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CURRENT INDICATORS OF ANTIFUNGAL RESISTANCE OF CANDIDA SPECIES

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Annotation:

The article presents the results of the evaluation of modern sensitivity indicators to antifungal preparations in 1052 strains of *Candida* species isolated from patients with urogenital candidiasis in the period from 2010 to 2015. Pathogen culture identified was examined to determine the sensitivity to amphotericin B, 5-fluorocytosine, fluconazole, itraconazole, ketoconazole, and miconazole. At present, along with a predominance of *Candida albicans*, the etiological range of causative agents of urogenital candidiasis is characterized by an increasing proportion of non-*albicans* species (*Candida glabrata*, *Candida krusei*, *Candida parapsilosis*). Heterogeneous specific structure of the disease and increase in resistance rates of *Candida* to commonly used azole antifungals (fluconazole, itraconazole, miconazole) necessitate permanent monitoring of the sensitivity of infectious agents to antifungals and optimizing treatment regimens based on these indicators.

Keywords: urogenital candidiasis, *Candida* species, antifungal drugs, itraconazole, fluconazole, miconazole, resistance.

Introduction:

As recommended World Health Organization wounds since 1999 urogenital candidiasis (UGK) is excluded from the list sexually transmitted diseases way, in connection with which the official UGC incidence rates in

There are no Russian Federation. At the same time, according to various authors, frequency of detection of case- teas for candidal vulvovaginitis (KVV) has doubled over the past 10 years, amounting to from 30 to 45% in the structure infectious-inflammatory times disorders of the lower genitourinary tract systems of women [1, 2]. Most high incidence rate candidiasis is registered in women levels between the ages of 20 and 40 and decreases in menopausal women



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period. It is known that candidiasis can cause about 20 species of fungi of the genus *Candida*. From 85 to 90% of yeast strains chewing mushrooms isolated from moisture worms, belong to *Candida albicans*, among non-*albicans* species most often. *Candida glabrata* occurs (5–10%), the next most frequently detected. Among the pathogens of UGK are *Candida tropicalis*, *Candida krusei*, *Candida parapsilosis* and *Saccharomyces cerevisiae*. *Candida* is isolated much less frequently kefir, *Candida guilliermondi*, even less commonly – other types, but virtually any *Candida* species may be the cause of vulvovaginitis [3–5].

Non-*albicans* species are capable of causing according to the majority, research dovatorov, clinically similar to *C. albicans* vaginitis, for which characterized by resistance to traditional on the drug therapy used - azole series miForeign authors include UGK caused by non-*albicans*- species, so-called complicated vulvovaginitis, making up approximately but 10% of cases of this disease. For complicated CVC it is typical more severe course and recurrent general nature of the disease.

The main goal of therapy for VVV is the elimination of etiological and pathogenetic prerequisites for the emergence of an infectious process. However, despite significant the role of various predisposing factors in the development of UGK, leading direction in the treatment of the disease still remains in use

introduction of antimycotic drugs. Currently in the arsenal of doctors there are a lot of highly effective funds for systemic and local treatment of VVV, the main ones of which are for more than 20 years the drugs have been azole groups (imidazole derivatives) *1a* and triazole). Dosage forms for treatment CVVs are represented by vaginal creams, suppositories and tablets. For treatment of the primary episode of disease *Levania* there is a wide choice highly effective local action drugs recommended suitable for use once or in within a few days. Results randomized clinical studies have demonstrated that intravaginal use imidazoles reduces the proportion of episodes diseases compared to placebo. Drugs are administered once per day, mainly at night, to ensure maximum body vaginal presence medicine. Some drugs (clotrimazole, miconazole) are produced in various concentrations, which is reflected in the duration course of treatment. As a rule, the long the effectiveness of topical therapy means varies from 1 to 7 days. Statistically significant differences in the effectiveness of treatment depending on depending on the duration of use, according to the results of various studies not established. Drugs



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are characterized by high proficiency and safety. It is known that 3–10% of the drug at local use comes from vagina into the systemic circulation.

In experiments on rodents there was embryotoxicity of imidazoles, but in humans the harmful age effects of azoles on the fetus when intravaginal use established but there was no [8]. Along with topical means for the treatment of VVV are used - There are systemic drugs (fluconazole, itraconazole), recommended caused by chronic relapses raging forms of the disease. Given type of suppressive therapy is presupposed avoids the use of antimycotic funds lasting up to 6 months. The peculiarity of these drugs is ease of use, which significantly increases the adherence to treatment. Oral use ofazole drugs some are also justified, in the opinion some authors, by necessity sanitation of extragenital areas gov infection. In particular, in work Z.F. Belikova noted the combination prevention of urogenital candidiasis with mycotic lesion of the cavity mouth, perianal area, groin femoral folds, disbacteriological intestinal zoom. According to the author, in 56.1% of examined patients with clinical manifestations of VVV gastrointestinal disturbances were observed th microocenosis with the release of gri- Candida bacteria in the amount of 104 CFU/ml and higher. In modern conditions it is impossible but ignore the heterogeneous feeling the validity of various types of mushrooms Bov Candida to a number of antimycotic drugs. Presence of non-albicans strains of Candida and other opportunistic nistic fungi serves as an important factor influencing the choice of schemes therapy and representing the main difficulty for empirical strategy therapy and prevention of VVV. The purpose of this study became the study of modern displays sensitivity factors of fungi of the genus Candida to antimycotic drugs Material and methods Sensitivity analysis was carried out resistance to antimycotic drugs there are 1052 strains of fungi of the genus Candida, isolated from patients with UGC during the period from 2010 to 2015: 92 strains – in 2010, 216 – in 2011, 223 – in 2012, 219 – in 2013, 198 – in 2014 and 104 strains – in 2015 Cultural species identification identification of Candida spp. was carried out with using selective media Candiselect (BIO-RAD, France). Identified culture diator was studied to determine sensitivity to antimycotic drugs. For this purpose, use micropanel 60 780 fungtest was installed,

where it was studied by dilution method sensitivity of fungi to 6 antimycotic drugs: amphotericin B, 5-fluorocytosine, fluconazole, itraconazole, ketoconazole, miconazole in two different concentrations Research results During the entire study period



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dominance of the dominant fungal species genus *Candida* among isolates isolated collected from patients with UGC, it turned out *C. albicans*, the frequency of detection of which the swarm was 90.2% in 2010, in 2011 – 87.0%, in 2012 – 86.1%, in 2013 – 86.3%, in 2014 – 85.8%, in 2015 – 85.6% (Table 2). However, it attracted attention increasing proportion of non-*albicans* strains *Candida* in the structure of the UGC for research period from 9.8% in 2010 to 14.4% in 2014–2015 Among non-*albicans* species *Candida* during 2010–2015 *C. glabrata* was most frequently isolated (5.6–6.8%), less often – *C. krusei* (2.3–5.6%) and *C. parapsilosis* (1.4–3.0%). The sensitivity of the selected iso- mushroom lats to antimycotic pre- parathas for the time periods studied are presented. According to the data received, on throughout 2010–2015 not marked resistance of the isolated strains to 5-fluorocytosine and amphotericin B, which is largely due to lack of application of pre-paratov in the treatment of urogenital candidiasis. Regarding ketoconazole, which is also not included in domestic and foreign recommendations on conduct-study of patients with UGC, 100% were observed high sensitivity of the isolated iso-lyatov *C. glabrata*, *C. krusei*, *C. parapsilosis* and low level of stability *C. albicans* without a pronounced trend to the dynamics of the v indicator (0–7.3%). Fluconazole and miconazole are some of the the most commonly used drugs com in the therapy of VVV. In the process of real The current study found that the sensitivity level is allocated strains of *C. albicans* to fluconaselu decreased during the study period from 100 to 83.1%, to miconazole – from 98.8 to 79.8%. There was also a decrease indicators of sensitivity to fluconazole of another UGK pathogen –*C. glabrata*: from 100 in 2010 to 85.7% in 2015 However, throughout the study period was not allocated no resistant strains of *C. Krusei* and *C. parapsilosis* to these drugs. The highest level of resistance stent *Candida* has been registered to itraconazole, while observing there was an increase in the number of insensitivities body isolates from all types of fungi from 2010 to 2015. Thus, the number of strains *C. albicans*, not sensitive to itraconazole, during the study period the increase grew from 14.5 to 55.3%, *C. glabrata* – from 66.7 to 100%, *C. krusei* – from 0 to 20%, *C. parapsilosis* – from 0 to 33.3%.

Conclusions

At the present stage, etiologicalical spectrum of urogenic pathogens total candidiasis along with the predominant incense of *C. albicans* is characterized by



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increasing proportion of non-albicans species (*C. glabrata*, *C. krusei*, *C. parapsilosis*). Heterogeneous species structure of the levania and increase in indicators resistance of fungi of the genus *Candida* widely used in therapyazole drugs (flucon-ash, itraconazole, miconazole) equipment express the need for constant sensitivity monitoring infectious agents to antimycotic technical means and circuit optimization therapy taking into account these indicators.

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