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Assessment of the State of Systemic Immunity in Patients with Inflammatory Periodontal Diseases

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ABSTRACT

Inflammatory periodontal diseases are characterized globally by a high prevalence of 55 to 98%, a variety of clinical manifestations, and a decrease in local or general factors of specific or nonspecific immunity. Immunological imbalance contributes to the chronicity of the course of somatic pathology, depletes compensatory mechanisms, and forms foci of chronic infection.

The study aimed to assess the state of systemic immunity in patients with inflammatory periodontal diseases.

Materials and methods: The general immune status was assessed in 120 patients of working age from 20 to 60 years. At the first stage, medical history and questionnaires were collected to identify immunopathological and immunodeficiency states. At stage II, the authors performed immunophenotyping of CD3, CD4, CD8, CD16, CD20 lymphocytes out according to level 1 tests (tests for confirming immunodeficiency), immunoglobulins (Ig A, M, G), circulating immune complexes, phagocytic, and oxygen-dependent metabolic activity of neutrophilic leukocytes. At stage III, level 2 tests (tests of differentiation of the damaged link), the immunoregulatory index, leuko T-cell index, leuko-B-cell index, and leukocyte-CD16+ index were determined.

Results and discussion: Analysis of the clinical manifestations of immunological disorders in inflammatory periodontal disease patients revealed a high percentage of people with chronic diseases: 12% had one somatic disease, 34% had 2, and 54% had three or more. 19.47% of the participants were referred to the first health status group, 37.17% to the second, and 43.36% to the third prophylactic observation group. The state of general immunity was characterized by a combined insufficiency of the cellular T-link, humoral B-link of lymphocytes (CD20+), oxygen-dependent metabolism of segmented neutrophils with an increase in the level of CD16+ cells, phagocytic activity, and circulating immune complexes in the blood. An increase in the circulating immune complexes in peripheral blood by 2-3 times may indicate active binding of antigens entering the bloodstream. T-lymphocyte indices (immunoregulatory index and leuko T-cell index) changed in different directions: the immunoregulatory index decreased with increasing severity, and the leuko T-cell index increased, which indicates an increase in the deficiency of T-lymphocytes, and impaired immunoregulation with an increase in the severity of inflammatory periodontal diseases. The suppression of the absorption, bactericidal activity, and reserve capabilities of phagocytes against the background of an increase in the content of immune complexes indicates the presence of an immunocomplex and an autoimmune component in the pathogenesis of inflammatory periodontal diseases.

Key words: Periodontitis, Cellular and humoral immunity, Immunoregulatory indices, Immunodeficiency states

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INTRODUCTION

Inflammatory periodontal diseases (IPDs) are characterized by a high prevalence according to the World Health Organisation (WHO) data (from 55 to 98%), a progressive course with a high recurrence rate, a variety of clinical manifestations of local and systemic immunity, an increase in the percentage of persons with secondary partial or complete adentia [1,2]. The inflammatory process can be limited to the gums (gingivitis) or affect all periodontal structures (periodontitis) [3-5]. The periodontal complex, on the one hand, reflects the general state of the body, and on the other hand, it can affect the course of general somatic diseases because of immunological, infectious, and toxic effects [6,7]. A decrease in the body's immune and anti-inflammatory defences increases the risk of infection and the development of complications of diseases of other organs and systems and forms various chronic infections. Immunological imbalance contributes to the chronicity of the course of somatic pathology, depletes compensatory mechanisms, leads to an increase in secondary immunological deficiency [8,9].

The study aimed to assess the state of systemic immunity in patients with inflammatory periodontal diseases.

MATERIALS AND METHODS

The studies were carried out at the Department of Propedeutics of Dental Diseases of the Federal State Budgetary Educational Institution of Higher Education "Bashkir State Medical University of the Ministry of Health of Russia" in 120 patients of working age (from 20 to 60 years) with inflammatory periodontal diseases who had given informed consent. The control group consisted of (n=20) practically healthy persons aged 20-50 years who did not have any dental or somatic pathology at the time of examination. The diagnosis of the disease was established according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). The study used clinical, instrumental, and immunological methods.

The general immune status was assessed in three stages. At the first stage, anamnesis data was collected containing complete information about the state of health and questionnaires to identify immunopathological disorders and immunodeficiency states. The general part of the questionnaire contained personal information (age, gender), physiological (blood pressure (BP), heart rate), anthropometric (weight, height, body mass index, waist circumference), and clinical data. A special part included questions to identify the presence of various types of immunopathology in the examined individuals.

Laboratory studies were carried out based on the laboratory of immunology of the Research Institute of Occupational Hygiene and Human Ecology and State Budgetary Health Institution "City Clinical Hospital No. 22" in Ufa. The study of the state of the general immunity of patients with IPDs began with the study of leukograms in the peripheral blood according to the standard method. The total number of leukocytes, erythrocytes in 1 litre of blood, the concentration of hemoglobin, erythrocyte sedimentation rate (ESR), the content of neutrophils, lymphocytes, monocytes, platelets were assessed. At stage II, the state of the general immune status in patients with IPDs was assessed according to the immunological indicators of level 1 tests (tests of confirmation of immunodeficiency): the humoral link of immunity was tested according to the number of CD20+ lymphocytes, the content of immunoglobulins of the main classes (Ig A, M, G) in the blood serum was assessed by the method radial immunodiffusion according to Mancini, the content of circulating immune complexes (CIC) was assessed by precipitation in a 4% polyethylene glycol solution; the state of natural defense factors was assessed by the phagocytic activity of neutrophils, and the complement activity by 50% hemolysis. Immunophenotyping of lymphocytes was carried out to confirm the diagnosis and monitor the state of the immune system: populations of T-lymphocytes were identified as CD3+, subpopulations of T-helpers as CD4+, T-cytotoxic as CD8+ cells in the reaction of indirect immunofluorescence using monoclonal antibodies from MedBiopekt, Moscow. The indices of natural killer (NK) cells CD16+ lymphocytes were determined. At stage III, level 2 immunological tests (differentiation tests of the damaged link), such as immunoregulatory index (IRI) (the ratio between CD4+ and CD8+ lymphocytes), and nitro blue tetrazolium (NBT) stimulation index (the ratio between spontaneous and stimulated NBT) were performed. We used leukocyte-T-cell (LTCI), leukocyte-B-cell (LBCI), and leukocyte-CD16+ cellular indices (the ratio of the total number of leukocytes to the absolute number of T-, B- or CD16+-lymphocytes) [8].

Statistical processing of the results was carried out using generally accepted standard methods. We determined the arithmetic mean (M), standard error of the arithmetic mean (Se), and standard deviation. The significance of the differences in indicators was assessed using the student's t-test. Differences were considered statistically significant at $p < 0.05$ [10].

RESULTS AND DISCUSSION

According to the results of our study, it was found that the group with K05.0 had more participants aged from 20 to 35 (54.6%), the group with K05.1 had more participants aged from 26 to 40 (56.2%), the group with K05.2 had more patients aged from 35 to 47 (45.9%), and the group with K05.3 had more patients aged 39 years and older (56.4%). Women were 3 times more likely to see a periodontist than men. The average age of women in all examined groups was higher than that of men, which may be due to higher motivation and desire to stay healthy among women. We found that with age, the severity, duration of the disease, and recurrence of IPDs increased in all groups and did not statistically differ based on gender.

At the next stage, we assessed the state of the immune system according to the anamnesis and questionnaires to identify immunopathological disorders and secondary immunodeficiency states. An analysis of the clinical manifestations of immunological disorders in patients with IPDs showed that the most frequent variant of immunological disorders was an infectious syndrome characterized by frequent colds, a high percentage of people with chronic diseases such as bronchitis, lymphadenopathy, autoimmune diseases, and allergies. According to our results, secondary immunodeficiency states were detected in 90.3% of patients with IPDs. Depending on the severity of IPDs, the immunodeficiency state (IDS) scores in patients increased from (5.1 ± 0.6) at K5.0 to (14.8 ± 1.6) at K05.3. The average score for the examined group was (10.2 ± 0.4) versus (3.3 ± 0.1) in the control group ($p < 0.001$). As a result of our study, the analysis of the clinical manifestations of IDS showed that the predominant form of immunopathology in patients with IPDs was a decrease in anti-infectious resistance, manifested by a high predisposition to infectious and inflammatory diseases of the upper respiratory tract with a tendency to relapse and a tendency to chronicity. The prevalence of all immunopathological syndromes in the group of IPD individuals exceeded the IDS data of the control group in the vast majority of IPD patients; with age, IDS indices, and severity increased.

Among the participants examined by us, 12% were found to have one somatic disease, 34% had 2, and 54% had three or more. 19.47% of the participants were referred to the first health status group, 37.17% to the second, and 43.36% to the third prophylactic observation group. Functional electrocardiogram (ECG) changes were identified in 58.4 percent of the examined persons, the highest heart rate indicators were found in participants aged 35-44 years. The blood glucose level was 5.4 mmol/l, total cholesterol was 4.9 mmol/l. The results obtained correlate with the age and severity of periodontitis. Our analysis of some physiological factors based on personal data in IPD patients showed insignificant changes in blood pressure and heart rate in comparison with the control group. It was observed that systolic and diastolic pressure in men significantly exceeded the values of pressure indicators in women. Body mass index (BMI) is an important physiological parameter that characterizes the characteristics of a person's constitution, the degree of their physical development, the level of their energy metabolism and is a criterion for the prognostic assessment of the compensatory and adaptive capabilities of the body. The study of anthropometric parameters in patients with IPD revealed an increase in body weight and BMI with an increase in the severity of periodontitis. A waist circumference of more than 80 cm in women and more than 94 cm in men was observed in 57.4% of the persons we had examined. The data obtained reflect the relationship between the development of periodontal pathology and the general state of the body and its dependence on age and body weight and amounted to BMI (21.9 ± 2.1) in the control group versus (26.6 ± 1.3) kg/m2 in the groups with K05.2 and K05.3 ($p < 0.05$). The BMI in men and women with IPD did not differ statistically ($p > 0.05$).

The blood system is a sensitive indicator of the reactive characteristics of the body. The results of general clinical studies of hematological blood parameters showed that the number of erythrocytes and hemoglobin did not reveal statistically significant deviations of their values from those of the control group. Indicators of leukocytes, lymphocytes, monocytes, platelets, and blood ESR carrying out nonspecific resistance of the organism in IPD patients, revealed an increase in the number of band neutrophils in the group of patients with K05.2 and K05.3. The number of monocytes, which are mononuclear phagocytes and precursors of tissue macrophages, increased by 1.5 times with K05.0. The number of band neutrophils increased in patients with periodontitis above the level in the control group and was the highest at K05.2 and K05.3 of periodontitis. The relative number of lymphocytes in patients with K05.2 and K05.3 was reduced. The level of ESR at K05.0 was 1.4 times lower and in patients with K05.1, it was lower than in the control group, while it was higher in the group of patients with K05.3. The data obtained indicate a defect in the bone marrow circulation and reflect a decrease in reactivity in the examined participants (Table 1).

Table 1: Hematological parameters in patients with inflammatory periodontal diseases (M ± m).

Indicators	Control (n=20)	K05.0 (n=30)	K05.1 (n=30)	K05.2 (n=30)	K05.3 (n=30)
Hemoglobin, g/l	124.11 ± 2.11	128.50 ± 5.51	132.42 ± 6.23	137.27 ± 6.31	136.11 ± 5.84
Erythrocytes x1012/g	4.55 ± 0.21	4.38 ± 0.16	4.47 ± 0.15	4.72 ± 0.09	4.91 ± 0.14
Leukocytes x109 /l	5.95 ± 1.33	6.53 ± 1.28	6.74 ± 0.38	7.65 ± 1.61	8.15 ± 1.76*
Eosinophils (%)	2.34 ± 0.21	1.60 ± 0.37	2.61 ± 0.10	2.62 ± 0.17*	2.71 ± 0.45*
Band neutrophils (%)	1.84 ± 0.54	2.21 ± 0.42	3.12 ± 0.23	3.80 ± 0.65*	4.24 ± 0.68*
Segmentonuclear neutrophils (%)	57.02 ± 8.5	56.20 ± 11.03	64.60 ± 3.2	55.70 ± 2.62	59.32 ± 3.20
Lymphocytes, (%)	30.12 ± 0.56	30.41 ± 0.47	30.23 ± 0.82	30.35 ± 0.76	31.43 ± 1.65*
Monocytes, (%)	5.80 ± 0.11	7.70 ± 0.73	5.62 ± 0.30	4.80 ± 1.03	4.05 ± 0.70*
Platelets, x109/l	255.2 ± 11.1	250.25 ± 12.3	235.78 ± 13.5	230.60 ± 15.1	248.61 ± 12.6
ESR mm/h	6.74 ± 2.50	7.74 ± 2.48	9.25 ± 2.18	9.42 ± 1.58	13.21 ± 3.20

Note: * - the difference with the control is statistically significant ($p < 0.05$); ** the difference with the control is statistically significant ($p < 0.001$).

Studies of the state of the cellular link of immunity in patients with IPDs showed a decrease in the number of CD4+, which ensures the inclusion of the B-system of lymphocytes and CD8+ cells in the immune response, which is an efferent link in the development of delayed-type hypersensitivity reactions (cellular reactions). The indices of T-lymphocytes (IRI and LTCI) changed in different directions: the IRI index (CD4/CD8) decreased as the severity increased and was especially low at K05.3; and LTCI significantly increased in all groups. Our results indicate an increase in T-lymphocyte deficiency and impaired immunoregulation of the cellular link of immunity in response to the effects of bacteria, viruses, protozoa, fungi, and other antigens, allergens, and is manifested by a decrease in anti-infectious resistance in patients with periodontitis.

The indices of the humoral link of immunity in the group of patients with K05.0 were characterized by a slight increase in the relative number of B-cells (CD20+) in comparison with the control group and a 2.4-fold decrease in the relative number of B-cells (CD20+) in the

group of patients with K05.3. The values of the LBCI significantly exceeded the values in the control group in the groups of patients with K05.1 and K05.3. The concentration of serum immunoglobulins reflects the functional state of the B-cell link of immunity, mediates the cascade development of the immune response, and can partially determine the effectiveness of the final, effector responses of cellular immunity in inactivating and eliminating bacterial, viral, and fungal antigens. The levels of immunoglobulins, the main classes in patients in our study did not significantly differ from the level of values in the control group. There was a tendency to an increase in these indicators, which reflects an increase in the failure of the functional state of the B-cell link of immunity. The indicators obtained by us show defects in the humoral link of immunity in patients with periodontitis. A decrease in the IgG concentration may be due to its participation in the formation of CIC. An increase in the CIC content in the peripheral blood may indicate an active binding of antigens entering the bloodstream. The CIC levels significantly increased in comparison with the control group by 2-3 times, which indicates the role of immunopathological reactions in the pathogenesis of IPDs, increasing in chronic infectious diseases, concomitant diseases in which the constant production of antigen by an infectious agent is combined with an immune response to it. The state of natural defense factors that carry out nonspecific protection against microorganisms (especially of a viral nature) and ensure, in general, the constancy of the cellular composition of the body, was characterized by an increase in the content of CD16+ lymphocytes (NK cells) in all groups of patients and a decrease in the leuko/CD 16 index in IPD patients, a decrease in the phagocytic, oxygen-dependent metabolic activity of leukocytes in patients with chronic generalized periodontitis (CGP), which indicates the suppression of the absorptive and bactericidal activity of phagocytes. The relative indices of the stimulated NBT-test decreased in the groups of patients with K05.2 and K05.3, which reflects a decrease in the reserve capacity of phagocytes. Oxygen-dependent metabolic activity of leukocytes, spontaneous and stimulated in patients with IPDs, decreased in comparison with the control group, which indicates the suppression of the absorptive and bactericidal activity of phagocytes. The NBT stimulation index also decreased in the groups with K05.0, K05.1, K05.2 and increased in the group with K05.3 above the level of the control group, which reflects a decrease in the reserve capacity of phagocytes (Table 2).

Table 2: ù Indicators of immunity in patients with iIPDs (M ± m).

Indicators	Control (n=20)	K05.0 (n=30)	K05.1 (n=30)	K05.2 (n=30)	K05.3 (n=30)
Leukocytes x109 /l	5.95 ± 1.33	6.53 ± 1.28	6.74 ± 0.38	7.65 ± 1.61	8.15 ± 1.76*
Lymphocytes, (%)	30.12 ± 0.56	30.41 ± 0.47	30.23 ± 0.82	30.35 ± 0.76	31.43 ± 1.65*
CD3, (%)	65.70 ± 1.11	66.13 ± 1.16	66.42 ± 2.44	56.13 ± 1.42*	58.78 ± 2.23 *
CD4, (%)	39.44 ± 1.12	39.14 ± 1.21	37.32 ± 1.26	36.33 ± 1.42*	34.35 ± 1.26*
CD8, (%)	27.62 ± 1.33	26.81 ± 1.24	27.42 ± 1.12	28.16 ± 1.24	28.38 ± 1.18
CD4/CD8	1.42 ± 0.15	1.45 ± 0.22	1.36 ± 0.14	1.29 ± 0.12	1.21 ± 0.11*
LTCI, units	5.72 ± 0.12	5.83 ± 0.16	7.84 ± 0.14**	9.22 ± 0.12**	8.01 ± 0.12**
CD20, (%)	12.16 ± 1.11	12.68 ± 1.53	11.12 ± 0.22	11.08 ± 0.21	8.14 ± 0.11**
IgA, (%)	10.36 ± 0.13	10.52 ± 0.22	10.20 ± 0.34	10.73 ± 0.14	10.36 ± 0.31
IgM, (%)	7.61 ± 0.13	7.78 ± 0.16	9.68 ± 0.38	9.88 ± 0.36	9.91 ± 0.28
IgG, (%)	80.76 ± 2.32	80.44 ± 2.28	80.13 ± 2.31	79.54 ± 2.40	79.42 ± 2.32
CIC, units	32.72 ± 2.64	65.36 ± 3.32**	67.34 ± 3.24**	70.34 ± 3.53**	93.13 ± 3.75**
LBCI	31.32 ± 1.11	29.68 ± 1.52	44.93 ± 1.64*	40.26 ± 1.57*	74.09 ± 1.82**
CD16, (%)	12.61 ± 1.17	16.57 ± 1.35	18.63 ± 1.54	26.79 ± 3.14*	27.86 ± 2.47*
Leuko/CD16	31.31 ± 1.18	26.12 ± 1.35*	30.64 ± 1.73	15.36 ± 1.25**	18.11 ± 1.26**
Segmentonuclear neutrophils (%)	56.88 ± 3.24	58.23 ± 1.71	60.35 ± 1.27	58.46 ± 2.41	59.48 ± 2.32
Leukocyte phagocytic activity (LPA), (%)	61.21 ± 1.63	65.22 ± 2.14	56.41 ± 2.23	39.14 ± 1.82*	34.66 ± 1.86*
Spontaneous NBT, (%)	17.24 ± 1.16	17.14 ± 1.12	17.03 ± 1.08	16.82 ± 0.23*	12.87 ± 0.74**
Stimulated NBT, (%)	24.51 ± 1.71	22.69 ± 0.76	24.32 ± 1.23	19.34 ± 0.74*	19.45 ± 0.74*
Stimulation index of NBT, units	1.42 ± 0.67	1.32 ± 0.06	1.43 ± 0.08	1.15 ± 0.09*	1.51 ± 0.08

Note: * - the difference with the control is statistically significant (p <0.05),

** - the difference with the control is statistically significant (p <0.01).

Therefore, the general pattern of the immune system's response in IPD is the development of T-link insufficiency (decrease in CD3, CD4, LTBI), immunoregulatory disorders (IRI), and an increase in B-link insufficiency with an increase in the severity of the disease. The state of natural defense factors in patients with IPDs is characterized by a decrease in phagocytic activity and reserve capacities of phagocytes in patients with K05.2 and K05.3 periodontitis. Chronic K05.3 periodontitis is characterized by a pronounced suppression of the T- and B-link, and a decrease in the immunoregulatory index with an increase in the number of CD16 lymphocytes, which indicates an inadequate immune response. The suppression of the absorption, bactericidal activity, and reserve capabilities of phagocytes against the background of an increase in the content of immune complexes indicates the presence of an immunocomplex autoimmune component in the pathogenesis of this disease. The presence of somatic pathology in patients weakens the body's defenses, indirectly creates conditions for negative effects on the periodontium of the microflora present in the oral cavity and endogenous periodontopathogenic factors that contribute to autosensitization and the development of immunopathological processes.

CONCLUSION

Thus, the state of general immunity in IPD patients is characterized by a combined insufficiency of the T-link, B-cell link of lymphocytes (CD20+), oxygen-dependent metabolism of segmentonuclear neutrophils with an increase in the level of NK cells CD16+, phagocytic activity, and CIC in the blood. The results obtained in our study suggest the need for a comprehensive examination and successive treatment of patients with IPDs by internal medicine specialists, a dentist specializing in periodontitis treatment, and an immunologist.

REFERENCES

1. Bulgakova AI, Medvedev YA, Zubairova GS. Immunological aspects of periodontitis. LAP Lambert Academic Publishing 2012; 125.
2. Bulgakova A, Shafeev I, Galeev R, et al. Clinical characteristics of patients with inflammatory periodontal diseases by prosthetic designs. Clin Periodontol 2015; 42:138-139.
3. Orekhova LY, Kudryavtseva TV, Cheminava NR, et al. Dental health problems in young people (literature review). Peridentol 2014; 2:3-5.
4. Yanushevich OO, Dmitrieva LA, Revazova ZE. Periodontitis in the 21st century. Moscow: MGMSU; 2012; 366.
5. Igic M, Kesic L, Lekovic V. Chronic gingivitis: the prevalence of periodontopathogens and therapy efficiency. Eur J Clin Microbiol Infect Dis 2012; 31:1911-1915.
6. Gilmiyarova FN, Radomskaya VM, Gilmiyarov EM. Phenotypic features of indicators of humoral immunity in patients with chronic generalized periodontitis with different blood groups. Biomeditsinskaya Khimiya 2011; 57:650-656.
7. Averyanov SV, Akateva GG, Pupykina EV. The prevalence and intensity of periodontal disease among students in Ufa. Stomatol Detskogo Vozrasta Profilaktika 2015; 3:51-54.
8. Khaitov RM, Ilina NI. Allergology and immunology: national guidelines. Moscow: GOETAR-Media 2009; 230.
9. Grudyanov AI, Tkacheva ON, Avraamova TV, et al. The issue of the relationship between inflammatory periodontal diseases and cardiovascular pathology. Stomatol 2015; 94:50-55.
10. Gareev EM. A brief overview of the basic methods of mathematical and statistical processing of biomedical information. Ufa: Publishing house of GOU VPO “Bashgosmeduniversitet” 2009; 109.