

АКУШЕРСТВО И ГИНЕКОЛОГИЯ

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STUDY OF VAGINAL MICROBIOTA IN POSTMENOPAUSAL WOMEN WITH SURGICAL CORRECTION OF GENITAL PROLAPSE

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Abstract. The study of the vaginal microflora of women with genital prolapse (GP), who are referred to surgical treatment, is of particular importance. Infectious and inflammatory complications after the surgical correction of GP significantly increase the recovery time, the length of the patient's hospital stay and the cost of treatment. It is important to be able to change the qualitative composition of microflora, thereby exerting a beneficial effect on the course of the postoperative period, affecting the outcome of surgical treatment. Evaluation of the vaginal microbiota by real-time polymerase chain reaction in postmenopausal women with surgical correction of genital prolapse against the background of using low-dose local therapy regimens with a drug containing estriol, progesterone and *Lactobacillus* culture.

Key words: genital prolapse, implant-associated complications, mesh implant, vaginal microbiota

Introduction. The inclusion of the study of vaginal microbiota in the fundamental international research project "Human microbiome project" (2008-2012), has greatly expanded the existing understanding of the microbiota of this biotope. Molecular studies based on the indication of 16S rRNA of bacteria revealed 265 species of microorganisms in the vagina [3,5,9]. Despite the existence of fundamental differences in the vaginal microbiota in women of different ages and ethnicity [2], *Lactobacillus* spp. are the dominant symbionts of this biotope. Currently, there is no single standard for the qualitative and quantitative composition of the vaginal microbiota in menopausal and postmenopausal women of various age groups.

The research conducted in 2016, the purpose of which was to study the vaginal microbiota in postmenopausal women with genital prolapse (GP) and healthy women, discovered some features [1]. In postmenopausal women (healthy and with GP) in the vagina there is no leukocyte reaction and, accordingly, the inflammatory process. *Lactobacilli* are recorded in 10.0% of cases in the vagina of postmenopausal healthy women. In women with GP, these microorganisms are absent. In the examined women of the above categories, coagulase-negative staphylococci and *Corynebacterium* spp. prevail among facultative anaerobic bacteria, while *Eubacterium* spp. prevail in the

group of non-clostridial anaerobic bacteria. In postmenopausal women, vaginal microbiota patterns were found that are characteristic for healthy women and for patients with genital prolapse.

GP in postmenopausal women can aggravate a woman's dysbiosis against the background of atrophy of the vaginal mucosa and an insufficient amount of estrogen [4,8,10]. The meta-analysis of N.D. Nelson (2004) proved that all routes of administration of estrogens (oral, transdermal, vaginal) are effective in alleviating the symptoms of menopause and favorably affect the vaginal microflora [6]. According to a number of authors, lactobacilli are absent in postmenopausal women who do not take estrogens, however, various taxa of anaerobic bacteria predominate [7, 11]. Thus, estrogen levels affect vaginal microflora patterns. As a result, the study of the microbiota of the vagina in menopausal and postmenopausal women is of particular importance.

At the same time, the study of the vaginal microflora of women with GP who are referred to surgical treatment is of particular importance. Obviously the microbial factor has an undeniable effect on the processes of vaginal tissue repair and long-term results after surgery. When the anatomy and topography of the urogenital tract organs are impaired, as well as anorectal dysfunction (with the development of rectocele, enterocele), pathogens of bacterial infections that cause colpitis, bacterial vaginosis, trophic changes in the tissue of the vagina and cervix (decubital ulcer of the cervix, bedsores of the vaginal walls) develop and persist for a long time, which requires complex therapy, taking into account the microbial factor and the severity of the inflammatory process, especially against the background of postmenopausal atrophy [11]. Different combinations of involutive, atrophic and inflammatory changes in the walls of the vagina are observed in case of prolapse of internal genital organs. The main factor here is the state of vascularization of the prolapsed vaginal wall and pelvic organs. The severity of atrophic and inflammatory changes is due to a decrease in vascularization and, accordingly changes of the mucous membrane, due to displacement of internal organs and changes of the vascular bed. Infectious and inflammatory complications after undergoing surgical correction of genital prolapse significantly increase the recovery time, the length of the patient's stay in the hospital and the cost of treatment. The saturation of the vaginal wall using local hormonal estriol-progesterone therapy, in combination with lactobacilli before surgery, as well as in the postoperative period, allows you to change the qualitative composition of the microflora, thereby having a favorable effect on the course of the postoperative period, affecting the outcomes of surgical treatment.

Materials and methods. The study involved 50 postmenopausal women suffering from genital prolapse of stage III, IV in combination with genitourinar menopausal syndrome. Patients were randomized into two groups. Three-component therapy was administered to the first group using vaginal forms of estrogen and progesterone preparations in combination with *Lactobacilli caseirhamnosus Doderleini* as a preoperative preparation of the vaginal mucosa and postoperative management of patients. The second group (comparison group) did not undergo

preoperative preparation and postoperative local therapy. All patients underwent clinical and laboratory examination: general examination and gynecological examination, cytological examination from the cervix and smears from the surface of the vagina, bacterioscopy of the contents of the vagina. As a diagnostic test to study the microbial composition of the vagina, the quantitative composition of the vaginal microbiota was determined by real-time PCR using the Femoflor-16 test system. Methods of parametric statistics were used.

Results and discussion. It was found that enrichment of the vaginal wall with hormones in combination with *Lactobacillus casei* in the perioperative period allows a statistically significant increase in the number of lactobacillary flora and a decrease in the number of anaerobic microorganisms in women after surgical treatment of genital prolapse after undergoing pelvic floor reconstruction with a mesh implant. A decrease in the pool of anaerobic microorganisms of women who underwent surgical treatment for pelvic organ prolapse can reduce the number of implant-associated complications.

Materials and methods of research

A comparative prospective randomized clinical trial was conducted on the basis of the gynecological department of the Ural Scientific Research Institute for Maternal and Child Care of the Ministry of Healthcare of Russian Federation for 2018-2019. The study included 50 women aged from 57 to 74 years with stage III, IV GP according to the international classification of Pelvic Organ Prolapse-Quantification (POP-Q). All women underwent various reconstructive plastic surgeries using mesh implants. Patients were randomized into 2 groups. The main (1) group consisted of 25 patients receiving three-component therapy, the control group (2) consisted of 25 people without the specified therapy. For women of the main group, hormones in combination with lactobacilli (estriol 0.2 mg, 2 mg of progesterone and *Lactobacillus casei* rhamnosus Doderleini) were prescribed according to the scheme: before surgery 2 capsules once a day for 2 weeks, then 1 week, 1 capsule per day, in the postoperative period 1 capsule twice a week for 2 months. The qualitative and quantitative composition of microflora was determined using the Femoflor-16 test. The diagnosis of normocenosis was determined by two indicators: the number of total bacterial mass (TBM) and *Lactobacillus* spp. Evaluation of aerobic microflora included determination of enterobacteria (*Enterobacterium* spp.), Streptococci (*Streptococcus* spp.), Staphylococci (*Staphylococcus* spp.). The amounts of *Gardnerella* / *Prevotellabivia* / *Porphyromona* spp., *Eubacterium* spp., *Sneathiaspp.* / *Lepperperpheri* *Sneathiaspp.* / *Leptotrihi* spp. / *Fusobacterium* spp., *Megasphaspp.* / *Veilonellaspp.* / *Dialister* spp., *Lachnobacterium* spp. / *Clostridium* spp., *Mobiluncusspp.* / *Corynebacterium* spp., *Peptostreptococcus* spp., *Atopobiumvaginae*, *Mycoplasma* (*hominis*+*genitalium*), *Ureaplasma* (*urealyticum*+*parvum*), were determined as anaerobic microorganisms. The number of *Candida* was also evaluated. The urogenital biota was quantified both in absolute terms (genome equivalents - GE / sample) and relative indicators (%), which were calculated using IQ5 Multicolor Real-Time PCR Detection System software provided by BIO-RAD (USA). The Femoflor-16 test was performed before surgery (after 1 month of

specialized preoperative preparation), and 2 months after surgical treatment. All data were statistically processed using the standard Microsoft Office 2010 software package (Microsoft Excel) and STATISTICA® for Windows 6.0. Quantitative indicators are presented in the form $M \pm SD$, where M is the arithmetic mean, SD is its standard deviation. Student's t criterion was used to determine confidence. Differences were considered statistically significant at $p < 0.05$.

Results of research and discussion.

Patients of the 1st and 2nd groups were comparable in age (62.5 ± 6 , and 65.27 ± 3.12 years, in the first and second groups, respectively, $p > 0.05$) and birth parity (2.6 ± 0.51 and 2.2 ± 0.8 births, $p > 0.05$).

When studying the microflora before surgical treatment, in women, against the background of local hormone therapy in combination with lactobacilli as a preoperative preparation, a higher content of lactobacilli was revealed in contrast to the control group (Table 1). Given that reconstructive plastic surgery in women with genital prolapse is performed under conditions of inflammation and atrophic changes, saturation of the vaginal wall with lactobacilli reduces the likelihood of postoperative complications and relapses of genital prolapse.

Table 1. The content of lactobacilli and the total bacterial mass in the vagina in women of the studied groups before / after surgical treatment

Indicators	Group 1	Group 2	p
Total bacterial mass (TBM) before treatment	7.8 ± 0.7	5.8 ± 0.7	>0.05
<i>Lactobacillus</i> spp. before treatment	7.0 ± 1.3	2.0 ± 1.5	<0.05
Total bacterial mass (TBM) after treatment	6.9 ± 0.3	6.8 ± 0.7	>0.05
Lactobacilli (<i>Lactobacillus</i> spp.) after treatment	6.3 ± 0.2	3.0 ± 1.1	<0.05

The content of lactobacilli in the vagina in women after surgical treatment using a mesh implant and low-dose local therapy with a drug containing estriol, progesterone and a culture of lactobacilli remained within normal limits, excess in the values in the control group ($p < 0.05$) was statistically significant (Table. 1).

Analysis of the qualitative and quantitative composition of the anaerobic flora of the vagina revealed differences in the number of individual bacterial species in the study groups. Before surgery, patients in both groups had an increase in *Gardnerella/Prevotellabivia/Porphyromonas* spp., *Eubacterium* spp., *Megasphaera* spp./*Veilonellas* spp./*Dialisters* spp., *Mobiluncus* spp./*Corynebacterium* spp., *Peptostreptococcus* spp.. The content of bacteria of *Gardnerella/Prevotellabivia/Porphyromonas* spp., *Megasphaera* spp./*Veilonellas* spp./*Dialisters* spp., *Mobiluncus* spp./*Corynebacterium* spp.

was significantly higher in the second group than in women with preoperative preparation (table. 2).

Table 2. Relative combination of anaerobic microorganisms in the vagina in women of the studied groups before surgical treatment

Microorganisms	Group 1 before treatment	Group 2 before treatment	Group 1 after treatment	Group 1 after treatment	p before treatment	P after treatment
<i>Gardnerella/Prevotellabivia/Porphyromonas</i> spp.	4.61±0.3	6.2 ±0.2	2.47±0.2	6.4 ±1.2	<0.05	<0.05
<i>Eubacterium</i> spp.	5.79±0.8	4.1±0.1	1.28±0.4	4.9±0.8	<0.05	<0.05
<i>Sneathiaspp./Leptotrihispp./Fusobacterium</i> spp.	0.3±0.9	0.4±0.3	0.5±0.3	1.8±0.2	p>0.05	<0.05
<i>Megasphaspp./Veilonellaspp./Dialisterspp.</i>	4.52±0.2	5.2±0.7	2.87±0.5	6.3±1.3	p=0.0001	>0.05
<i>Lachnobacterium</i> spp./ <i>Clostridium</i> spp.	1.93±0.1	1.1±0.5	2.3±0.8	1.8±0.7	<0.05	<0.05
<i>Mobiluncusspp./Corynebacterium</i> spp.	4.31±1.1	5.7±0.2	5.2±1.5	6.3±1.4	<0.05	<0.05
<i>Peptostreptococcus</i> spp.	4.47±1.0	3.1±1.2	1.1±0.5	1.2±1.5	p=0.0001	>0.05
<i>Atopobiumvaginae</i>	0.5±0.2	0.8±0.5	0.3±0.1	0.5±0.3	<0.05	<0.05

In the group of patients who received local forms of hormones in combination with lactobacilli, the number of samples demonstrating pathogenic and opportunistic vaginal microflora significantly decreased. A significantly lower proportion of patients with a pathogenic state of the vaginal microbiota after three-component therapy is noteworthy.

As a result of the analysis of the composition of the vaginal microflora 2 months after surgical treatment in the 1st group, a significant decrease in the content of some anaerobic microorganisms, such as *Gardnerella/Prevotellabivia/Porphyromonas*spp., *Eubacterium*spp., *Megasphaspp./Veilonellaspp./Dialisterspp.*, *Peptostreptococcus*spp. was revealed (tab. 2).

The results obtained allow us to conclude that it is the reduction in the pool of anaerobic microorganisms in women who underwent surgical treatment for pelvic organ prolapse that allows to reduce the number of implant-associated complications, such as erosion of the vaginal mucosa at the site of the mesh implant installation, as well as possible infectious complications.

Conclusion:

1. Thus, women with genital prolapse have a significant disturbance of the vaginal microflora due to a decrease in the number of lactobacilli. The restoration of the microbiota of the vaginal epithelium during atrophic changes in patients with genital prolapse, the increase in the resistance of the epithelium to infectious and inflammatory processes establishes the demand for preoperative preparation of the vaginal walls using preparations containing estriol and progesterone in combination with *Lactobacillus*.

It was found that the decrease in the content of anaerobic microorganisms in the vagina in patients with pelvic floor reconstruction with a mesh implant, against the background of the use of low-dose local therapy regimens with a drug containing estriol, progesterone and *Lactobacillus* culture in the postoperative period, allows to indirectly influence the outcomes of surgical treatment, reducing the frequency of implant-associated complications, in particular, such as erosion of the vaginal mucosa.

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ОЦЕНКА РИСКОВ ВОЗМОЖНЫХ ОСЛОЖНЕНИЙ БЕРЕМЕННОСТИ
ПРИ ПРОВЕДЕНИИ КОМБИНИРОВАННОГО СКРИНИНГА В I
ТРИМЕСТРЕ**

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**Arebyev E.V., Vshivtsev K.S., Kudryavceva E.V
RISK ASSESSMENT OF POSSIBLE PREGNANCY COMPLICATIONS
DURING COMBINED SCREENING IN THE FIRST TRIMESTER**

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Аннотация. В настоящей статье представлена оценка взаимосвязи биохимических и ультразвуковых показателей комбинированного скрининга в I триместре беременности с риском осложнений из группы «больших акушерских синдромов».

Annotation. This article presents an assessment of the relationship between biochemical and ultrasound indicators of combined screening in the first trimester of pregnancy with the risk of complications from the group of "great obstetric syndromes".

Ключевые слова: пренатальный скрининг, преэклампсия, комбинированный скрининг I триместра

Key words: prenatal screening, preeclampsia, combined first trimester screening