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The role of the system of hemostasis of blood and saliva in the development of the inflammatory process in the periodontium in patients with cardiovascular pathology

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Abstract:
The aim of this study was to assess the state of indicators of the hemostasis system of blood and saliva in patients with CGP concomitant CHF. 109 people aged 40 to 60 years, with signs of chronic generalized periodontitis (CGP) concomitant CHF were examined. In accordance with the objectives of the study, 3 groups were formed: Group I - 50 patients (39 men and 11 women) with chronic generalized periodontitis on the background of AH and IHD, Group II - 34 patients (22 men and 12 women) with CGP on the background of AH and IHD combined adentia, group III - 25 patients (15 men and 10 women) with periodontal pathology (CGP), without diseases of the cardiovascular system (CVS). Revealed hyperhomocysteinemia and an increase in the procoagulant activity of saliva and blood, which is a consequence of not only CGP, but also atherosclerotic process, in which a thrombogenic threat is created due to the involvement of endothelial cells of the oral mucosa in this process.

1. INTRODUCTION

One of the pressing problems of dentistry is periodontal disease, which is associated with a high prevalence, intensity of the process, the subsequent formation of a chronic odontogenic focus of infection and its adverse effect on the body. According to WHO statistics (2010), the frequency of periodontal disease in different countries of the world ranges from 80 to 100%, and the prevalence of chronic inflammatory periodontal diseases is steadily increasing not only among the elderly, but also among young people. Therefore, the widespread prevalence of inflammatory periodontal diseases is an urgent medical and social problem. The results of studies over the past two decades indicate significant clinical and pathogenetic relationships between periodontal diseases and internal organs. One of the pressing issues today is the question of the association of dental diseases with pathology of the cardiovascular system.

For example, in patients with cardiovascular diseases, there is a greater degree of damage to periodontal tissues, in comparison with patients without them. Analysis of accumulated factors and observations leads to the understanding that the development of a generalized inflammatory process in the periodontium occurs against the background of complex disorders of homeostatic balance in the body. were found and large changes in the hemomicrocirculation of periodontal tissues in these patients.

According to modern data, persistent oral microflora can cause the development of cardiovascular pathology in two ways: direct - bacteria penetrate the vascular endothelium through the bloodstream, causing endothelial dysfunction, inflammation and atherosclerosis, and / or indirectly - through stimulating the production of mediators with atherogenic and

pro-inflammatory systemic effects. The researchers reported that for every 20% increase in bone loss, there is a 40% increase in the likelihood of heart disease. Cardiovascular diseases are the unfavorable background against which, with the participation of other unfavorable factors, various pathological changes in the body can develop, in particular, in the oral cavity. Manifestations of changes in the oral cavity in IHD are determined by the duration and severity of the disease. The results of many studies indicate the existence of a significant relationship between periodontal disease and coronary heart disease, confirmed the need to implement effective programs for the prevention and treatment of dental diseases for patients with ischemic heart disease. Patients with coronary heart disease, upon admission to the hospital, require a planned dental examination, and, if necessary, medical measures. The high prevalence of dental diseases and their close relationship with cardiac pathology convinces of the need to assess its pathogenesis from the standpoint of systemically acting mechanisms that should be taken into account when developing comprehensive approaches to their friendly treatment. The analyzed information sources on the state of the periodontium in patients with cardiovascular pathology indicate a high prevalence of dental diseases in patients with disorders of the cardiovascular system. Despite numerous studies in this direction, the problem of oral diseases in patients with cardiovascular pathology, in particular, ischemic heart disease, remains insufficiently studied. This states the need for in-depth research on this issue. The aim of this study was to assess the state of indicators of the hemostasis system of blood and saliva in patients with CGP concomitant ischemic heart disease.

2. MATERIALS AND METHODS OF THE STUDY

We examined 109 people aged 40 to 60 years, all patients showed signs of chronic generalized periodontitis (CGP). In accordance with the objectives of the study, 3 groups were formed: Group I - 50 patients (39 men and 11 women) with chronic generalized periodontitis against the background of AH and IHD: exertional angina pectoris II-IV functional class (according to the Canadian classification), aged from 43 to 60 years. Group II - 34 patients (22 men and 12 women) with CGP on the background of AH and IHD combined adentia who are at the stages of treatment for CVD, Group III - 25 patients (15 men and 10 women) with periodontal pathology (CGP), without diseases of the cardiovascular system (CVS) at the age of 40 to 60 years. It was mandatory for all study participants to read and sign an informed consent approved by the local ethics committee of the Ministry of Health of the Russian Federation. It should be noted that all patients included in the groups were examined by a cardiologist. To clarify the diagnosis of coronary artery disease, all patients underwent physical and instrumental examination: ECG at rest in 12 conventional leads, two-dimensional echocardiography, coronary angiography, 24-hour blood pressure monitoring, 24-hour Holter monitoring and laboratory studies. All patients were examined by a dentist. A standard clinical dental examination was carried out: assessment of patient complaints, medical history and life, objective status, assessment of periodontal indices. The level of individual hygiene and the state of periodontal tissues were assessed in all patients. The hygienic state of the oral cavity was determined by the Green - Vermillion (OHI-S) method (Simplified Oral Hygiene Index). The depth of the periodontal pocket (PC) and the loss of the periodontal attachment (PZP) were measured. Gingival bleeding was assessed using the H.R. Muhleman. Tooth mobility was determined using the Miller scale (modified by T.J. Fleszar). To identify the developed forms of periodontal pathology used the periodontal index (PI, Rüssel, 1956); the degree of gingival recession according to P.D. Miller (1985). To determine the qualitative and quantitative composition of microorganisms in periodontal pockets, the method of polymerase chain reaction in "real time" was used. X-ray methods made it possible

to assess the depth and severity of periodontal lesions, focusing on the level of bone resorption of the alveolar parts of the jaws. Blood and saliva were collected on an empty stomach before and after the course of treatment. In saliva, procoagulants were determined (prothrombin and thrombin time, activated partial thrombin time (APTT) and fibrinolytic activity, and in the blood, the content of fibrinogen and soluble fibrin-monomeric complexes (RFMK) was additionally assessed. All methods used are described in the Barkagan hemostasis system study guide. .S.,Momot AP (2001). The concentration of homocysteine and haptoglobin was determined by the enzyme immunoassay using kits from the company "HUMAN" Determination of the content of free hemoglobin as a marker of intravascular hemolysis in patients was carried out using the method recommended by V.I. Kozlovsky and A.V. (2014). Statistical processing of the obtained results was carried out using the methods of parametric and nonparametric statistics. Methods of descriptive statistics consisted in assessing the arithmetic mean (M), the mean error of the mean (w) - for features with a continuous distribution, as well as the frequency of occurrence of the feature in with a discrete value. To assess the intergroup differences in the mean values of features with continuous distribution, we used t - Student's test.

3. RESULTS OF THE STUDY AND ITS DISCUSSION

When analyzing the dental status of patients, more pronounced changes in the periodontal indices were found, which indicate inflammatory processes in the periodontium of patients of the first and second observation groups. The average value of the PMA index in the observation group was 63% (in the comparison group - 34%), the periodontal index Russel-PI = 4.9 ± 0.3 (in the comparison group - 1.4 ± 0.1). The PBI bleeding index in the observation group is almost three times higher than in the comparison group (3.1 and 1.1, respectively), although the mean values of the OHI-S hygiene index in patients of the observation group and the comparison group differ slightly: 2.5 and 2.3 ...

The main factor affecting the state of the periodontium in patients without concomitant pathology is the hygienic state of the oral cavity. The values of hygiene indices in the observation group were statistically significantly higher than in the comparison group, which indicated a deterioration in the state of oral hygiene. Based on the complaints identified, it should be assumed that the majority of patients with coronary heart disease have bleeding gums; they associate this with the intake of antiplatelet agents and anticoagulants, and not with unsatisfactory hygienic care. Analysis of the obtained research results showed that the majority of patients of group I complained of bleeding gums (spontaneous, when eating and brushing teeth) - 57.9%. In patients of group II, bleeding gums were observed only in 68.7%. Painful sensations when chewing food and brushing teeth were more often observed in patients of group II - 69.4%, in group II - 20%. No less characteristic complaint in generalized periodontitis is tooth mobility, so. group I patients noted this symptom in 65.1% of cases, versus 72% of group II patients.

Table 1 Patientcomplaints

	Group 1 Patients n=50	Group 2 patients n= 34	Comparisongroupn=25
Bleedinggums	31 (61%)	28 (83%)	6 (25%)

Painful sensations (when experiencing food, brushing teeth)	26 (52%)	24 (71%)	4 (17%)
Toothmobility	27 (54%)	23(67%)	5 (18%)
Drymouth	31 (62%)	27 (78%)	10 (39%)
Burningtongue	15 (29%)	12 (34%)	5 (18%)
Smellfromthemouth	38 (76%)	28 (84%)	11 (42%)

Thus, all patients of groups I and II presented complaints. The study of periodontal pockets revealed that in patients of group I, the average value of the pocket depth was 3.7 ± 1.5 mm. in patients of group II - 4.1 ± 0.3. To assess the state of the periodontium, the CPITN index was calculated. These tables show that more severe periodontal damage is observed in the second group than in the first group of patients, this is shown by high values of the CPITN index. Analysis of the OHI-S hygiene index (G&V) shows that higher values are noted in both the first and second groups. The PI index, which reflects the severity of periodontal lesions, in the first group is 3.9 ± 0.5, and in the second group, 4.1 ± 0.3. At the same time, the maximum value of the PI index was noted with CGP against the background of coronary artery disease with combined adentia. It is 4.1, which corresponds to a moderate-severe degree of chronic generalized periodontitis.

To determine the qualitative and quantitative composition of the microflora of periodontal pockets in the groups, five periodontal pathogens were studied: A. actinomy-cetemcomitans, P. gingivalis, T. forsythensis, P. intermedia, T. denticola, which are the most significant in the development of generalized periodontitis. The results of the analysis of microflora in the area of the gingival pockets, carried out using PCR in "real time", are presented in the table.

Table 2 The frequency of detection of periodontal pathogens in different groups

	Group 1 Patients n=50	Group 2 patients n= 34	Comparison group n=25
A.actinomycetemcomitans	36 (71%)	27 (80%)	7 (28%)
P. gingivalis	38 (76%)	30 (89%)	7 (27%)
T. forsythensis	31 (61%)	22 (66%)	9 (36%)
T. denticola	29 (58%)	21 (61%)	8 (34%)
P. intermedia	27 (54%)	21 (62%)	7(28%)

Most often found in group II with combined pathology: DNA of Porphyromonasgingivalis (Pg) in 89% of people and DNA of Tannerellaforsythensis (Tf) in 66% of cases, DNA of Tannerellaintermedia in 62% of cases and DNA of Treponemadenticola in 71% of cases (table). In the control group the following prevailed: Least of all in the group with combined

pathology of the cardiovascular system there was a periodontopathogen: Aggregatibacteractinomycetemcomitans (Aa) in 28%, and in the control group Prevotellaintermedia (Pi) in 28% of cases. Thus, it can be stated that all patients with cardiovascular pathology have one or another degree of bacterial damage to periodontal tissues, where Porphyromonasgingivalis and Aggregatibacteractinomycetemcomitans were more often observed in the first and second groups of patients.

In the studies of I.I. Chukuaev, (2007), it is indicated that P. gingivalis uses hemin (the breakdown product of hemoglobin) as food in the inflammatory exudate (periodontal fluid). To obtain hemin, the bacterium uses specific receptors of the outer membrane, proteases (gingipains) and lipoproteins. Therefore, the causative agent of gingivitis intensely destroys red blood cells and increases the amount of free hemoglobin in the blood. As can be seen from the presented research results (table 3), the level of haptoglobin in the blood has a peculiar dynamics. In the 1st group of patients, the haptoglobin index is 41.5% lower than the indicators of the comparison group, while in the patients of the 2nd group it did not decrease by 56% when compared with the indicators of the comparison group. Consequently, an increase in free hemoglobin in the blood activates the synthesis of haptoglobin by the liver for the binding of free hemoglobin in patients with a combined form of the disease and the formation of a haptoglobin / hemoglobin complex.

Table 3 The content of haptoglobin and the level of free hemoglobin in the blood in patients with CGP concomitant ischemic heart disease

	Group 1 Patients n=50	Group 2 patients n= 34	Comparisongroupn=25
Haptoglobinmg / dl	72.54±6.35*	54.38±4.17*	124.32±10.46
Freehemoglobin g / l	0.079±0.001*	1.06±0.09*	0.044±0.002

Note: * - reliability of differences P <0.05 relative to the comparison group

It should be noted that each mechanical damage to the periodontal tissues with gingivitis leads to an increase in the formation of free hemoglobin, which is food for P. gingivalis and its reproduction. In turn, the local activation of this process leads not only to destruction and reparative processes in the periodontal tissues but also affects the coagulation system of both saliva and blood. In the case of ongoing tissue destruction or the presence of an infectious process, these endogenous toxins can persist for a long time in the body and cause a systemic and local inflammatory reaction in the cardiovascular system.

The observed increase in the concentration of free hemoglobin in the blood, against the background of a low level of haptoglobin, can adversely affect the functional state of platelets and, in turn, can contribute to the hemostatic system in this contingent of patients. As can be seen from the results of the studies presented in Table 4, we observed significant changes in the parameters of the hemostasis system in saliva in the examined patients. Thus, an increase in procoagulant and a decrease in fibrinolytic activity was revealed in saliva. The concentration of homocysteine in saliva in the examined patients was also increased.

The revealed hyperhomocysteinemia and an increase in procoagulant activity in saliva are a consequence of not only CGP, but also a violation of microcirculation, which creates a thrombogenic threat due to the involvement of endothelial cells of the oral mucosa in this process.

Table 4

Indicators of the hemostasis system and the level of homocysteine in saliva in patients with CGP concomitant ischemic heart disease

	Group 1 Patients n=50	Group 2 patients n= 34	Comparisongroupn=25
Prothrombintime,%	61.43±5.04*	60.12±5.21*	76.87±4.18
APTT,%	66.72±4.83*	60.34±6.04*	82.01±5.34
Thrombintime,%	61.54±4.67*	57.78±4.67*	81.56±5.53
Fibrinolysis,%	84.51±5.43	88.53±6.06*	74.83±4.28
Homocysteine, μmol / L	0.71±0.14*	0.83±0.15*	0.32±0.03

Note: * - reliability of differences P <0.05 relative to the comparison group

The revealed hyperhomocysteinemia and an increase in procoagulant activity in saliva are a consequence of not only CGP, but also a violation of microcirculation, which creates a thrombogenic threat due to the involvement of endothelial cells of the oral mucosa in this process.

Analysis of the hemostatic system and homocysteine parameters in the blood of the examined patients with CGP combined ischemic heart disease showed a state of hypercoagulability, as evidenced by a shortening of prothrombin time, APTT, thrombin time, an increase in the concentration of fibrinogen, an increase in fibrin-monomer complexes (RFMC), inhibition of fibrinolysis (Table 5). The concentration of homocysteine in the blood in patients of both groups was also increased in relation to the indicators of the comparison group by almost 1.5-2 times.

Thus, in patients with CGP combined with IHD, especially in the group of patients with edentulous blood and saliva, a high procoagulant potential was noted against the background of inhibition of fibrinolysis and an increase in the concentration of homocysteine, which is apparently due to an increase in free hemoglobin, which activates the vascular-platelet link of the hemostatic system.

Table 5
Indicators of the blood coagulation system and homocysteine metabolism in patients with CGP concomitant ischemic heart disease

	Group 1 Patients n=50	Group 2 patients n= 34	Comparison group n=25
Prothrombintime,%	16.53±0.89*	16.21±1.02*	22.16±1.23
APTT, s	30.54±2.64*	28.97±2.36*	43.54±2.63
Thrombintime, s	16.11±0.87	16.0±0.63	19.54±1.18
Fibrinogen, g / l	4.83±0.37*	5.69±0.33*	3.31±0.24

RFMK, mg / 100 ml	7.91±0.56*	8.14±0.62*	3.43±0.28
Fibrinolysis, min	176.73±8.39	179.67±9.01	138.51±7.58
Homocysteine, μmol / L	14.52±1.32*	17.34±0.71*	8.19±0.72

Note: * - reliability of differences P <0.05 relative to the comparison group

On the other hand, structural hypercoagulation observed in patients with impaired functional state of the cardiovascular system may be a risk factor for thrombotic complications. At the same time, against the background of the observed microcirculation disorders, trophic insufficiency in the periodontal tissues and destructive processes, a new recurrence of inflammation in the periodontal tissues may occur.

Thus, in the process of studying the dental status in patients with chronic inflammatory diseases of the periodontal tissues of concomitant cardiovascular pathology, the most informative hygienic and periodontal indices were established, the characteristic features of reactive glycoprotein and some indicators of the blood and saliva coagulation system were identified, which can be used as a control. for dental support of patients with coronary artery disease during dental implantation.

4. CONCLUSIONS

1. It was revealed that each mechanical damage to the periodontal tissues with gingivitis leads to an increase in the formation of free hemoglobin against the background of P. Gingivalis toxins, which in turn can cause not only destructive and reparative processes in the periodontal tissues but also affect the coagulation system and saliva and blood.
2. Revealed hyperhomocysteinemia and an increase in procoagulant activity in saliva are a consequence not only of CGP, but also a violation of microcirculation, in which a thrombogenic threat is created due to the involvement of endothelial cells of the oral mucosa in this process.
3. In patients with CGP combined with ischemic heart disease, especially in the group of patients with edentulous blood, a high procoagulant potential was noted against the background of inhibition of fibrinolysis and an increase in the concentration of homocysteine, which is apparently due to an increase in free hemoglobin, which activates the vascular-platelet link of the hemostasis system.

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