cysts of the jaws. *Materials and methods of research.* To assess the state of microcirculation by LDF examined 60 patients with odontogenic cysts of the jaws, including 26 men and 34 women. The mean age of patients was 35.42±2.1 years. The study was performed at the preoperative stage, on days 7 and 30 after cystectomy. Recording of each LDF-gram was performed at a temperature of 22° C, from 10.00 to 11.00 in the morning. To assess the parameters of the microcirculatory tract, the following indicators were taken: the mean value of tissue perfusion (TP), determination of the level of "flax" (SCO) – the standard deviation of the oscillations of the TP in a given period of time. Under conditions of normocirculatory type of periodontal tissue microcirculation, the lowest fixed parameter is in the projection of odontogenic cyst, where the amplitude of endothelial oscillations AmaxE (Hz) = (0.120±0.005) compared with intact periodontal AmaxE (Hz) = (0.210±0.032). Indicators of active flax motions have a similar amplitude, with a difference of ± 0.008 Hz. On the 7th day of observation, the patients have a hyperemic type of microcirculation. In 28% of cases during surgery, there is a stagnant type of microcirculation. On the 30th day of follow-up, normocirculatory, spastic and hyperemic types of microcirculation were recorded in both groups, but the number of patients with normocirculatory type increased by 16%, and with hyperemic type – decreased by 3%.

Key words: periodontitis, periodontitis, odontogenic cyst, microcirculation

Рецензент – проф. Ткаченко І. М.
Стаття надійшла 19.12.2020 року

DOI 10.29254/2077-4214-2021-2-160-280-283
UDC 616.314-77266: 616.31-002-08(043.3)

Badalov R. M., Kovalenko G. A.

PREVENTION AND TREATMENT OF PROSTHETIC STOMATITIS IN PATIENTS WITH DIABETES MELLITUS TYPE 2

Kharkiv Medical Academy of Postgraduate Education (Kharkiv)
galinadib@gmail.com

The connection of the publication with planned research works. The present research is a part of the research project "Improvement of prosthetic techniques and materials quality in the treatment of dental patients", state registration № 0115U000146

Introduction. The emergence of prosthetic stomatitis (PS), as evidenced by numerous publications, remains a significant problem in modern dentistry. Despite the widespread use of modern materials and manufacturing techniques of the prostheses themselves, as evidenced by publications, PS is observed in about 70% of people using a prosthesis for more than 1 month [1]. And with a longer period of using the prosthesis, this figure is higher. And in about 90% of cases, the causative agents of PS are fungi of the genus Candida, in the overwhelming number of cases it is C. albicans, which in most cases are present in association with the bacterial flora [1, 2]. All this outlines the essential features of the course of this pathology, the treatment of which is difficult in practice. PS should be distinguished from subprosthetic stomatitis, which is also often associated with dental prosthetics. However, the cause of its development is trauma of the oral mucosa due to defects in the prosthesis, improper fit, etc. It is subprosthetic stomatitis, in contrast to prosthetic stomatitis, that is considered a risk factor for the occurrence of precancerous and malignant neoplasms of the oral cavity [3]. The generally recognized factors that contribute to the manifestations of PS from a clinical point of view, according to authoritative researchers, are the elderly and senile age of the patient [4], the constant wearing of a full upper denture (replacing all upper teeth in the upper jaw). The likelihood of developing this pathology is higher when the prosthesis constantly remains in the mouth and is not removable during sleep. Other factors include xerostomia (dry mouth), diabetes mellitus, chronic digestive disorders, and a high-carb diet [1, 4]. The infectious carriage of C. albicans also plays a role. Moreover, the carriage of these opportunistic microorganisms goes far beyond the purely dental problem. In general, it has a clear population tends to increase and is considered by many authors as a typical opportunistic infection [5]. According to the modern studies, during the twentieth during the twentieth century, the carriage of C. albicans on the oral mucosa increased from 10% in the 1920s to 46–52% in the 1970s and is now detected in about 30–50% of the healthy population as a component of normal microflora of the oral cavity [6].

Other factors in the promotion and maintenance of PS are widely discussed. In particular, they are noted as possible violations of the manufacturing technology of prostheses associated with errors in the clinical stages of their production or the pathological effect of chemical ingredients that make up the manufacturing material [2]. Compliance with the patient's oral hygiene and the rules for caring for dentures is also important. However, most researchers tend to associate the widespread prevalence of candidiasis in PS (like stomatitis itself) with hypovitaminosis caused by impaired carbohydrate metabolism. This is especially evident in diabetes mellitus and leads to exacerbations of mycotic diseases [6].

Modern researches show the significantly higher prevalence of Candida albicans in patients with diabetes versus healthy subjects [6, 7]. Poor glycemic control in patients with DM Type 2 correlates with higher probability of presence of Candida albicans in the oral cavity [8]. The longitude of the disease is also a predisposing factor for the lesion of the oral musoca with various fungi of Candida family [9, 10].

We can conclude that the role of diabetes mellitus and the associated with it decrease of the tissue tolerance to elevated glucose levels may be a highly underestimated factor in the onset and chronicity of PS.

Aim of the research: to evaluate the effect of prostheses on the seeding of the oral mucosa by the Candida fungus in patients with diabetes mellitus type 2, as

well as the effectiveness of prevention and treatment of prosthetic stomatitis.

Object and methods of the research. To evaluate the features of fungal seeding in prosthetic stomatitis in patients with diabetes mellitus type 2, we studied the prevalence of Candida fungal infection of prosthetic beds and prostheses in 66 patients with diabetes mellitus before and after prosthetics. The study included patients with a verified diagnosis of type 2 diabetes proved by an endocrinologist at least three years ago. All studied patients used acrylic plate prostheses of various configurations, including both full and partial plate structures. All of them were divided into three study groups depending on the prophylaxis of candidiasis of the oral mucosa and the treatment of PS. The 1st group consisted of 11 people who were recommended to thoroughly carry out daily hygienic care of prostheses. They compiled a conditional control group for the effectiveness of drug prevention and treatment of PS. The second group consisted of 43 patients who took Fluconazole orally at a dose of 200 mg once a day and rinsed the mouth with alkaline solutions for 14 days. Patients of the third group (12 people) used applications under the base of prostheses of 1% cream "Clotrimazole" twice a day, immediately after a meal. The treatment duration were 14 days. The composition of the study groups did not differ significantly with the Kennedy classification. Adherence to recommendations and drug intake were monitored through daily patient self-records.

To assess the microbial contamination in all subjects before the study, 7 days after the installation of the prosthesis and the start of prophylaxis and treatment, 14 days after and 30 days after, a morning smear taken from the mouth before any oral hygiene actions. Next, a series of tenfold dilutions in isotonic sodium chloride solution was prepared from the test material and inoculated into tubes with Sabouraud agar, considering the cultivation conditions. At the end of the incubation period, the number of colony-forming units (CFU) in 1 ml was counted, thus concluding the total microbial contamination. The isolated microorganisms were identified by conventional methods, considering the morphological, cultural, and biochemical properties based on the traditional classical bacteriological methods [5].

The results of the research. Our researches showed that the oral cavity in 65.9% of the studied patients of all study groups was significantly seeded with Candida. Moreover, in patients using complete removable plate prostheses, the rate of contamination was significantly higher **(Fig.).**

The dynamics of the results of observation of the contamination of the oral cavity with Candida fungi in various researched groups of patients are presented in the **table**.

Our experimental data show the initial level of the seeding of Candida albicans in patients included in the study was significantly higher than the literature data for the healthy individuals. That proves the previous data on vulnerability of diabetes patients for oral candidiasis.

The obtained microbiological results show that in patients with type 2 diabetes without specific drug therapy (group 1) during the first week after the installation of the prosthesis had a significant increase by 78.5% of the population of Candida albicans. On the 14th day after the installation of the prosthesis in group 1, the number of colonies exceeded the initial value by 36.6% from (20.5±0.10) * 10^7 to (28.0±0.4) * 10^7 colonies. Further, the growth rate of Candida albicans colonies decreases: when observed after 1 month, by 5.3% compared to the level of 14 days: from (28.0±0.40) * 10^7 to (26.5±0.30) * 10^7 colonies ($p<0.01$).Perhaps this trend shows, on the one hand, an increase in resistance to infection due to immune mechanisms, and on the other hand, it demonstrates the patient's mastery of the skills of hygienic care of prostheses.

Table – Indicators of the intensity of seeding with Candida fungi in the oral cavity of patients with diabetes mellitus type 2 who used plate prostheses, colonies*10^7, M±m

Researched groups	The observation period after the start of treatment, days			
	0	7	14	30
Sowing before placing the prosthesis – 20.50±0.10				
1st group	20,50±0,10	36,6±0,5	28,0±0,4	26,5±0,3
2nd group	22,0±0,8	18,8±0,5*	9,5±0,9*	0,50±0,05*
3rd group	21,20±0,7	0,05±0,001*	—	—

Note: * – reliability compared to group 1.

In patients receiving general antifungal treatment (group 2), the intensity of excretion gradually decreased on the 14th day of treatment to the level of (9.5±0.9) * 10^7, and after a month it was (0.50±0.05) * 10^7 colonies, which, respectively, were 2.3 and 44 times lower than the initial level ($p<0.001$). In this regard, in our opinion, it was worth paying attention to the significant differences between PS and candida stomatitis of a different etiology. In the first case, the process has a predominantly atrophic form of inflammation, and the effect of drug therapy, as a rule, occurs quickly (within 14 days). Also, as shown by further observation of patients in this group, they were not prone to relapse.

In patients of group 3, already 7 days after the start of local treatment, there was a 400-fold decrease in the intensity of isolation of colonies, and already on the 14th day, specific fungal inoculation was absent in 100% of patients. At the same time, the absence of Candida fungi in certain concentrations was absent even two weeks after the end of treatment with Clotrimazole cream. At the same time, when applying applications under the bases of the prostheses of this cream in pa-

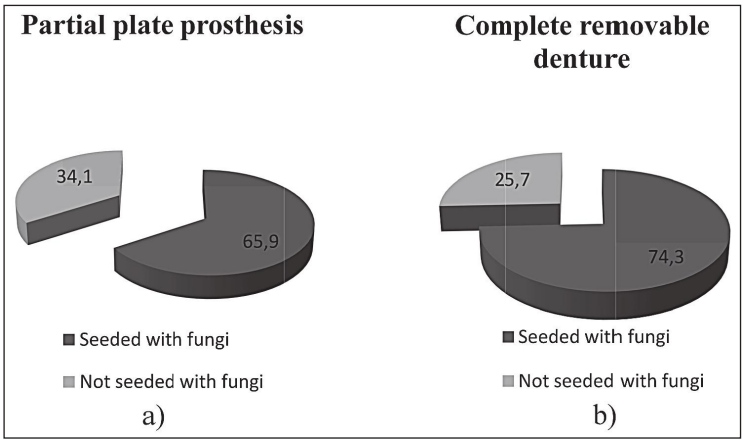

Figure – The dissemination of the oral cavity in patients with diabetes mellitus type 2, using partial (a) and full (b) removable plate prostheses (in %).

tients with type 2 diabetes mellitus with the presence of Candida lesions of the oral cavity, we received a significant decrease in the intensity of growth. Effective relief of the mycotic component of the course of PS was clinically significant. The oral mucosa regained its natural appearance, and the clinical symptoms of PS completely disappeared.

The discussion of results of the research. In the recent literature, there is an opinion about PS as an atypical ongoing fungal infection. This is usually confirmed by the absence of signs of full-thickness lesions of the mucous membrane, characteristic of candidiasis of other localizations and nature [10]. This gives grounds for some researchers to consider PS as a nonspecific reaction to various microorganisms under the prosthesis. In this case, the surface of the prosthesis shows a positive reaction for Candida, but with a biopsy of the mucous membrane, there is usually no penetration of the fungal hyphae into the epithelium. Although the stratified squamous epithelium lining the oral cavity is a typical site for Candida fungi [6].

It is known that fungi of the genus Candida albicans, belonging to the deuteromycetes, are able to exist in the form of single cells, pseudohyphae and hyphae forms. Thanks to this, they do not need invasion of the mucous membrane.

They are also widely represented in the normal human microflora (excreted from the oral mucosa in 25% of healthy individuals, from the stomach – in 20%, with bile – 50%, from the intestines – up to 85%, into the blood – they are usually absent). They are also a component of normal gut microbiota, the growth of which is controlled by gut microorganisms, and they are present in stable amounts [11, 12]. Thus, even in patients without concomitant diseases, the main factor in the development of PS and the persistence of candidiasis in the oral cavity may be the presence of dentures, which alters the microbiota of the oral cavity.

Thus, even in patients without concomitant diseases, the main factor in the development of PS and the persistence of candidiasis in the oral cavity may be the presence of dentures, which in itself alters the microbiota of the oral cavity. Thus, the environment under the prosthesis is more acidic and less susceptible to the cleansing action of saliva, which contributes to the high enzymatic activity of the fungal flora and causes inflammation of the mucous membrane [1].

Chronic candidal stomatitis of various origins (against the background of long-term treatment with antibiotics, cytostatics, corticosteroid drugs, etc.), even without the presence of an irritating factor of dentures, is difficult to treat [10]. Experts describe them as hyperplastic forms of oral candidiasis and note the low effectiveness of monotherapy with antimycotics, which prompts the use of two or three drugs in these cases.

In addition, patients often have a typical chronic fungal infection with damage to various parts of the gastrointestinal tract [1]. Early impact on prosthetic stomatitis and prevention of its transition to a chronic form of the disease should be one of the therapeutic goals of the practicing dentist when installing dentures. Patients with type 2 diabetes are a particularly vulnerable group.

Conclusions. Based on the results of our research and the high significance of the results of microbiological studies in the oral cavity and the clinical course of PS, we recommend the use of 1% cream “Clotrimazole” during the first two weeks after the initial installation of the prosthesis as a method of prevention and treatment of the fungal component of PS in patients with type 2 diabetes mellitus.

When assessing the dental status of patients, a prerequisite is the identification of endocrine pathology, especially the degree of diabetes compensation.

Prospects for further research. To improve the design of partial dentures used for orthopedic treatment of defects of the dentition in patients with type 2 diabetes mellitus.To substantiate and develop a method for the prevention of prosthetic stomatitis in patients with type 2 diabetes mellitus using removable plate prostheses made of acrylic plastics.To study the immediate and long-term results of the prevention of prosthetic stomatitis in patients with type 2 diabetes mellitus using removable acrylic denturesand to assess the quality of treatment.

References

1. Salvi GE, Cosgarea R, Sculean A. Prevalence of Periimplant Diseases. Implant Dent. 2019;28(2):100-102. doi: 10.1097/ID.0000000000000872.
2. Grizodub DV, Badalov RM. Otsenka mikrobnoi obsemenennosti polosti rta patsientov, stradayushchikh neperenosimostyu bazisnykh materialov s`emykh zubnykh protezov. Vistnik problem biologii imeditsiny. 2015;2.2(119):48-52. [in Russian].
3. Piemonte E, Lazos J, Belardinelli P, Secchi D, Brunotto M, Lanfranchi-Tizeira H. Oral cancer associated with chronic mechanical irritation of the oral mucosa. Med Oral Patol Oral Cir Bucal. 2018 Mar 1;23(2):151-160. doi: 10.4317/medoral.22017.
4. Bianchi CM, Bianchi HA, Tadano T, Paula CR, Hoffmann-Santos HD, Leite DPJr, et al. Factors related to oral candidiasis in elderly users and non-users of removable dental prostheses. Rev Inst Med Trop Sao Paulo. 2016;58:17. doi: 10.1590/S1678-9946201658017.
5. Soni AP, Astekar M, Metgud R, Ramesh G, Sharma A, Verma M. Candidal carriage in diabetic patients: a microbiological study. J Exp Ther Oncol. 2019 Jan;13(1):15-21.
6. Javed F, Al-Kheraif AA, Kellesarian SV, Vohra F, Romanos GE. Oral Candida carriage and species prevalence in denture stomatitis patients with and without diabetes. J Biol Regul Homeost Agents. 2017;31(2):343-346.
7. Zomorodian K, Kavoosi F, Pishdad GR, Mehriar P, Ebrahimi H, Bandegani A, et al. Prevalence of oral Candida colonization in patients with diabetes mellitus. J Mycol Med. 2016;26(2):103-110. doi: 10.1016/j.mycmed.2015. 12.008.
8. Matic Petrovic S, Radunovic M, Barac M, Kuzmanovic Pficer J, Pavlica D, Arsic Arsenijevic V, et al. Subgingival areas as potential reservoirs of different Candida spp in type 2 diabetes patients and healthy subjects. PLoS One. 2019 Jan 10;14(1):e0210527. doi: 10.1371/journal.pone.0210527.
9. De la Torre-Luna R, Domínguez-Pérez RA, Guillén-Nepita AL, Ayala-Herrera JL, Martínez-Martínez RE, Romero-Ayala ME, et al. Prevalence of Candida albicans in primary endodontic infections associated with a higher frequency of apical periodontitis in type two diabetes mellitus patients. Eur J Clin Microbiol Infect Dis. 2020 Jan;39(1):131-138. doi: 10.1007/s10096-019-03702-z.
10. Jhugroo C, Divakar DD, Jhugroo P, Al-Amri SAS, Alahmari AD, Vijaykumar S, et al. Characterization of oral mucosa lesions and prevalence of yeasts in diabetic patients: A comparative study. Microb Pathog. 2019 Jan;126:363-367. doi: 10.1016/j.micpath.2018.11.028.
11. Millsop JW, Fazel N. Oral candidiasis. Clin Dermatol. 2016;34(4):487-494. doi: 10.1016/j.clindermatol.2016.02.022.
12. Polesello V, Segat L, Crovella S, Zupin L. Candida Infections and Human Defensins. Protein Pept Lett. 2017;24(8):747-756. doi: 10.2174/0929866 524666170807125245.

ПРОФІЛАКТИКА ТА ЛІКУВАННЯ ПРОТЕЗНИХ СТОМАТИТІВ У ХВОРИХ ЦУКРОВИМ ДІАБЕТОМ 2 ТИПУ

Бадалов Р. М., Коваленко Г. А.

Резюме. Виникнення протезних стоматитів є досить мультиетіопатогенетичним процесом. Сучасні дослідження виявляють значно вищу поширеність Candida albicans у пацієнтів з діабетом порівняно зі здоровими суб'єктами. Це пов'язано з гіповітамінозами, викликаними порушенням вуглеводного обміну. Наявність підвищеного вмісту глюкози в крові та слині призводить до загострень мікотичних захворювань, що, зі свого боку, й провокує значне зростання мікрофлори. Роль цукрового діабету та пов'язане з ним зниження толерантності тканин до підвищеного рівня глюкози може бути вкрай недооціненим фактором початку та хронізації протезного стоматиту. Вивчали вплив зубних протезів на мікробну контамінацію слизової оболонки ротової порожнини грибами роду Candida у пацієнтів з цукровим діабетом 2 типу та ефективність профілактики та лікування протезного стоматиту.

В дослідженні прийняли участь 66 пацієнтів з цукровим діабетом 2 типу. Всім обстеженим пацієнтам вперше були встановлені протези з акрилових пластмас різної конфігурації. Пацієнти були розділені на три групи: контрольну групу, групу, яка приймала флуконазол всередину в дозі 200 мг 1 раз на добу та групу, що застосовувала аплікації під основи протезів 1% кремом «Клотримазол» 2 рази на день. Для оцінки мікробної контамінації всі пацієнти були обстежені до початку до початку дослідження, через 7, 14 та 30 днів після корекції зубних рядів та початку профілактики та лікування.

Отримані дані показали, що у 65,9% обстежених пацієнтів всіх груп були виділені гриби роду Candida albicans. Крім цього, у пацієнтів, що користувалися повними знімними протезами, рівень контамінації був значно більшим. Застосування 1% крему клотримазол місцево показало найбільш високу ефективність щодо зниження контамінації слизової оболонки ротової порожнини грибами роду Candida в порівнянні з іншими групами.

Даний метод може бути рекомендований до використання на протязі перших двох тижнів після встановлення протезу вперше як метод профілактики та лікування грибкового компоненту ПС у пацієнтів з цукровим діабетом 2 типу.

Ключові слова: протезний стоматит, цукровий діабет 2 типу, мікробіологічна оцінка, ефективність використання, клотримазол

PREVENTION AND TREATMENT OF PROSTHETIC STOMATITIS IN PATIENTS WITH DIABETES MELLITUS TYPE 2

Badalov R. M., Kovalenko G. A.

Abstract. The occurrence of prosthetic stomatitis is a multiethiopathogenetic process. Modern researches show the significantly higher prevalence of Candida albicans in patients with diabetes versus healthy subjects This is due to hypovitaminosis caused by a violation of carbohydrate metabolism. The presence of elevated blood glucose and saliva leads to exacerbation of fungal diseases, which, in turn, provokes a significant increase in microflora. The role of diabetes mellitus and the associated with it decrease of the tissue tolerance to elevated glucose levels may be a highly underestimated factor in the onset and chronicity of prosthetic stomatitis. The purpose of the present research to evaluate the effect of dental prostheses on the contamination of the oral mucosa with Candida fungi in patients with type 2 diabetes mellitus, as well as the effectiveness of prevention and treatment of prosthetic stomatitis.

The research included 66 patients with type 2 diabetes. All examined patients received prostheses made of acrylic plastic materialof various configurations for the first time. The patients were divided into three groups: a control group, a group taking fluconazole orally in the dose of 200 mg once a day, and a group using applications under the bases of prostheses with 1% Clotrimazole cream 2 times a day. To assess microbial contamination, all subjects were examined before the start of the research, 7, 14 and 30 days after the installation of the prosthesis and the start of prophylaxis and treatment.

The obtained data showed that Candida albicans fungi were isolated in 65.9% of the examined patients of all groups. Moreover, the level of contamination was significantly higher in patients using complete removable plate dentures. The use of 1% clotrimazole cream locally showed the highest efficiency in reducing the contamination of the oral mucosa with Candida fungi in comparison with other groups.

This method can be recommended for use during the first two weeks after the installation of the prosthesis for the first time as a method of prevention and treatment of the fungal component of PS in patients with type 2 diabetes mellitus.

Key words: prosthetic stomatitis, type 2 diabetes mellitus, microbiological assessment, efficiency, clotrimazole.

Рецензент – проф. Ткаченко І. М.

Стаття надійшла 04.01.2021 року