearance of new drugs on the pharmaceutical market will allow us to develop the tactics of complex etiopathogenetic therapy of vaginitis in postmenopause.

The aim of the study was to evaluate the clinical effectiveness of complex therapy of AV in postmenopausal women, including the use of vaginal cream, the use of butoconazole 2%, clindamycin 2%, for vaginal use, followed by the use of suppositories with estriol.

Materials and Methods of research:

74 women with AV, who were sent for an outpatient examination of the 3rd polyclinic of the city of Samarkand, took part without fail. All patients were registered during the study and signed a notice of participation in it.

Inclusion criteria: age from 50 to 70 years, postmenopause, confirmation of the diagnosis of AV, consent to participate in detection.

Exclusion criteria: age younger than 50 years or older than 71 years, absence of postmenopause, hypersensitivity to the component of the drug, use of systemic or antibacterial therapy for 2 weeks, sexually transmitted infections.

The main group consisted of 54 women (average age - 60.4 ± 0.6 years), attracted intravaginally with the help of an applicator cream butoconazole+clindamycin 5 g daily for 6 days and then - vaginal suppositories with estriol 1 candle 1 time a day at night for 15 days. The comparison group consisted of 20 women (average age - 61.1 ± 0.9 years) who received appropriate suppositories only with estriol.

Evaluation of the effectiveness of treatment was carried out by the presence/absence of complaints, the results of bimanual examination, examination in mirrors, microscopic examination of vaginal secretions stained by Gram, cytological examination of cervical smears, polymerase chain reaction (PCR) in real-time protocol (Femoflor test) with quantitative determination of fetal DNA associated with vaginitis (*Gardnerella vaginalis*, *Atopobium vaginae*, *Ureaplasma urealyticum*, *Mycoplasma hominis*, *Prevotella* spp., *Megasphaera* spp., etc.). Control studies were conducted before treatment, 2 weeks and 1 month after the end of therapy.

Research results:

According to the age of the study participants, the results of clinical and laboratory studies were the subject of study.

At the beginning of the study, women have complaints of burning, dryness of the vaginal mucosa, scanty yellowish discharge. Determination of acidity within pH $6,7 \pm 0,4$ and $6,6 \pm 0,4$, in smears the average number of leukocytes in the field of view $58, 8 \pm 5,6$ and $63,0 \pm 7,2$ respectively, smear microscopy revealed populations of small bacillus ($31,6 \pm 1,1\%$ and $10,5 \pm 1,2\%$), mixed ($21,1 \pm 1,2\%$ and $29,0 \pm 1,5\%$), cocco-bacillary flora ($47,4 \pm 1,9\%$ and $59,1 \pm 2,1\%$) respectively.

Thus, before treatment, women with AV had pronounced changes in vaginal microcenosis. Concentrations of various diseases causing inflammation of lactobacilli were most often detected.



2 weeks after the end of treatment, 6 (11.1%) of 54 patients (compared to the data before treatment) of the main groups had complaints of burning sensation, while all had no complaints of vaginal dryness, the acidity of the vaginal contents recovered to the average norm, falling within the pH range of 4.5 [2, 5, 6], the number of leukocytes in vaginal secretions decreased by more than 10 times, the representation of small bacillus in the vaginal flora increased by an average of 2.3 times, while the proportion of mixed and on average 9 times cocco-bacillary flora increased by an average of 2.3 times. In contrast to patients receiving complex therapy, 6 (30.0%) out of 20 patients who took only candles with estriol after the course of treatment against the background of signs of clinical disease (absence of dryness). there was a burning sensation in the vagina, the laboratory dynamics of indicators was multidirectional and poorly expressed. Thus, the pH of the vaginal contents does not normalize and is released without dynamics, the average content of leukocytes in the smear Consumption was less significant in the vaginal flora, the representation of small bacillus significantly prevailed in dynamics with a simultaneous combination of a mixed proportion and cocco-bacillary flora.

A month after the end of therapy, positive dynamics of clinical and laboratory parameters is recorded in patients of the main group, which takes into account their recovery. At the same time, there are no significant changes in such indicators in women after monotherapy, while 8 (40.0%) patients retain a burning sensation in the vagina, all retain a reduced acidity of the vaginal content.

Study of the vaginal microbiocenosis of a woman with AV by PCR in a long-term trial using the Femoflora test a month after treatment using a combined manifest examination model an increase in the content of lactobacilli and a decrease in the content of obligate anaerobes (*Staphylococcus* spp., *G. vaginalis*, *Bacteroides*) spp., *Peptostreptococcus*, *Megasphaera* spp., *Leptotrichia* spp./*Sneathia* spp., *Lachnobacterium* spp., *A. vaginae*, *M. hominis*, *Ureaplasma* spp.) and fungi (*Candida* spp.).

In women who took only candles with estriol, a weakly positive dynamics was noted. At the same time, against the background of concentration, obligate anaerobic flora (*Staphylococcus* spp., *Enterobacteriaceae*, *G. vaginalis*, *Leptotrichia* spp./*Sneathia* spp., *Lachnobacterium*, *A. vaginae*, *M. hominis*, *Ureaplasma* spp.) and *Candida* spp. are often detected.

Thus, already 2 weeks after the course of taking prescribed medications, a more pronounced effectiveness of the combined AB treatment regimen was noted. In general, monotherapy with *Ovipol Clio* does not cause normalization of vaginal biocenosis.

Despite the absence of the desired effect of therapy in some patients, all the women who participated in the study underwent treatment well, allergic reactions and other consequences were absent.

It is known that hormonal disorders in a woman's body are a favorable background for the development of the inflammatory process of the acute genital region due to changes in the reactivity of the vaginal mucosa. In the MPE of the vagina and the vaginal part of the cervix, proliferation in the basal and parabasal layers, accumulation of intermediate layer cells with accumulation of glycogen in them; cultivation of excessive cells with accumulation in keratin are detected. the most frequent forms of age-related changes in the vagina and cervix in postmenopause are AV and cervicitis [2-4, 8]. The active secretion of the vaginal epithelium depends on estrogens: the follicular phase of the menstrual cycle is characterized by the identification of cells with the formation of a layer, for luteal – mainly intermediate cells,

against the background of hypoestrogenism – basal and parabasal [2, 8]. Against the background of estrogen deficiency in postmenopause, due to a decrease in the proliferative activity of the basal and parabasal layers of the MPE, thinning and a decrease in the elasticity of the atrophied epithelium, a decrease in the volume of the submucosal vascular network, the development of colon ischemia, and a decrease in transudation occur. Atrophic changes in the vaginal mucosa make it easily vulnerable, which causes complaints of discomfort, dryness, burning, watery or bloody discharge [4].

Throughout a woman's life, vaginal cells and ectocervix cells secrete protons through the apical plasma membrane, mixing with the pH of the vagina in the acidic direction. With a pronounced pH of the vaginal environment on the alkalization side, the total number of pathogens, primarily lacto- and bifidobacteria, decreases to 5.5-7.5, which occurs in the microflora, obligate-anaerobic tissues that provoke inflammatory processes predominate [9]. Activation of conditionally pathogenic microflora is possible, causing the manifestation of colonization resistance of the mucous membrane of the vagina and cervix, the amount of facultative microflora, which leads to favorable conditions for the development and chronization of the inflammatory process. It is important to note that in postmenopause, due to the inhibition of tissue resistance, the vaginal epithelium becomes even more sensitive to infection and ulceration, contributing to colonization of the vagina and consumption of the urinary tract by conditionally pathogenic flora (mainly the ingestion of bacilli and the typical disappearance of the microflora of the skin) and their secondary infection. As a result, secondary inflammatory processes, bacterial vaginosis, recurrent vaginitis develop, which contribute to the development of dyspareunia [2].

The results of the study indicate a higher positive effect of treating patients with AV according to a combined scheme (intravaginal cream butoconazole + clindamycin and further suppositories with estriol), which obviously has pharmacological properties and etiopathogenetically justified use.

Estriol, when exposed to a set of vaginal epithelial tissues, normalizes the pH of the medium and the microflora of the urogenital tract, and also leads to the ingress of the main elements of connective tissue – collagen and elastin [3, 4].

Clindamycin, binding to the 50S subunit of ribosomes, synthesizes protein in the microbial cell, thereby having a high spectrum of protection against groups including *G. vaginalis*, *Peptococcus* spp., *Peptostreptococcus* spp., *Bacteroides* spp., *Fusobacterium* spp., etc. The fungicidal and antimicrobial mechanisms of action of butoconazole consist in blocking the formation of ergosterol from lanosterol in the cell membrane and the formation of membrane permeability, which leads to the lysis of a fungus or bacterium cell [7].

When analyzing the dynamics of clinical and laboratory parameters in postmenopausal women with AV, it should be noted that monotherapy with an estriol-containing blood preparation of the cellular composition of the vaginal mucosa, which is an increase in the secretory activity of epithelial cells. At the same time, in the presence of dysbiotic diseases in the vagina, characteristic of the postmenopausal period, the restoration of secretory activity becomes a favorable disease for the development of pathogenic flora. This is manifested by its growth against the background of the detection of lactobacilli. In this regard, the early use of the drug with a certain spectrum of antimicrobial and fungicidal action allows to prevent the progression of dysbiotic disorders of the function of the cells of the vaginal mucosa during postmenopausal treatment.



Conclusion:

Postmenopausal hypoestrogenism leads to a reduction of vulvovaginal perfusion, a decrease in the number of cells in the layers of the vaginal MPE, a decrease in their glycogen content, the severity of secretory activity of the mucous membrane, the volume of vaginal microbiocenosis. Adequate and effective drug correction of dysbiotic processes of the vaginal microsystem in postmenopause should take into account the peculiarities of pathogenesis, based on the social aspects of women's life, as well as age-related changes in the quantitative and qualitative composition of the vaginal microbiota. The use of polymicrobial etiology of the vaginal microflora is widespread.

In this regard, candles with estriol, intended for topical use in the detection of vaginitis in postmenopause, the optimal use of antibacterial drugs that have a positive effect on the vaginal microbiota, are largely applicable. Complex therapy with the use of a combined cream for intravaginal use.

References:

1. Analysis of the course of pregnancy in women infected with *Ur.urealyticum*, depending on the degree of colonization of the genital tract. A. Melnikova, M.M. Padrul, E.S. Horowitz, G.I. Rabotnikov. *Perm Medical Journal*. - 2017.- Vol. 34, No. 2. - pp. 26-30.
2. Boymamatova P. F. Dyscirculatory encephalopathy: principles of treatment // *Eurasian Medical Research Periodical*. - 2022. - T. 13. - C. 128-132.
3. Furkatjonovna B. P., Ukurova S. G. Assessment of the role of ent pathology in the development of facial pain // *Academicia Globe: Inderscience Research*. - 2022. - T. 3. - №. 03. - C. 56-63.
4. Ismatiloevna Y. F. TREATMENT OF VAGINAL DYSBIOTIC DISORDERS IN PREGNANT WOMEN BEFORE CHILDBIRTH // *World Bulletin of Public Health*. - 2022. - T. 12. - C. 86-89.
5. Ismatiloevna Y. F., Islamovna Z. N., Utkurovna S. G. DYSBIOSIS OF THE VAGINAL MICROBIOTA IN GYNECOLOGICAL DISEASES // *Thematics Journal of Education*. - 2022. - T. 7. - №. 2.
6. Ismatiloevna Y. F., Utkurovna S. G., Islamovna Z. N. THE OUTCOME OF PREGNANCY AND CHILDBIRTH IN WOMEN WITH IMPAIRED VAGINAL BIOCECENOSIS // *World Bulletin of Public Health*. - 2022. - T. 13. - C. 85-87.
7. Karapetyan, T.E. Aerobic Vaginitis and pregnancy T. E. Karapetyan, V. V. Muravyeva, A. S. Ankirskaya *Obstetrics and gynecology*. - 2013.- No. 4.- pp. 25-28.
8. Kostin, I.N. The significance and results of the international research project "Human Microbiome" I.N. Kostin, L.Yu. Kuvankina, H.Yu. Simonovskaya *Status Praesens*. - 2013. - №5(16). - Pp.9-15.
9. Kuzmin *Gynecology*. - 2015.- No. 2.- pp. 21-26 Laboratory diagnostics of bacterial vaginosis: methodological recommendations of A.M. Savichev, M.A. Bashmakov, T.V. Krasnoselskikh. - St. Petersburg: Publishing House N-L, 2011.-28 p.
10. Nikonov AP, Astsaturova OR, Chilova RA, Ishchenko AI, Rafal'skii VV. Infections in obstetrics and gynecology: diagnosis and antimicrobial chemotherapy. A manual for doctors. M.: PAgRI, 2006. 28 p. Russian (Nikonov A.P., Ascaturova O.R., Chilova R.A., Ishchenko A.I.,



- Rafalsky V.V. Infections in obstetrics and gynecology: diagnostics and antimicrobial chemotherapy. Manual for doctors. M.: PAgRI, 2006. 28 p.)
- 11.Nikonov AP, Astsaturova OR, Chilova RA, Ishchenko AI, Rafal'skii VV. Infections in obstetrics and gynecology: diagnosis and antimicrobial chemotherapy. A manual for doctors. M.: PAgRI, 2006. 28 p. Russian (Nikonov A.P., Astsaturova O.R., Chilova R.A., Ishchenko A.I., Rafalsky V.V. Infections in obstetrics and gynecology: diagnostics and antimicrobial chemotherapy. Manual for doctors. M.: PAgRI, 2006. 28 p.)
- 12.Safoeva Z. F. Comparative characteristics of neurological symptomatology in children depending on the type of delivery //Youth and medical science in the XXI century. – 2018. – C. 61-63.
- 13.Safoeva Z. F., Utkurovna S. G. DYSBIOTIC UPPER AIRWAY DISORDERS IN CHILDREN WITH ACUTE STENOTIC LARYNGOTRACHEITIS LARYNGOTRACHEITIS //World Bulletin of Public Health. – 2022. – T. 11. – C. 1-4.
- 14.Safoeva Z., Samieva G. TREATMENT OF CHILDREN WITH ACUTE STENOSING LARYNGOTRACHEITIS IN CONDITIONS OF PROLONGED TRACHEAL INTUBATION //Eurasian Journal of Medical and Natural Sciences. – 2022. – T. 2. – №. 6. – C. 185-190.
- 15.Tavo, V. Prevalence of Mycoplasma hominis and Ureaplasma urealyticum among women of reproductive age in Albania V. Tavo Med.arch. - 2013. - Vol. 67, No. 1. - pp. 25-26. doi:10.5455 medarch.2013.67.25-26
- 16.Temporal and spatial changes of the human microbiota during pregnancy D.B. DiGiulio, B.J. Callahan, P.J. Mcmurdy PNAS. -2015. - Vol. 112, No. 35. -pp.11060-11065. doi:10.1073pnas.150287511
17. The composition and stability of the vaginal microbiota of normal pregnant women differ from the composition of the microbiome of non-pregnant women R. Romero, S.S. Hassan, P. Hajer. - 2014. - Vol.2, No. 1. - p.4. doi:10.1186/2049-2618-2
- 18.Utkurovna S. G., Farkhodovna S. Z., Furkatjonovna B. P. Optimization of the treatment of acute rhinosinusitis in children //Web of Scientist: International Scientific Research Journal. – 2022. – T. 3. – №. 3. – C. 769-773.
19. Yuldasheva F. I. FEATURES OF VAGINAL MICROBIOTA DYSBIOSIS IN GYNECOLOGICAL DISEASES //Conferencea. – 2022. – pp. 85-87.
- 20.YULDASHEVA F. I., SAMIEVA G. U., ZAKIROVA N. I. FEATURES OF CHANGES IN THE MICROFLORA OF THE VAGINA TO WOMEN //ЖУРНАЛ БИОМЕДИЦИНЫ И ПРАКТИКИ. – 2022. – Т. 7. – №. 3.
- 21.Сафоева З. Ф., Хусаинова Ш. К., Умарова С. С. Сравнительная оценка неврологической симптоматики у новорожденных, рожденных естественным путем и путем операции кесарева сечения //Достижения науки и образования. – 2021. – №. 1 (73). – С. 53-57.
- 22.Урунова Ф., Сафоева З. Функциональное состояние почек у недоношенных новорожденных родившихся от матерей с преэклампсией //Журнал вестник врача. – 2018. – Т. 1. – №. 1. – С. 80-83.
- 23.Safoeva Z. F., Samiyeva G. U. CLINICAL AND IMMUNOLOGICAL FEATURES AND THERAPY OPTIONS FOR RECURRENT LARYNGOTRACHEITIS IN CHILDREN //Theoretical aspects in the formation of pedagogical sciences. – 2022. – Т. 1. – №. 4. – С. 105-106.

