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SORPTION ACTIVITY OF THE EPITHELIUM OF THE ORAL CAVITY IN RESIDENTS OF ARKHANGELSK DEPENDING ON BODY MASS INDEX

The purpose of the study: to study the features of the sorption activity of the epithelium of the oral mucosa, depending on the body mass index. A survey of 61 practically healthy women living in Arkhangelsk aged 19 to 45 years was conducted. According to the results of the distribution, two groups were formed depending on BMI: BMI > 25 (30 people) and BMI < 25 (31 people). To exclude the metabolic syndrome, a study of the main parameters of the lipid profile was conducted. The sorption activity of the epithelium in the separated oral mucosa in the group with a BMI >25 was lower compared with the group of subjects with normal weight. The average number of peripheral blood leukocytes in the examined group with a BMI>25 was statistically significantly higher (6.67±0.88 ×10^9 cells/l compared with 4.94±0.06 ×10^9 cells/l) due to neutrophil granulocytes (3.75±0.27 ×10^9 cells/l versus 2.50±0.18 ×10^9 cells/l). Their content levels did not go beyond the reference values. The average level of the proinflammatory cytokine IL-1β in the supernatant of oral fluid in individuals with a BMI >2.5 was twice as high (20.19±2.95 pg/ml compared with 10.95±1.80 pg/ml). The average levels of IL-1β in peripheral blood in individuals of both groups studied do not exceed the physiological norm, and the average levels of this proinflammatory cytokine in the supernatant of oral fluid are 2-4 times higher than in the cut, it can be assumed that the local synthesis of this cytokine. low levels of sorption activity of the oral epithelium in individuals with a BMI >25 may indicate a risk of developing metabolic syndrome.

Thus, in individuals with a BMI > 25, a decrease in the levels of sorption activity of the oral epithelium was revealed, as well as a twofold increase in the average levels of IL-1β in the supernatant of the oral fluid, which suggests a more intense inflammatory reaction of the oral mucosa, the chronization of which can lead to metabolic changes, and, as a result, can contribute to the development of metabolic syndrome. At the same time, the average levels of IL-1β in peripheral blood do not change, which emphasizes the relative autonomy of the local immune response. Concentrations of the proinflammatory cytokine IL-1β in the oral fluid, which are many times higher than the average levels of IL-1β in peripheral blood, indicate a predominantly local synthesis of this inflammatory mediator.

Keywords: Sorption, epithelium, obesity.

Introduction. The innate immune system of the oral cavity functions as the first line of defense against infection, provides immune tolerance to commensal bacteria and food antigens. Epithelial cells of the mucous membranes of the oral cavity are the main components of the innate immune system, providing relative impermeability of the epithelial barrier to microorganisms. The microbiota of the oral cavity plays an important role in maintaining the health of the human body. Deviation from the symbiotic balance between the host and the microbiota can lead to oral and systemic diseases. Epidemiological studies confirm the connection between oral dysbiosis and metabolic dysregulation. Dysbiosis of the oral microbiome can contribute to inflammatory changes and impaired metabolic regulation in obesity. Significant differences in the composition of the oral microbiome between people with normal weight and obesity have been revealed [3, 7, 8].

Increased permeability of the intestinal wall in obesity is associated with changes in the composition of proteins of dense compounds and thinning of the mucous layer of the epithelial barrier, which leads to translocation of food and bacterial antigens into the bloodstream. The microflora of the oral cavity initiates immune reactions and contributes to increased metabolic inflammation of adipose tissue. Two approaches linking oral bacteria with inflammatory and metabolic effects in distant organs are discussed in the literature. Translocation of oral bacteria into the intestine and effects on the composition of the intestinal microbiome are one of the approaches. Translocation of oral bacteria and inflammatory molecules into the bloodstream leads to bacteremia, systemic damage and various immune reactions. This causes systemic inflammation and local inflammation in remote areas [6]. Local increase in proinflammatory cytokine levels and remodeling of dense compound proteins play a key role in the manifestation of epithelial barrier dysfunction in obesity [2].

There are fundamental restrictions on the capture of bacteria by epithelial cells in the gastrointestinal tract and other cavities. Endocytosis, as a consequence of the fundamental principles of biology, is based on molecular and cellular recognition, which plays an important role in bacterial adhesion to host cell receptors. Adsorption and receptor-mediated protein endocytosis is a universal property of cells, and especially in the epithelium of mucous membranes. Some absorbed proteins are transported intact through the cells and thus provide specialized functions, such as the transfer of immunity from mother to child. However, mostly absorbed proteins are transported to lysosomes, where they undergo complete hydrolysis to amino acids. This process is important for the homeostasis of circulating proteins [9].

The sorption activity of the epithelium depends on the size of the sorbed particles. Studies of the sorption capacity of epithelial cells of the mucous membranes of the esophagus show that latex microspheres larger than 1 μm adhered to epithelial cells, but were not subjected to phagocytosis [4]. Microspheres with a diameter of 0.01 and 0.1 microns. microspheres, but not 1.0 microns, were internalized rather than simply attached to the outer surface of the cell [5].

Studies simulating the consequence

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of diabetes mellitus in the oral cavity have demonstrated a decrease in the sorption capacity of oral epithelial cells against the background of an increase in the number of heterogeneous microflora and low leukocyte activity. There were also trends towards a significant decrease in the index of cellular differentiation and an increase in the nuclear-cytoplasmic ratio against the background of intensive processes of desquamation of the mucosal epithelium, exacerbating local inflammatory reactions [10].

At the local level, cytokines ensure the development of all stages of the immune response to the influence of a pathogenic factor: they limit its spread, removal and restoration of damaged tissue. Low concentrations of cytokines form adequate local inflammation, higher ones cause a systemic inflammatory reaction of a protective nature, extremely high ones lead to the development of pathological conditions. The source of cytokines in the oral fluid is serum transudate and salivary glands, and they are also produced by epithelial cells of the oral mucosa upon contact with microorganisms. In addition, cytokines are actively produced by lymphocytes and macrophages embedded in the epithelial layer of the mucous membrane. Separately, it should be noted that the content of cytokines in the oral fluid does not correlate with their level in the blood, which indicates the relative autonomy of local immunity. The diagnostic value of determining cytokines increases when they are examined directly in the focus of inflammation.

The initial mucosal response is triggered by the activation of toll-like receptors, which act as the most important inflammatory mediators within the innate immune system. Activation of immune cells such as macrophages and T cells contributes to the creation of a pro-inflammatory environment, which leads to an increase in the level of inflammatory cytokines such as TNF-α, IFN-γ, IL-6, IL-13 and IL-1β. Moreover, inflammatory cytokines can affect the main regulator of the function of dense compound proteins.

Studies prove that metabolic inflammation of adipose tissue in individuals with a high body mass index has a negative effect on the epithelial layer of the mucous membranes, weakening the secretion of proteins of dense compounds, increasing the permeability of the epithelial layer due to paracellular transport. The degree of permeability of the epithelial barrier is regulated by proteins of intercellular tight contacts both under physiological conditions and under conditions of a pathological process [1].

Table 1

Average levels of body mass index and peripheral blood lipid metabolism, depending on BMI

Parameters	BMI >25, M±m	BMI <25, M±m
Body Mass Index	31.59±3.65*	21.84±2.25
Total cholesterol, mmol/l	3.54±0.47	3.98±0.74
Triglycerides, mmol/l	0.83±0.33	0.96±0.20
Phospholipids, mmol/l	2.08±0.60	2.48±0.70
Glucose, mmol/l	5.02±0.43	5.26±0.41
aspartate transaminase, E/L	21.42±6.14	20.77±3.07
Alanine aminotransferase, E/L	12.71±4.78	15.16±3.70
Gamma-glutamyltranspeptidase, E/L	20.37±21.22	20.72±14.22
Amylase, E/l	49.25±18.07	49.23±19.84

* - p<0.05

Table 2

The sorption activity of the epithelium in the oral fluid of the subjects, depending on BMI

Parameters	BMI > 25	BMI < 25
Average sorption activity of the epithelium, bacterium / cell	69.66±3.92*	86.29±2.25
% of individuals with epithelial sorption activity <100 bacterium / cell	55.17	32.29
% of individuals with epithelial sorption activity <50 bacterium / cell	27.59	0

* - p<0,05

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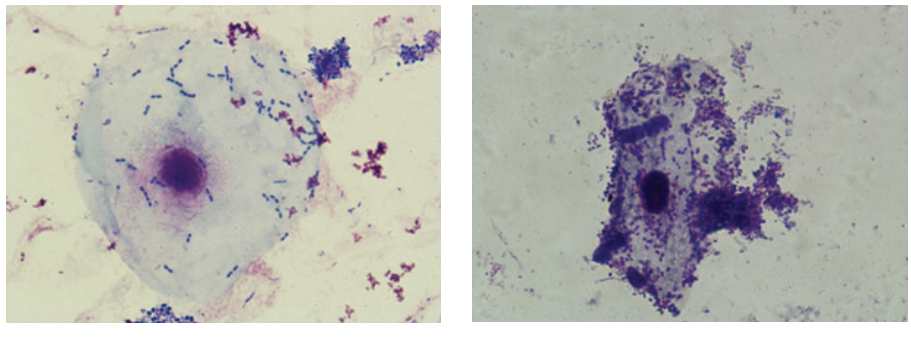

Epithelial cell of the oral cavity with a low number (a) and a large number (b) of sorbed microorganisms. Staining according to Romanovsky-Giemsa. Magnification ×1000

The purpose of the work: to study the features of the sorption activity of the epithelium of the oral mucosa depending on the body mass index.

Materials and methods. On the basis of the Laboratory of Environmental Immunology of the Institute of Physiology of Natural Adaptations of the the N. Laverov Federal Center for Integrated Arctic Research of the Ural Branch of the Russian Academy of Sciences, a survey of 61 practically healthy women living in Arkhangelsk aged 19 to 45 years was conducted. The average age of the subjects was 33.52±8.17 years. The examination was conducted during the absence of exacerbation of chronic diseases. All studies were conducted with the consent of volunteers and in accordance with the requirements of the Helsinki Declaration of the World Medical Association on Ethical Principles of Medical Research. Permission was received from the Ethical commission of the Institute of Physiology of Natural Adaptations of the the N. Laverov Federal Center for Integrated Arctic Research of the Ural Branch of the Russian Academy of Sci-

Table 3

Erythrocyte and leukocyte indices of peripheral blood depending on BMI

Parameters	ИМТ >25, M±m	ИМТ <25, M±m
Erythrocytes, 10^6 cells/µl	4.81±0.49	4.79±0.39
Hemoglobin, g/l	132.40±18.64	131.06±14.93
Hematocrit, %	37.11±4.34	37.11±3.33
Red blood cell volume, fL	77.25±5.91	77.59±4.32
The volume of hemoglobin in erythrocytes, pg	27.53±2.74	27.38±2.15
The average concentration of hemoglobin in erythrocytes, g/l	355.83±13.74	352.42±11.86
Platelets, 10^3 cells/µl	281.67±64.97	256.00±53.53
The estimated width of the distribution of red blood cells by volume, standard deviation, fL	38.63±3.06	36.80±2.18
The calculated width of the distribution of erythrocytes by volume, coefficient of variation, %	14.21±2.00	13.36±1.26
Estimated platelet distribution width, fL	14.40±2.48	13.90±2.19
Platelet volume, fL	11.03±1.04	10.79±0.89
The coefficient of large platelets, %	34.17±8.30	32.31±7.15
Thrombocrit, %	0.31±0.06	0.27±0.05
White blood cells, 10^9 cells/l	6.67±0.88*	4.94±0.06
Neutrophils, 10^9 cells/l	3.75±0.27*	2.50±0.18
Neutrophils, %	55.86±0.90	50.39±0.51
Lymphocytes, ×10^9 cells/l	2.12±0.79	1.82±0.62
Lymphocytes, %	32.10±0.50	36.82±1.18
Monocytes, ×10^9 cells/l	0.56±0.15	0.45±0.11
Monocytes, %	1.87±0.07*	1.55±0.07
The ratio of neutrophils to lymphocytes (NLR)	8.60±0.60	9.26±0.87
Eosinophils, ×10^9 cl/l	0.19±0.14	0.16±0.11
Eosinophils, %	2.98±0.01	3.15±0.05
Basophils, ×10^9 cells/l	0.03±0.02	0.02±0.01
Basophils, %	0.44±0.06	0.41±0.02

* - p<0.05

ences (Protocol No. 8 dated March 30, 2022) to conduct the study.

All the subjects had their height and body weight measured, and the body mass index was calculated using the formula: BMI = weight (kg) / height $(m)^2$.

Oral fluid was taken in the morning, on an empty stomach, into plastic tubes, which were immediately frozen for 72 hours, then unscrewed on a centrifuge. A smear was made from the sediment and stained according to Romanovsky-Gimse. The average number of microbial bodies per 100 epithelial cells was calculated in the smear. The infusion fluid was used to determine IL-1β by enzyme immunoassay.

The complex of immunological research included the study of a hemogram of venous blood taken on an empty stomach in the morning (the number of platelets, erythrocytes, leukocytes, total hemoglobin in the blood, leukograms) on an automatic hematology analyzer XS–500i (Sysmex, Japan). Cytokines IL-1β, IL-6, TNF-α, IL-10 (Vector Best, Russia) of peripheral blood and the supernatant of oral fluid were determined by the enzyme immunoassay using the Multiskan FC enzyme immunoassay analyzer (Thermo Scientific, USA).

The study of the lipid profile included the determination of total cholesterol, glucose, triglycerides, phospholipids, and insulin using a Shimadzu UV-1800 spectrophotometer (Japan) and Vector–Best reagents (Russia).

Statistical processing with the determination of the arithmetic mean and standard error (M ± m) was carried out using the Microsoft Excel software package. The significance of the differences was assessed using the Student's t–test when conducting statistical analysis using the Statistica software package. The significance of the differences was taken into account at $p < 0.05$.

Table 4

Average levels of peripheral blood cytokines and oral fluid supernatant

Cytokines	BMI >25, M±m	BMI <25, M±m
IL-17F, pg/ml	26.54±23.93	28.47±13.62
IL-1β, pg/ml	4.75±1.92	4.63±3.65
IL-1β (saliva), pg/ml	20.19±2.95*	10.95±1.80
IL-4, pg/ml	11.88±1.85	10.17±2.71
IL-6, pg/ml	2.72±2.06	3.2±2.47
TNF-α, pg/ml	6.21±6.9	7.04±6.2
IL-10, pg/ml	4.53±4.1	5.03±6.44

* - p<0.05

Results and discussion. According to the results of the distribution, two groups were formed depending on BMI: BMI > 25 (30 people) and BMI < 25 (31 people). To exclude the metabolic syndrome, a study of the main parameters of the lipid profile was conducted. The results of the lipid metabolism parameters studied by us are shown in Table 1.

The main parameters of the lipid profile in all subjects did not exceed the limits of the physiological norm.

We found that a high body mass index is associated with a decrease in the sorption activity of epithelial cells of the mucous membranes of the oral cavity. The average levels of sorption activity of epithelial cells of the oral fluid, as well as the percentage of persons with reduced sorption levels are shown in Table 2.

The sorption activity of the epithelium in the separated oral mucosa in the group with a BMI >25 was lower compared with the group of subjects with normal weight (Figures 1, 2). At the same time, the average level of epithelial cell sorption capacity did not reach 100 bacterium / cell. in half of the subjects in the BMI group >25, and 50 bacterium / cell in a third of the volunteers in this group. A decrease in the levels of the sorption capacity of epithelial cells may indicate a weakening of the protective properties of epithelial cells of the mucous membranes of the oral cavity in persons with high BMI due to the negative influence of factors of metabolic inflammation of adipose tissue.

Figure 1. Epithelial cell of the oral cavity with a low number of sorbed microorganisms. Romanovsky-Giemse coloring. Increase ×1000.

To clarify the nature of metabolic inflammatory processes, it was of interest to study peripheral blood parameters, the results of which are presented in Table 3.

The indicators of erythrocyte and platelet components of peripheral blood in both groups of subjects had no significant differences and were within the physiological norm.

The average number of peripheral blood leukocytes in the examined group with a BMI>25 was statistically significantly higher (6.67±0.88 ×10^9 cells/l compared with 4.94±0.06 ×10^9 cells/l) due to neutrophil granulocytes (3.75±0.27 ×10^9 cells/l versus 2.50±0.18 ×10^9 cells/l). Their content levels did not go beyond the reference values. To assess the likely systemic inflammation, the average values of the neutrophil-lymphocytic index in the subjects were calculated, it was determined that those with a high BMI were higher than those of volunteers with normal body weight (1.87±0.07 compared with 1.55±0.07).

The average concentrations of the mediators of inflammatory reactions of peripheral blood and the supernatant of oral fluid studied in individuals with different BMI levels are shown in Table 4.

The studied levels of peripheral blood cytokines in the subjects in both groups had no statistically significant differences. However, the average level of the proinflammatory cytokine IL-1β in the oral fluid supernatant in individuals with a BMI >2.5 was twice as high (20.19±2.95 pg/ml compared with 10.95±1.80 pg/ml). Elevated levels of the inflammatory mediator IL-1β in the oral fluid indicate a local immune response, play an important role in the development of inflammation and a decrease in the effectiveness of the protective function of the epithelial barrier in obesity. Since the average levels of IL-1β in peripheral blood in individuals of both groups studied do not exceed the physiological norm, and the average levels of this proinflammatory cytokine in the supernatant of oral fluid are 2-4 times higher than in the cut, it can be assumed that local synthesis of this cytokine. It is important to keep in mind that the average values may vary depending on the individual characteristics of the body.

The relatively elevated level of c-reactive protein (2.46±0.17 micrograms/ml compared with 1.97±0.19 micrograms/ml), even with normal cholesterol levels in practically healthy individuals, makes it possible to predict the risk of metabolic disorders that can lead to the development of metabolic syndrome, since individuals with a BMI > 30 have average concentrations of c-reactive protein. proteins tend to increase (4.20±1.86 micrograms/ml).

Conclusion. Thus, in individuals with a BMI > 25, a decrease in the levels of sorption activity of the oral epithelium was revealed, as well as a twofold increase in the average levels of IL-1β in the supernatant of the oral fluid, which suggests a more intense inflammatory reaction of the oral mucosa, the chronization of which can lead to metabolic changes, and, as a result, can contribute to the development of metabolic syndrome. At the same time, the average levels of IL-1β in the peripheral blood do not change, which highlights the relative autonomy of the local immune response. Concentrations of the proinflammatory cytokine IL-1β in the oral fluid, which are many times higher than the average levels of IL-1β in peripheral blood, indicate a predominantly local synthesis of this inflammatory mediator.

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