



COMBINED IMMUNOTHERAPY IN THE TREATMENT OF CANDIDASIAN INFECTIONS OF THE URINARY ORGANS

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Abstract: *Candidiasis is an infectious disease of the skin and mucous membranes caused by Candida species, most commonly Candida albicans. The infection can affect any part of the skin, and most often the process is localized in the skin folds, interdigital folds, in the genital area, nail cuticles and on the oral mucosa*

Key words: *t-cell mediated immunity, dermatovenereology, candida endocrinopathy syndrome*

Introduction

Candidiasis most commonly occurs in intertriginous areas such as the axillae, groin and gluteal folds (eg, diaper rash), interdigital folds, glans penis, and sub mammary folds. Vulvovaginal candidiasis is common among women. After improperly done manicure, dishwashers and people who often work with their hands in water can develop candidal lesions of the nail plates and [paronychia](#) ([Onychomycosis](#)). In obese patients, Candida infection may occur in the pannus (in the folds of the abdomen).

Oropharyngeal candidiasis is a common symptom of local or systemic immunosuppression. In chronic mucocutaneous candidiasis, the nails, skin, and oropharynx are usually affected. Patients have no skin defenses against *Candida* , *no proliferative response to Candida* antigen (but retain a normal proliferative response to mitogens), and a normal antibody response to *Candida antigens* and other antigens. They also have impaired T-cell mediated immunity.



Chronic mucocutaneous candidiasis can develop as an autosomal recessive disease associated with hypoparathyroidism and Addison's disease (*Candida* endocrinopathy syndrome). Symptoms of candidiasis in men and women are different. Candidiasis or thrush is an extremely unpleasant fungal disease that often appears on the genital mucosa and indicates the fact of reduced human immunity.

Candidiasis, otherwise known as "mucosal thrush", mainly appears as isolated or continuous patches of white plaque. Places that are affected by thrush are usually painless, however, with the formation of cracks or hardening of the plaque, mild pain may appear. With the development of candidiasis, redness, skin maceration, itching in and around the anus appear.

An urgent task of dermatovenereology will always be the search and development of new methods of therapy for patients with various urogenital infections. This search is carried out in two directions - the creation and improvement of traditional antimicrobial, antifungal, antiviral drugs or the development of fundamentally new drugs with a combined etiopathogenetic effect. These drugs include new immunomodulators " Gepon" and "Immunomax".

Purpose of the study: In our study, we tried to study the clinical efficacy and safety of using the combination of Gepon with Immunomax for the treatment of patients with one of the most common and frequently recurrent infections of the skin and mucous membranes, an infection caused by fungi of the genus *Candida* .

Materials and Methods: The study included 50 patients aged 25 to 40 years, of whom there were 30 women and 20 men. The inclusion criteria for the study were: the presence of clinical manifestations of the skin and mucous membranes caused by fungi of the genus *Candida* ; unsuccessful treatment of these infections with other drugs; microscopic (bacteriological) confirmation of *Candida* infection .

Diseases	Number of patients
Vulvovaginal candidiasis	30
<i>Candida</i> balanoposthitis	4
Candidal balanoposthitis in combination with candidal urethritis	6
Candidal balanoposthitis in combination with candidal lesions of the oral mucosa	4
<i>Candida</i> urethritis	4
Candidal paronychia	2
TOTAL	50

The duration of the disease varied from 2 weeks to 6 years.

The clinical structure of morbidity is presented in Table 1.



In their manifestations, candidal lesions had a classic clinical picture. The main complaints of women were itching and discharge from the genital tract; men - itching, burning, discomfort in the glans penis and urethra. During a clinical examination, all women revealed hyperemia and swelling of the mucous membranes of the genital tract, the presence of abundant milky or curdled discharge in the vagina; in men, redness of the mucous membrane of the glans penis (14 people) and the presence of a whitish plaque (12 people), redness of the urethral sponges and the presence of mucous secretions (10 people), hyperemia, swelling of the mucous membrane and the presence of curdled plaque on the tongue and corners of the mouth (4 people), the presence of redness, erosion and peeling on the skin of the nail folds of the fingers (2 people). Previous therapy was carried out in all 50 patients and included both local (nystatin, clotrimazole, nizoral, pimafulcin, pevaril) and general treatment (nystatin, nizoral, pimafulcin, orungal, lamisil). The method of using the drug in women consisted in irrigation with a 0.04% solution of Gepon of the mucous membrane of the vulva and vagina; in men in the form of lotions of 0.04 % Gepon solution for lesions of the mucous membranes of the glans penis and oral cavity and instillations into the urethra for urethritis. The procedures were performed 1 time per day with an interval of 1-3 days, 5 procedures per course. In addition to the above-mentioned use of Gepon, all patients were recommended to take Immunomax intramuscularly at a dose of 200 IU once a day. The course of treatment is 6 injections on days 1, 2, 3, 8, 9, 10 of treatment.

Results and discussion : When examining patients after treatment, a pronounced effect of the drug on the clinical condition of patients was noted. The disappearance of signs of inflammation, observed already after the first procedures, was achieved in practice in which very strong inflammatory phenomena were observed before treatment, and slight hyperemia of the mucous membranes remained after treatment (clinical efficiency - 88%). Such a pronounced clinical anti-inflammatory effect was accompanied by positive dynamics of microscopic studies. Immediately after treatment, the disappearance of spores and mycelium of fungi of the genus *Candida* from the urogenital tract and other mucous membranes was noted in 22 women and 18 men (microbiological efficiency - 80%). In 2 men, a small amount of fungal spores was found in the material from the mucous membrane from the urethra, in 8 women, a small amount of spores and mycelium of fungi were also found in the material from the vagina and cervical canal. The obtained positive changes were quite stable when examining patients 1 month after treatment, recurrence of candidiasis was detected only in one patient. In 2 patients, in whom, after the first examination, despite the clinical cure, mycelium and fungal spores were found, microscopic examination after 1 month revealed their disappearance. Thus, the final indicator of clinical and etiological efficacy was 84%. There were no side effects in any of the studied patients. Immunomax enhances immunological defense mechanisms in infections caused by viruses (human papillomavirus, herpes simplex virus, parvovirus, canine distemper virus) or bacteria (*E. coli*, salmonella, staphylococcus, chlamydia, mycoplasma, ureaplasma). This effect of the drug is manifested in adults and newborns with the introduction of Immunomax in various ways: intramuscularly, intraperitoneally, orally . .

The active component of the drug "Gepon" (HEPON) is a synthetic tetradecapeptide of the formula: Thr - Glu - Lys - Lys - Arg - Arg - Glu - Thr - Yal - Glu - Arg - Glu - Lys - Glu . The drug "Gepon" - lyophilized powder of 1.2 or 10 mg in vials is produced by LLC IMMAFARMA (Russia), contains, respectively, 1.2 or 10 mg of the indicated synthetic tetradecapeptide, does not



contain other components. The drug is registered by the Ministry of Health of Russia (registration certificate R No. 000015 / 01-2000 dated 12.07.2000, FSP 42-0012-0015-00). Instructions for the medical use of the drug Gepon approved by the decision of the Pharmacological Committee of the Ministry of Health of the Russian Federation (Minutes No. 8 dated October 7, 1999 г). The drug belongs to the group of immunomodulators, is indicated to increase the effectiveness of immune protection against infections, treatment and prevention of opportunistic infections caused by bacteria, viruses or fungi. The drug "Gepon" has interferon-inducing activity, induces the synthesis of alpha and beta interferons in a wide range of doses. The impact of Gepon on lymphocytes does not cause polyclonal activation of divisions, activation of CD69 and polyclonal synthesis of cytokines. The effect of the drug on lymphoid cells consists in the induction of receptors for cytokines (in particular, for IL 2), in a pronounced increase in the response to other activation signals.

Gepon induces the production of MIF-cytokines and L-selectins by T-cells, which enhance the activity of granulocytes and cause selective chemotaxis of macrophages. Oral administration of the drug causes normalization of the content of CD 4+, CD 8+-lymphocytes, as well as NK-cells, increases the content of activated T-lymphocytes and neutrophilic granulocytes, enhances the production of IgG antibodies to confection agents relevant to this patient. During the first phases of clinical trials of Gepon in patients with severe immunodeficiency, it was found that repeated use of Gepon not only optimizes the immune status, but also has a therapeutic effect on nasopharyngeal infections caused by fungi of the genus *Candida* and other opportunistic microorganisms. The developers of the drug suggested a local effect of Gepon. These data are from post-registration clinical trials. As a result of the study, we have expanded the medical indications for the use of Gepon and developed a new method of its use. The priority in the treatment of candidiasis is the rapid relief of clinical symptoms that significantly reduce the quality of life of patients. In this regard, the pronounced effect of the drug on the clinical condition of patients draws attention.

Almost all patients observed a rapid subsidence of inflammation in the urogenital tract. Perhaps this is due to the inhibition of the production of proteinases by fungi, which are one of the leading components of inflammation. When evaluating microscopic data before and after treatment, we drew attention to a decrease in the number of leukocytes in smears from the urethra, vagina and cervical canal, the disappearance of spores and mycelium of *Candida* fungi in 84% of patients. Detection in 5 patients immediately after treatment of a small amount of spores and mycelium of the fungus, which we regarded as a negative result, in fact, is not such. Firstly, because *Candida* belongs to the opportunistic microflora, and, therefore, simply finding it in the material from the urogenital tract in the absence of clinical symptoms cannot always be regarded as a disease. Secondly, in 2 patients, during a repeated control study, fungi were not detected by microscopy.

The obtained positive results turned out to be quite stable: when observing patients for 2-3 months, a relapse of the disease, accompanied by clinical symptoms, was observed only in 1 patient. When conducting therapy, it is very important to take into account the localization of the infectious process. So, for example, in the treatment of women, it is necessary to take into account the possibility of a candidal process in the intestines and the likelihood of penetration of pathogenic strains of *Candida* from the rectum into the genital tract, which may affect the effectiveness of local therapy. In the treatment of balanitis and balanoposthitis in men, it is necessary to remember the



possible localization of the infection in the urethra, which can be eliminated by adding Gepon instillations into the urethra. The proposed scheme for the use of the drug is conditional. Each doctor, based on the experience of practical application of Gepon, and also depending on the activity of the clinical manifestations of the disease, can change the intervals between procedures and increase their number (more than three).

Of course, during treatment and for the period of follow-up, patients should use barrier contraceptives during sexual intercourse. In order to prevent recurrence, the doctor should give detailed recommendations on the prevention of candidiasis and advice on personal hygiene.

Conclusions: Thus, the indicated effects of Gepon and Immunomax on the immune system as a whole lead to a significant increase in the body's immune defense against infections. A drug Immunomax, when combined with Gepon in the form of topical application of a 0.04% solution, has a pronounced clinical anti-inflammatory effect, allows achieving a clinical and etiological cure in 96% of patients with urogenital candidiasis. The drug can be recommended for the local treatment of infections of the skin and mucous membranes caused by fungi of the genus *Candida*, as well as for the prevention of these infections. Given the high clinical and etiological efficacy of Gepon and Immunomax in patients with candidiasis that has already developed, it can be assumed that the drug will also be effective in the prevention of this disease, in particular, when prescribing antibiotics.

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