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**A NEW SOLUTION TO THE PROBLEM OF RECURRENT UROGENITAL
CANDIDIASIS.**

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Abstract

AIM: We monitored 20 patients with recurrent urogenital candidiasis who received topical application of activated silica solution for rapid disease progression and prevention of recurrences. The purpose of our study is to improve the effectiveness of the treatment of urogenital candidiasis and reduce the number of relapses, given the local immune response. The problem is solved by the fact that in the developed method of treatment, which includes a comprehensive therapy (antimycotic drugs, vitamins, anti-inflammatory therapy), in addition locally in the form of sanations - vaginal irrigation is used activated silica solution.

Keywords: recurrent urogenital candidiasis, activated silica solution, local immune response, yeast-like fungi.

抽象的

目的：我们监测了 20 名复发性泌尿生殖道念珠菌病患者，这些患者接受了局部应用活化二氧化硅溶液以快速疾病进展和预防复发。鉴于局部免疫反应，我们研究的目的是提高泌尿生殖道念珠菌病治疗的有效性并减少复发次数。该问题通过以下事实解决：在已开发的治疗方法中，包括综合疗法（抗真菌药物、维生素、抗炎疗法），此外在局部以卫生的形式 - 阴道冲洗使用活性二氧化硅溶液。

关键词：复发性泌尿生殖道念珠菌病，活性二氧化硅溶液，局部免疫反应，酵母样真菌。

Introduction

The problem of urogenital candidiasis is one of the most urgent and complicated in the practice of modern dermatovenereologists. Its high social significance is due to its wide prevalence, especially among women of reproductive age, and its tendency to recurrent course, which worsens the quality of life of patients. Urogenital candidiasis is the second most common disease of the female genital system after bacterial vaginosis [1]. Worldwide, about 10 million women visit gynecologists every year for vaginitis [1,2]. Many studies [3,4] report that three-quarters of these women (75%) have already experienced an episode of urogenital candidiasis, at least 50% of them will have a second episode, and 5-10% of all women have recurrent urogenital candidiasis, that is, ≥ 4 episodes of urogenital candidiasis per year.

The aim of our study is to improve the effectiveness of the treatment of urogenital candidiasis and reduce the number of relapses, given the local immune response, which responds more intensively to excessive growth of opportunistic microflora than to fungal infection, which may be due to the ability of fungi to suppress local immune defense or other factors that lead to the formation of an incomplete immune response in recurrent urogenital candidiasis.

Materials And Methods

The problem is solved by the fact that in the developed method of treatment of recurrent urogenital candidiasis, including comprehensive therapy (antimycotic drugs, vitamins, anti-inflammatory therapy), in addition locally in the form of sanations - vaginal douches, activated silica solution - 150 ml "Fatiderm" - once a day

for 7 days is used. Fatiderm - organic mineral water, consisting of complexes of siliceous minerals of Uzbekistan SiO₂ (36mg/l), Na (319mg/l), K (13mg/l), Ca (28 mg/l), Fe (0.3 mg/l), Co (0.0002 mg/l), Ni (0.002 mg/l, as well as Au, Tb, Sm, Dy, Gd, Er, Ho, Tm. pH -7.9. Activated silica solution activates regeneration processes of skin cells, mucous membranes, has anti-inflammatory effect, inhibits the growth of conditionally pathogenic microorganisms (Staphylococcus spp. E. Coli, Candida spp), restores pH. Microelements contained in the solution affect local immunity, increasing resistance to various pathogens.

According to Costernon J. W. (1995) most of the above-mentioned infections occur with biofilm formation. Gintsburg A.L., Ilyina T.S. et al. (2003) revealed the role of trace elements, especially iron, copper, potassium, magnesium in metabolic processes that affect biofilm formation. These trace elements are involved in the activation of oxidative processes, enzyme systems, and energy production occurring in mitochondria [5,6].

Due to biofilms, microorganisms increase their resistance by 50-500 times to the action of disinfectants, antibacterial agents, bacteriophages, antibodies and phagocytes. This phenomenon on the part of microorganisms is the main etiopathogenetic factor of chronicity and frequent recurrence of the disease, which in turn leads to antibacterial resistance [7]. A study by Helen Knight (2015) at the Massachusetts Institute of Technology found that chelating proteins in the neutrophils of the human immune system play an important role in fighting infections. One of the main representatives of the protein fraction is calprotectin protein, which binds zinc, manganese and iron ions, thereby inhibiting the spread of both bacteria and infectious fungi. Experimental studies have established that

the protein does deplete iron from the medium, and that the presence of excess calcium in the medium leads to a much greater depletion of iron, which stops bacterial growth. Using radioactive isotopes, it has been shown that the protein indeed prevents microbes from absorbing the coveted trace element [2,5,7].

Results

20 patients with recurrent urogenital candidiasis were examined. Smears of all patients showed increased leukocytosis, fungi, and key cells (bacterial vaginosis) in 11 of them. *Candida albicans* was detected in 12 patients and *Candida tropicalis* in 8 patients.

All patients complained of vaginal discharge of a curd-like nature, itching and burning. All patients had relapses of the disease 3-4 times a year.

All 20 patients underwent vaginal sanitation-springing procedures with the activated flint solution "Fatiderm" - 150 ml for 7 days once a day. Using a gynecological mirror, a bath with

activated silica solution "Fatiderm" - 150 ml with a single dose - 20.0 ml, and then the solution was held for 5 minutes, then washed off and dried with a cotton tampon. The course of local douches was only 7 days.

Fifteen patients with urogenital candidiasis formed a control group. Betadine or Citeal solution was used. In this contingent of patients, subjective and objective manifestations disappeared on day 5-6 of treatment.

Two patients in this category of patients had fungi detected in smears after treatment, *Candida albicans* in culture, and all patients had recurrences of the disease.

The dynamics of clinical observation showed that on the 3rd day of treatment there was a reduction of discharge, itching, inflammatory manifestations (edema, redness) disappeared. After sanitation on the 7th day of treatment, bacteriological examination did not reveal fungi and key cells in smears and bacteriological culture, the number of leukocytes decreased markedly.

Table 1. Comparative clinical characteristics of topical treatment of urogenital candidiasis with aqueous silica solution "Fatiderm" (in days)

Patient group	Reducing hyperemia	No white plaque On the vaginal mucosa	Reducing inflammation on the vaginal mucosa	The disappearance of the itching
Main group of patients with recurrent urogenital candidiasis N=20	2,7+0,4*	1,8+0,5*	2,5+0,5*	2,8+0,5*
Control group Patients with recurrent urogenital candidiasis N=15	4,2+0,3	3,3+0,4	4,1+0,5	3,3+0,4

- reliability index in relation to the indicators of the control group (P < 0.05)

Indicators	Absence of Candida fungi	Absence of Gardnerella vaginalis	Absence of St. aureus	Absence of Ureaplasma urealitycum
Main group of patients with R recurrent urogenital candidiasis N=20	6,2	5,2	7,2	10,1
Control group Patients with recurrent urogenital candidiasis N=15	7,2	7,2	9,2	12,1

Table 2. Comparative characteristics of laboratory examination of smears and bacterial culture of recurrent urogenital candidiasis against the background of local treatment (in days)

The follow-up results showed that the patients did not reapply within 1 year, since no recurrence of the disease was observed.

As a result of treatment: decreased discharge, eliminated itching, inflammatory manifestations (swelling, redness) within 7 days, pain and burning stops, in bacteriological studies there is a decrease in white blood cell count, disappearance of key cells, activated local immunity, thus eliminating recurrent relapses, accelerated regeneration processes, normalization of the vaginal microflora.

Discussion

The traditional way of treating vulvovaginal candidiasis according to the recommendations of American experts is known, in which patients with recurrent course of the disease are prescribed fluconazole 150 mg orally every 72 hours three times, and then as a maintenance therapy fluconazole is prescribed once a week 150 mg for 6 months. This treatment regimen has proven to be effective in 90% of cases, but relapses still occur in patients, which may be explained by the presence of fluconazole-

resistant *C.albicans*, as well as a wider spread of *C.non-albicans* to date [8,9,10,11,12].

Other oral antimycotic regimens are also known, such as ketoconazole 100 mg orally once daily, itraconazole 200mg twice daily once a week, but administration of these drugs is limited due to their high hepatotoxicity.

However, using only systemic drugs in recurrent urogenital candidiasis treatment is insufficient and is followed by relapses in 70% of cases in 6 months after the completed course of treatment, and in 40-50% of cases in 12 months after the complete course of systemic therapy. Therefore, the solution to this problem should be approached in a comprehensive manner, taking into account the fact that in women with recurrent urogenital candidiasis dysbiotic disorders of the vaginal microflora are observed, as well as the marked changes in the local immune system of the urogenital tract mucosa [13,14,15,16,17,18].

There are various methods of local treatment of recurrent urogenital candidiasis, which, apart from the traditional prescription of systemic drugs, use the following: clotrimazole in the form of 500mg suppositories once a week

or 200mg twice a week; up to 70% of the cure rate in the presence of *C.glabrata* resistant to azole antimycotics has been observed after using gelatin capsules with boric acid vaginally in a dose of 600mg every 14 days. Another alternative is topical administration of 17% flucytosin cream for 14 days, which has also proven effective against *C.non-albicans*, but this method is limited in use because of its high cost [19,20,21,22].

The disadvantage of this method is that the local application of only antifungal drugs does not eliminate the frequent relapses of the disease, because it does not affect the local immunity. Also the accompanying vaginal microflora is not normalized, which is a key link, because the disturbed microflora aggravates the course of vulvovaginal candidiasis. This method can only temporarily alleviate the condition of patients for a short time, after this method of treatment the complaints are renewed.

There is also known a complex method of recurrent urogenital candidiasis treatment, in which the etiotropic therapy with systemic fluconazole (50 mg once a day for 7 days) and topical immunomodulatory therapy with interleukin 2 - Roncoleukin (in two points into the anterior abdominal wall, taking into account the lymph outflow - 0.5 ml three times with an interval of 72 hours) were used [23,24,25].

But even this method was accompanied by subsequent relapses and, despite the treatment, microbiological examination in a number of patients revealed the same strain of candidiasis as before the treatment - *C.glabrata*. Also, this method is invasive and traumatic, and many patients refuse this therapy.

Conclusion

Thus, the development of recurrent urogenital candidiasis is a multifactorial process in which both the properties of yeast fungi and various disorders of the vaginal microflora play a role, contributing to the development of inflammatory process and recurrence of urogenital candidiasis, which creates considerable discomfort to patients, and therefore requires further more detailed and in-depth study of this pathology with regard to violations in the microflora and local immunity of the vaginal biotope. It follows that to achieve the best therapeutic effect, the treatment of recurrent urogenital candidiasis, which develops against the background of vaginal microflora disorders, should be comprehensive, aimed not only at fungal, but also at the bacterial opportunistic microflora, which can provide the best therapeutic effect and prevent recurrence of the disease.

The results of numerous studies indicate that an in-depth examination of patients with recurrent urogenital candidiasis, aimed not only at the detection of fungi, but also at the assessment of the state of the bacterial flora, is necessary. The application of an activated silica solution locally in combination with complex broad-spectrum drugs aimed at eliminating dysbiotic disorders of the vaginal microflora contributes to the normalization of the vaginal microbiota, as well as a significant reduction in the recurrence of urogenital candidiasis in the examined women. This complex application of the local method of treatment ensures the creation of a highly effective minimally invasive method for the treatment of vulvovaginal candidiasis, the complete cure of the disease, which is not accompanied by side effects, allows to reduce the treatment period, eliminates

recurrent relapses and provides for outpatient treatment.

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