STATE OF MICROBIOCENOSIS AND LOCAL IMMUNE STATUS OF THE ORAL CAVITY IN TROPHIC ULCERS OF PATIENTS WITH POST-COVIDED SYNDROME

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Abstract: In bacterial pneumonia in patients who underwent COVID-19, a microbiota inhabited by oral pathogens was found in the mucous membrane of the oral cavity and periodontium. The development of trophic ulcers is usually caused by gram-positive cocci, the growth of which is promoted by pulmonary hypoxia and typical symptoms of COVID-19.

Keywords: COVID-19, trophic ulcer, microbiota, pathogenic microorganisms, gram-negative microflora.

A threat to the general health of the population, as well as to the dental condition of the oral mucosa during the COVID-19 pandemic, is its causative agent SARS Cov-2. This fact was recognized by WHO on January 30, 2020 that the COVID-19 epidemic is a public health emergency for all countries of the world. Oral lesions seen in COVID-19 patients, especially after pneumonia, include taste disturbance, non-specific ulcers, gingivitis, spots on the oral mucosa and lips. Candidiasis, aphthous stomatitis, herpetiform lesions, vasculitis, mucositis, drug rash, necrotic periodontal lesions, angular cheilitis, Melkerson-Rosenthal syndrome are also observed [1,4,6,14].

On March 31, 2020, a 67-year-old European man was admitted to Alvorado Hospital (Brazil) with symptoms of pneumonia: weakness, cough, shortness of breath, fever and diarrhea. On the twenty-fourth day of hospitalization, dentists observed a persistent white coating on the back of the tongue, in addition, the dentist found multiple ulcers on the back of the tongue. There were no skin manifestations in the patient, the saliva was viscous, there were no indications for the biopsy method. The patient used mouth rinses and daily applications of 1% hydrogen peroxide. [5,8,9,12].

In bacterial pneumonia in patients who underwent COVID-19, a microbiota inhabited by oral pathogens was found in the mucous membrane of the oral cavity and periodontium. The development of trophic ulcers is usually caused by gram-positive cocci Staphylococcus aureus, Streptococcus, Candida albikans, Fusobacterium nucleatum, much less often Prevotella intermedia, Porphyromonas gingivalis, which cause infection of the lower respiratory tract. [7,10,,11,13].

Of note, pulmonary hypoxia and typical symptoms of COVID-19 promote the growth of anaerobes and facultative anaerobes derived from the oral microbiota. The oral cavity contains the second largest microbiota in the human body, which can

include bacte In patients in these cases, there is a thick white-gray coating on the tongue in the form of white plaques. [2,3].

The aim of the study was to assess the microbiological and immunological status of patients with trophic ulcers who underwent COVID-19.

Materials and methods. The study involved patients of both sexes with a history of COVID-19 and the appearance of a trophic ulcer on the oral mucosa. For control, the study included people without severe background pathology of the same age who were not infected with the virus.ria, fungi, viruses. 125 people were examined, of which 104 were patients with trophic oral ulcers after COVID-19 and 21 were healthy individuals who were included in the control group. The study included people aged 18-70 years, including 61 men and 43 women. The average age of the subjects was 56.7±0.9 years.

The study included 104 patients with a trophic ulcer on the ORM with a confirmed diagnosis of COVID-19 (according to PCR and CT of the lungs), complicated by pneumonia and signed consent to the study. Clinical and laboratory research methods were carried out.

Clinical research methods included the collection of an anamnesis of the disease and complaints of a patient who had COVID-19 with a trophic ulcer based on extracts from the case histories and an assessment of the clinical course of the disease. Dental examination of patients was carried out according to the generally accepted scheme: examination, determination of color, humidity and localization of lesions on the oral mucosa, in addition, an assessment was made of the condition of the teeth, dental plaque, data on the rehabilitation of the oral cavity. 97% of patients with trophic ulcers that developed after suffering COVID-19 complained of bad breath (halitosis).

Microbiological studies of the oral cavity with a trophic ulcer included quantitative and qualitative indicators of the microflora of the oral fluid. The collection of material from patients (Efimovich O.I., 2002) was delivered to the laboratory within two hours and a number of test tubes with serial dilution were prepared. After egogo, they were seeded on highly selective nutrient differential diagnostic media: endo medium, yolk-salt agar, blood agar, Sabouraud agar, etc.; anaerobic microbes were used for the growth of anaerobic microbes. The inoculum was placed in a thermostat at a temperature of 37°C for 24 hours; after the expiration, the cultural and tinctorial properties and the type of microbe were studied. Quantitative indicators of the oral fluid flora were expressed in logarithms: K=Ax200xP (CFU/ml) where, K is the number of microbes of one species; A - the number of colonies in the last dilution, where there is microbial growth; 200 is the coefficient that brings the loop inoculation in accordance with 1 ml; P is the degree of dilution. The number of microbial species of each species was expressed in Lg CFU/ml.

Immunological studies (according to Mancini) were carried out to determine the level of secretory immunoglobulin class A (sIgA) in the oral fluid. To do this, holes were cut out on the agar layer and filled with oral fluid. The culture medium of the well was treated with monospecific sera.

The data obtained during the study were subjected to statistical processing on a Pentium-IV personal computer using the Microsoft Office Excel-2016 software package, including the use of built-in statistical processing functions. Variation statistics methods were used with the calculation of the arithmetic mean of the studied indicator (M), standard deviation (□), standard error of the mean (m), relative values (frequency, %). Results. According to our microbiological studies in healthy individuals (n=21), the density of the microbial population of the oral cavity was a fundamental characteristic and mainly depends on the topography of the ecological niche. In terms of species composition, it is most of all represented by gram-positive flora, most pronounced on the tongue and palate, less on the gingival mucosa. In this regard, the frequency of occurrence of trophic ulcers is most common in these areas of the oral mucosa (Fig. 1,2). In patients with trophic ulcers on the oral mucosa after covid pneumonia, gram-negative microflora was noted, which was clinically manifested by halitosis. In 62% of patients with trophic ulcers, the microflora of the oral cavity was represented by fungi of the genus Candida, which are opportunistic flora, there is a white coating on the tongue (Fig. 3)

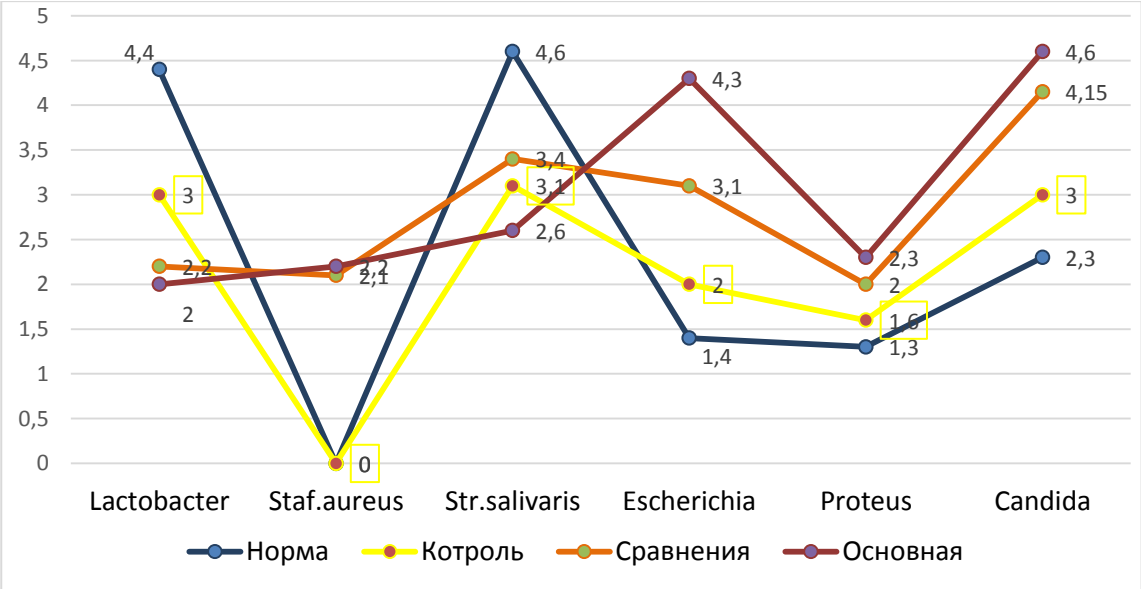
Pic. 1 Trophic ulcer on the gum

2 Trophic ulcer on the tongue

In patients with COVID-19 infection, oral opportunistic microorganisms of the oral microbiota reflect unsatisfactory and poor oral hygiene and disseminate to the lower respiratory tract through aspiration or intubation. The most pronounced significant changes in the studied groups (main and comparisons) reveal a significant decrease in the number of anaerobes, coccal flora and an increase in fungi of the genus Candida, as well as cultures of Staphylococcus aureus and Escherichia, which are aggressive.

Fig. 3 Candidal plaque on the tongue

The COVID-19 pathogen SARS-CoV-2 may interact with members of the oral microbiota in both the lungs and mouth. Negative risk factors such as poor oral hygiene, coughing, rapid breathing under various conditions, and mechanical ventilation are the main routes for oral microbiota to enter the respiratory tract. In addition, pulmonary hypoxia can stimulate the growth of anaerobes and facultative anaerobes derived from the oral microbiota. Together, all these factors lead to respiratory dysbacteriosis.



Pic. 4 The state of the microflora of the oral cavity in trophic ulcers in patients who have undergone Covid 19.

As can be seen from Fig. 4 in patients with trophic ulcers in patients who have undergone Covid 19, cultures of Staphylococcus aureus, Escherichia, Proteus are determined in the oral fluid. These microbial strains are the most aggressive, apparently these properties determine the monitoring of the disease. Fungi of the genus Candida also grew significantly and amounted to Lg 4.60 ± 0.3 CFU / ml and almost double the norm (Fig. 4). The study of colonization by yeast-like fungi of the oral cavity of patients with trophic ulcers after suffering covid pneumonia makes it possible to say that the density of colonization by these microbes has increased. Fungi of the genus Candida colonized the mucous membranes of the gums, tongue and palate, where their number exceeded the content on the surface of the cheek. In the species structure of fungi, the appearance of species unusual for microbiocenosis in healthy individuals was noted.

Secretory immunoglobulin A (sIgA) plays an important role in the local immune defense of the oral mucosa. Thus, sIgA inhibits the ability of bacteria and viruses to adhere to the surface of the epithelium, thereby preventing the penetration of pathogenic microbes into the body. Secretory immunoglobulin A is secreted by plasma cells of the submucosal layer of the tonsils and lamina propria cells. Saliva contains a large amount of secretory immunoglobulin sIgA than other immunoglobulins. A decrease in the level of sIgA in post-COVID syndrome is defined by us as a secondary immunodeficiency and, as a rule, accompanies inflammatory and destructive processes on the oral mucosa. In addition, the oral mucosa, with a decrease in the level of sIgA, becomes vulnerable to viruses and bacteria, as well as to various traumatic factors, such as plaque and deposits, carious cavities and chipped teeth, smoking, alcohol intake, and others. In this regard, we found that insufficient sanitation of the oral cavity or its absence in patients with trophic ulcers who underwent covid pneumonia leads to a decrease in the level of sIgA, and, ultimately, to a violation of the local barrier function of the oral mucosa. As a **result** of this thesis, we came to the conclusion that professional oral hygiene for patients with trophic ulcers will contribute to the improvement of the oral mucosa. Immunological studies of secretory immunoglobulin A in the oral fluid showed a significant decrease in its level in patients after covid pneumonia, especially in the main group(Table 1).

Table 1

Characteristics of the level of sIgA in the oral fluid in patients with trophic ulcers after Covid 19 (M±m)

Index	Study groups		
	Control n=21	Comparison group n=52	Main group n=52

sIgA, mg/ml	0,62±0,13 p≥0,05	0,46±0,04* p≤0,05	0,37±0,05*ð p≤0,05

Note: * - p≤ 0,05; ** - p≥0,05 compared to the control group
ð - p≤ 0,05; ðð- p≥0,05 compared with the comparison group.

As can be seen from Table 1, in patients of the main group, the sIgA in saliva was in the range of 0.37+0.05 mg/ml, which was significantly (p□0.05) lower than in the comparison group of 0.46+0.04 mg /ml and significantly (p□0.05) lower than in the control group 0.62+0.13 mg/ml. The difference between the indicators in the comparison group and in the control group was statistically significant (p□0.05).

Conclusions: 1. Clinically, the most common trophic ulcers in patients who had Covid 19 were detected on the tongue and palate, less often on the gingival mucosa;

2. Microbiological studies revealed a significant decrease in the number of anaerobes, coccal flora, an increase in fungi of the genus Candida, the appearance of a culture of Staphylococcus aureus and Escherichia;

3. Immunological studies of sIgA in the oral fluid showed a significant decrease in its level in patients with a trophic ulcer after covid pneumonia, the most pronounced in the main group.

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