

The role of disturbances in vaginal microbiocenosis in recurrent urogenital candidiasis

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ABSTRACT: Purpose: This study aims to investigate the role of disturbances in vaginal microbiocenosis in recurrent urogenital candidiasis (UGC), focusing on the type of fungus present and the bacterial mass, using PCR diagnostics. Methods: Twenty-two women diagnosed with chronic vulvovaginal candidiasis were examined. PCR diagnostics, including the Mycoso-Screen analysis for fungal pathogens and the Femoflor-16 PCR test system for vaginal dysbiosis, were performed to determine the type of fungus and bacterial mass present. Results: *Candida albicans* was found in 36% of patients, *Candida glabrata* in 32%, *Debaryomyces hansenii* in 12%, *Pichia kudriavzevii* in 12%, and *Saccharomyces cerevisiae* in 12%. Moreover, dysbiosis of vaginal microbiota was observed in 77% of patients, characterized by decreased lactobacilli and increased opportunistic microflora, contributing to the recurrence of UGC. Conclusion: Recurrent urogenital candidiasis is influenced by various factors, including the properties of yeast fungi and disturbances in vaginal microbiota. Comprehensive treatment addressing both fungal and bacterial components of dysbiosis may provide better therapeutic outcomes and reduce the recurrence of UGC. Further research is warranted to elucidate the mechanisms underlying these interactions and optimize treatment strategies.

KEYWORDS: Recurrent urogenital candidiasis, vaginal microbiocenosis, PCR diagnostics, dysbiosis, antifungal therapy.

Diseases Genital candidiasis is one of the common causes of reproductive dysfunction, affecting the quality of life of women, as well as an etiological factor in ante- and intrapartum infection of the fetus. An important role in the chronicization of candidiasis infection of the genital tract is played by a violation of the local anti-infective protection of the vagina and systemic immunity, which determines the need to develop new pathogenetically based approaches to the treatment of this pathology, taking into account concomitant urogenital infections and immune disorders.^[1,2,3]

Today, the diagnosis of candidiasis remains problematic, since determining the type of fungus and its sensitivity to antimycotics is a costly and lengthy process and takes more than 7-8 days. It is known that candidiasis occurs when the microflora is disturbed, and without logically identifying it, it is difficult to cure the infection. Studying the composition of the microbiota: determining each bacteria by bacteriological culture, firstly, is expensive and takes time (7-9 days). Treatment is also not based on data from etiopathogenetic factors, and is limited only to an antimycotic drug that has not been confirmed by the type of fungus

and sensitivity to which antimycotic, which gives an incomplete cure and subsequently relapses occur. The study of vulvovaginal candidiasis is considered relevant and timely today due to frequent relapses, the difficulty of identifying associated STIs, and difficulty in treatment. It is necessary to use therapeutic regimens that involve eliminating or weakening the influence of factors of the onset, persistence and progression of the disease. This will allow you to select the most appropriate etiotropic treatment and achieve the fastest positive result with the acceleration of reparative processes in the vaginal biotope.^[2,3,4,5] An important role in the chronicization of candidiasis infection of the genital tract is played by a violation of the local anti-infective defense of the vagina and systemic immunity, which determines the need to develop new pathogenetically based approaches to the treatment of this pathology, taking into account concomitant immune disorders.^[3,4] Meanwhile, this is of great practical interest, since the association of candidiasis with many urogenital infections is widespread and most often it is they that cause a more severe course and the development of relapses of the disease, which creates considerable suffering for patients.

It is known that in maintaining the homeostasis of the vaginal microbiota, along with the immune system, lactobacilli play an important role, which colonize the vagina and are normally the dominant microorganism in the vaginal microflora. As a result of their vital activity, lactobacilli produce various active substances (lactic acid, bacteriocins, hydrogen peroxide), which create unfavorable conditions for the development of UPM and pathogenic microorganisms.^[2,5] They also release exopolysaccharides into the extracellular environment, which promote their adhesion to the mucous membrane and ensure the stability of the mucosal layer and resistance to UPM. It is generally accepted that a decrease in the number of lactobacilli and an increase in the number of UPM are mainly associated with BV, but not with VVC.^[1,3,4] However, the results of our study showed that in 75.4% of patients with VVC it occurred against the background of vaginal dysbiosis. Moreover, we have shown that in the presence of dysbiotic disorders of the vaginal microflora, relapses of VVC occur significantly more often than with preserved normal flora. It is also impossible to exclude general genetically determined features of the immune system that reduce resistance to UPM.

An important factor in maintaining the balance of vaginal microflora and protecting the body from the development of VVC is the local immune response. Fungal spores, entering the vagina, adhere to the surface of epithelial cells and are recognized by pattern recognition receptors. This leads to the launch of intracellular signaling pathways, activation and induction of transcription of genes involved in the formation of the immune response.^[6]

Purpose of the study. Study of the microflora of the vaginal biotope in recurrent urogenital candidiasis with determination of the type of fungus and bacterial mass by PCR diagnostics.^[7]

MATERIALS AND METHODS

22 women aged from 22 to 47 years old with a diagnosis of "Chronic vulvovaginal candidiasis" were examined at the RSNPMCDVC. All patients had complaints of discharge from the genital tract, burning and itching. These patients received treatment for several years, but the treatment showed a short-term effect. In 17 patients, relapses of the disease were observed 3-4 times a year. Basically, all patients received treatment in the form of course doses of Flucanazole.

During an objective examination in a gynecological speculum: all patients had white, curd-like discharge, the vaginal walls were hyperemic and swollen.

Colposcopic examination revealed cervical erosion, acetowhite epithelium, and iodine-negative zone in 10 patients; in the remaining patients, the colposcopic picture was within normal limits.

To determine the type of fungus, PCR "Mycoso-screen" was performed. Mycoso-Screen is an analysis for identifying and typing pathogens of fungal infections of the genus *Candida*, *Malassezia*, *Saccharomyces* and *Debaryomyces* by polymerase chain reaction with detection of results in real time; semi-quantitative multiplex analysis in preparations obtained from human biological material.

RESULTS

Table-1 Mycozoscreen test – 14 species of yeast fungi quantitatively by real-time PCR.

Table -1 shows that of the 22 examined women with urogenital candidiasis, *Candida albicans* was found in the patients, *Candida glabrata* in 5, *Debaryomyces hansenii* (*C.famata*) in 2, *Pichia kudriavzevii* (*C.krusei*) in 2, *Saccharomyces cerevisiae* in 3. Data indicate that there is an increase in other yeast-like fungi of the genus *Candida non albicans*.

Since vaginal dysbiosis and a decrease in the number of lactobacilli aggravate the course of candidiasis and cause frequent relapses, all patients underwent the following examinations: to study opportunistic microflora (OPM), the use of the Femoflor-16 PCR test system for qualitative and quantitative assessment of vaginal dysbiosis. The presence of UPM and its quantity and the amount of lactobacilli in relation to the total bacterial mass (TBM) were taken into account. (table 2). The table shows that only 3 patients have normocenosis, the remaining 17 patients have the absence of lactobacilli and a violation of the vaginal microbiocenosis with the identification of certain bacteria.

bacterial mass (BMW). [Table 2]. The table shows that only 3 patients have normocenosis, the remaining 17 patients have the absence of lactobacilli and a violation of the vaginal microbiocenosis with the identification of certain bacteria.

Groups of microorganisms are divided into the following types:

1. Facultative anaerobic microorganisms:
2. Obligate anaerobic microorganisms
3. Yeast-like fungi *Candida* spp.
4. *Mycoplasma* *Mycoplasma hominis* *Ureaplasma* (*urealyticum* + *parvum*)
5. Pathogenic microorganisms: *Mycoplasma genitalium*

Table-1 Mycozscreen test – 14 species of yeast fungi quantitatively by real-time PCR.

		Patients n=22
1	<i>Meyerozyma guilliermondii</i> (C. guilliermondii)	
2	<i>Candida albicans</i>	7 (36%)
3	<i>Candida tropicalis</i>	
4	<i>Debaryomyces hansenii</i> (C. famata)	2 (12%)
5	<i>Candida glabrata</i>	5 (32%)
6	<i>Kluyveromyces marxianus</i> (C. kefyr)	
7	<i>Pichia kudriavzevii</i> (C. krusei)	2 (12%)
8	<i>Candida auris</i>	
9	<i>Clavispora lusitanae</i> (Candida lusitanae)	
10	<i>Candida dubliniensis</i>	
11	<i>Candida parapsilosis</i>	
12	<i>Saccharomyces cerevisiae</i>	3 (12%)
13	<i>Malassezia</i> spp.	
14	<i>Malassezia furfur</i>	

Table 2: Femoflor-16

Group	indicators	Patients n=25
Diagnosis of normocenosis	<i>Lactobacillus</i> spp.	<N y 17 (80%) Не выявлено у 5 (20%)
Aerobic microorganisms	<i>Enterobacteriaceae</i>	20 (80%)
	<i>Streptococcus</i> spp.	22 (88%)
	<i>Staphylococcus</i> spp.	19 (76%)
Anaerobic microorganisms	<i>Gardnerella vaginalis</i> / <i>Prevotella bivia</i> / <i>Porphyromonas</i> spp.	16 (64%)
	<i>Eubacterium</i> spp.	12 (48%)
	<i>Sneathia</i> spp./ <i>Leptotrichia</i> spp./ <i>Fusobacterium</i> spp.	9 (36%)
	<i>Megasphaera</i> spp./ <i>Veillonella</i> spp./ <i>Dialister</i> spp.	8 (32%)
	<i>Lachnobacterium</i> spp./ <i>Clostridium</i> spp.	5 (20%)
	<i>Mobiluncus</i> spp./ <i>Corynebacterium</i> spp.	8 (32%)
	<i>Peptostreptococcus</i> spp.	7 (28%)
	<i>Atopobium vaginae</i>	11 (44%)
Microplasm	<i>Mycoplasma genitalium</i>	Не выявлено
	<i>Mycoplasma hominis</i>	7 (28%)
	<i>Ureaplasma</i> spp.	11 (44%)
Yeast-like fungi	<i>Candida</i> spp.	11 (44%)

CONCLUSION

Thus, the development of vulvovaginal candidiasis is a multifactorial process in which both the properties of yeast fungi and various disorders of the vaginal microflora play a certain role, which contribute to the development of the inflammatory process and the recurrence of UGC, which creates considerable discomfort for patients, and accordingly requires further more detailed and in-depth studies of this pathology, taking into account disturbances in the microflora and local immunity of the vaginal biotope. It follows from this that in order to achieve a better therapeutic effect, treatment of UGC, which develops against the background of a disorder of the vaginal microflora, should be comprehensive, aimed not only at fungal, but also at bacterial opportunistic microflora, which can provide a better therapeutic effect and prevent relapses of the disease. Subsequently, the use of antifungal therapy in combination with complex broad-spectrum drugs aimed at eliminating dysbiotic disorders of the vaginal microflora helps to normalize the vaginal microbiota, subsequently leading to a significant reduction in relapses of UG in the women studied.

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