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DISTINCTIVE ASPECTS OF CANDIDAL STOMATITIS TREATMENT IN THE PRESENCE OF CONCURRENT MEDICAL CONDITIONS

Purpose of the study. To study the effectiveness of the treatment complex, which includes CANDIVAC in patients with manifestations of candidal lesions of the oral mucosa with a recurrent course on the back of chronic viral hepatitis B in the replication phase. **Research methods.** Patients with chronic viral hepatitis B (CHBV) in the replication phase, who were diagnosed microscopically and through laboratory tests with 4 cases of candidal stomatitis over the past 12 months, were subject to observation. The diagnosis of recurrent candidal stomatitis was substantiated on the basis of clinical manifestations and microscopic and bacteriological examination of pathological material from the lesion. The effectiveness of therapy was monitored immediately before the appointment of CANDIVAC and 21 days after the start of treatment, and was also repeated in 9 and 12 months. **Scientific novelty.** The dynamics of subjective complaints and microbiological studies showed positive changes during treatment, namely: already after 21 days of treatment, 64 % of the examined patients noted the disappearance of the symptoms of the disease, and there was also no pathogen in smears from the oral cavity and in the intestine. It is worth noting that in persons with CVHB, in whom the replication phase lasted no more than 2 years, a more pronounced effect of the treatment complex was recorded. Analysis of the effectiveness of medical examinations 9 and 12 months after the introduction of CANDIVAC showed a significant improvement in the assessment of subjective complaints and microbiological parameters. At the same time, in patients with CVHB who had a replication phase of more than 5 years, the reduction of contamination of the oral and intestinal mucosa was less effective. **Conclusions.** The data obtained indicate a favorable effect of CANDIVAC in the complex treatment of the recurrent course of candidal stomatitis, which led to a statistically significant decrease in the frequency of relapses and the intensity of patients' subjective complaints.

Key words: recurrent candidal stomatitis, chronic viral hepatitis B, treatment, CANDIVAC.

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ОСОБЛИВОСТІ ЛІКУВАННЯ КАНДИДОЗНОГО СТОМАТИТУ НА ТЛІ СОМАТИЧНОЇ ПАТОЛОГІЇ

Мета дослідження. Вивчення ефективності лікувального комплексу до складу якого входить CANDIVAC у хворих з проявами кандидозного ураження СОПР з рецидивуючим перебігом на тлі хронічного вірусного гепатиту В в фазі реплікації. **Методи дослідження.** Спостереженню підлягали хворі на хронічний вірусний гепатит В (ХВГВ) в фазі реплікації, у яких було діагностовано мікроскопічно та лабораторно 4 випадки кандидозного стоматиту впродовж останніх 12 місяців. Встановлення діагнозу рецидивуючого перебігу кандидозного стоматиту обґрунтовували на підставі клінічних проявів, шляхом мікроскопічного та бактеріологічного дослідження патологічного матеріалу з вогнища ураження. Контроль ефективності терапії проводилось безпосередньо перед призначенням CANDIVAC в складі комплексної терапії та через 21 день після початку лікування, а також повторювалось у віддалені строки 9 та 12 місяців. **Наукова новизна.** Динаміка суб'єктивних скарг та мікробіологічного дослідження показала позитивні зміни в перебігу лікування, а саме: уже через 21 день лікування у 64 % обстежених відзначалось зникнення симптомів захворювання, а також спостерігалась відсутність збудника інфекції в мазках зі СО рота та в кишечнику. Звертає увагу той факт, що у осіб з ХВГВ в яких фаза реплікації продовжувалась не більше 2 років реєструвався більш ефективний вплив лікувального комплексу. Аналіз ефективності диспансеризації через 9 та 12 місяців після введення CANDIVAC показав значне покращення в оцінці суб'єктивних скарг та мікробіологічних показників. В той час у пацієнтів ХВГВ фаза реплікації у яких була тривалістю більше 5 років зниження обсіменіння слизової рота та кишечника було менш ефективне. **Висновки.** Отримані дані свідчать про сприятливий вплив CANDIVAC під час комплексного лікування рецидивуючого перебігу кандидозного стоматиту, що призводило до статистично значущого зниження частоти рецидивів та інтенсивності суб'єктивних скарг пацієнтів.

Ключові слова: рецидивуючий кандидозний стоматит, хронічного вірусного гепатиту В, лікування, CANDIVAC.

Formulation of the problem. The recurrent course of oral candidiasis is a problem that requires complex and multidisciplinary approaches both in diagnosis and in the tactics of treatment and prevention, since, in most cases, fungal lesions are a manifestation of numerous somatic diseases [1, 8, 10].

The conducted studies indicate that the problem of recurrent candidiasis is not related to infection with a new type of yeast fungus, it lies in susceptibility to infection with one's own already existing type of yeast fungus [13, 14].

The analysis of literary sources gives reason to assert that the main direction of treatment of fungal lesions of oral mucosa should be the restoration of the biocenosis of the entire gastrointestinal tract. For this purpose, local and systemic therapy of symbiotic flora and complex immunomodulators of bacterial origin are used, namely: vaccines, biological supplements, eubiotics, probiotics, symbiotics, bacteriophages. [1, 3, 12] Despite the achieved progress, the problem of treatment of the recurrent course of oral candidiasis remains relevant [5, 7].

In order to achieve effective and sustainable results of treatment, a complex approach and the development of new methods of therapy for fungal infection of the oral mucosa are necessary [6, 9, 14].

The objective of the research. The study of the effectiveness of the treatment complex, which includes CANDIVAC, in patients with manifestations of candidal lesions of oral mucosa with a recurrent course against the background of chronic viral hepatitis B in the replication phase.

The materials and methods of the research. The following group was observed: 17 people aged from 28 to 67 years old with chronic viral hepatitis B in the replication phase, who were diagnosed microscopically and laboratory with 4 cases of oral candidiasis during the last 12 months.

Among this contingent of patients, 8 cases of chronic atrophic oral candidiasis (CAOC) and 9 cases of chronic hyperplastic candidiasis of the oral cavity (CHCOC) were found. The most common form of oral candidiasis was mycotic glossitis (MG) (82.3 %) (Table 1). 13 people (76.5 %) had candidal intestinal dysbacteriosis of varying degrees of severity.

The diagnosis of recurrent course of oral candidiasis was established based on clinical manifestations, through microscopic and bacteriological examination of pathological material from the lesion. The control of the therapy effectiveness was carried out immediately before the prescription of CANDIVAC and 21 days after the start of treatment, it was also repeated after 6 months (the end of the planned treatment), in the follow-up periods of 9 and 12 months.

It is well known that CANDIVAC contributes to the recognition and formation of local specific protection against infectious agents of candidal infections, namely: stimulates the protective activity of macrophages; increase in the population of T-lymphocytes (CD4); increase the concentration of secretory IgA on the surface of mucous membranes [14].

The composition of CANDIVAC includes: inactivated microorganisms in the form of frozen lyophilized forms – 5 mg, including:

- Propionibacterium acnes lysatum cryodessicatum (CCM 7083) – 2,50 mg;
- Candida albicans lysatum cryodessicatum (CCM 8355) – 0,83 mg;
- Candida krusei lysatum cryodessicatum (CCM 8357) – 0,83 mg;
- Candida glabrata lysatum cryodessicatum (CCM 8356) – 0,83 mg.

CANDIVAC was administered orally according to the instructions: 3 cycles of 10 days with a subsequent 20-day break. Daily dose – 1 capsule on an empty stomach.

Local treatment included sanitizing of the oral cavity and its antiseptic treatment with 0.05 % chlorhexidine solution once a day. Complex therapy was supplemented with vitamin therapy with Milgamma 1 pill once a day for 10 days, intake of antihistamine Diazoline 1 pill twice a day for 10 days, and immunotropic drug Imudon – 6 pills a day also for 10 days.

Results and their discussion. The analysis of the dependence of the dynamics of subjective complaints and microbiological research on the immediate results of treatment with the use of CANDIVAC showed positive changes, namely: already after 21 days of treatment, the symptoms of the disease disappeared in 64% of people, and the absence of an infectious agent in swabs of oral mucosa and in the intestine

Table 1

Contingent of patients with oral candidiasis

Type of disease	Total	Number of patients	%
chronic atrophic oral candidiasis	17	8	47.1
chronic hyperplastic candidiasis of the oral cavity		9	52.9

was observed. 5 % of the examined subjects showed a decrease in *Candida* seeding in swabs of oral mucosa and in the intestine – 0.2 ± 0.03 Lg CFU/ml and 0.4 ± 0.2 Lg CFU/ml, respectively (before treatment – 2.3 ± 0.03 Lg CFU/ml and 4.5 ± 0.4 Lg CFU/ml respectively) in the background of absence of disease symptoms. In the background of the absence of clinical symptoms of candidiasis and fungi in the oral cavity, the causative agent of candida infection was found in 3 patients at a concentration of 10^2 CFU/ml during the examination of the intestinal contents.

It is worth to note that the treatment complex was more effective for the patients with chronic viral hepatitis B, who had the replication phase for no more than 2 years. The decrease of *Candida* seeding in swabs of oral mucosa and in the intestine was noted – 0.1 ± 0.03 Lg CFU/ml and 0.8 ± 0.1 Lg CFU/ml, respectively (before treatment – 2.1 ± 0.03 Lg CFU/ml and 3.9 ± 0.4 Lg CFU/ml, respectively). At that time, patients with chronic viral hepatitis B, who had the replication phase for more than 5 years, showed less effective decrease of *Candida* seeding in swabs of oral mucosa and in the intestine – 0.3 ± 0.03 Lg CFU/ml and 1.4 ± 0.3 Lg CFU/ml, respectively (before treatment – 2.5 ± 0.04 Lg CFU/ml and 4.8 ± 0.3 Lg CFU/ml, respectively).

The revealed regularities in the development of oral candidiasis provide grounds for asserting that patients with chronic viral hepatitis B have general pathological changes, which contribute to the occurrence and progression of fungal infection. This statement is confirmed by the fact that positive tests for the presence of markers of HBV replication (HbsAg, HbeAg, anti-HBcIgM, HBV DNA) in the blood serum coincide with a significant decrease in the mixed oral fluid S Ig A, Ig M and an increase in the content of Ig G [4].

A dynamic follow-up efficacy analysis 9 and 12 months after CANDIVAC administration showed positive changes in the assessment of subjective complaints and microbiological indicators. Thus, 70.6 % of patients, who were under our observation, showed the prolongation of remission period up to 1.5-2 years. And under the condition of compliance with the rules of oral hygiene, the condition of the oral mucosa significantly improved compared to the condition in the period before treatment (Fedorov-Volodkina index was 2.7 ± 0.1 points before treatment and 1.5 ± 0.1 points after treatment, respectively). The most important indicator of the effectiveness of the treatment complex was a significant reduction in the number of relapses. Thus, 1 case of relapse was noted in 11.8 % of patients and more than 2 relapses in 17.6 % of the examined patients.

Conclusions.

1. The obtained data indicate the beneficial effect of CANDIVAC during the complex treatment of the recurrent course of oral candidiasis that led to a decrease in the frequency of relapses in 70.6 % of the examined patients and the intensity of subjective complaints of patients.

2. The use of CANDIVAC extends the period of remission of oral candidiasis without the use of antimycotic drugs to 1.5-2 years.

3. In order to achieve an effective and stable result of the treatment of recurrent oral candidiasis, it is necessary to take into account the indicators of the patient's dental status, the presence of general diseases, laboratory test data.

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