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The State of the Kallikrein-Kinin System in Patients with Periodontal Diseases on the Background of Primary Arterial Hypotension

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Abstract

The level of blood supply to individual organs and tissues, including periodontal tissues, directly depends on the state of central hemodynamics. Consequently, a decrease in systemic blood pressure in primary arterial hypotension leads to a change in blood flow in the microcirculatory bed of the periodontium and complicates the course of pathological processes in it. In the available literature, there are only isolated works devoted to the study of the kallikrein-kinin system of blood in primary arterial hypotension. The study involved 60 patients with chronic inflammatory periodontal diseases and background primary arterial hypotension (group i), 60 patients with inflammatory periodontal diseases and normal blood pressure (group ii), and 40 patients with intact periodontal condition and normal blood pressure (control). Thus, the characteristic of the dental status of patients with different levels of systemic blood pressure indicates a deterioration in the indicators of hygienic indices with background primary arterial hypotension.

Discipline: Medicine, Dentistry.

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1 Introduction

The increasing prevalence of chronic gingivitis and periodontitis over the past decade indicates the need to develop new modern, effective methods of treatment and prevention. In recent years, there has been an increase in the interest of dentists in the problem of microcirculatory disorders in the tissues of the dental system, as one of the risk factors for the development of periodontal pathology [1]. This is due to a large number of factors that can cause them, both exogenous and endogenous. The problem of periodontal diseases is very relevant now. Thus, more than 60% of the population under the age of 40 suffer from various periodontal diseases, in the older age group this indicator reaches 100% [2]. Periodontal diseases often occur against the background of concomitant diseases – digestive disorders, metabolic disorders, cardiovascular and endocrine diseases, sensitization, and infection of the body [3-6].

2 Literature Review

Over the past decade, interest in the relationship of periodontal diseases with atherosclerosis, and as a consequence of the development of this pathology – cardiovascular diseases, has grown significantly. According to modern concepts, the mechanism of influence of inflammatory diseases on atherogenesis is considered as follows: periodontal pockets, being a reservoir of pathogenic microorganisms, secrete bacterial components (endotoxins) into the bloodstream, which mediately, with the help of anti-inflammatory cytokines and other inflammatory mediators that are produced by responder cells, cause vascular alteration, hyperlipidemia and lipid infiltration of the vascular wall, and they also stimulate and support the inflammatory response [7-9]. Thus, the atherogenic process is started and maintained.

In periodontal diseases against the background of coronary heart disease, there is a higher level of violations of regional hemodynamics, microcirculation, activation of free radical oxidation with a decrease in the antioxidant activity of the blood and disorders in the hemostasis system [10-12]. The clinical course of inflammatory and dystrophic-inflammatory periodontal diseases is significantly affected by microcirculatory disorders in its tissues, often predestined by cardiovascular pathology and traumatic lesions of the spinal cord. Arterial hypertension causes lymphostasis and increased permeability of the capillary wall, which is accompanied by severe edematous syndrome and bleeding gums [13,14].

The level of blood supply to individual organs and tissues, including periodontal tissues, directly depends on the state of central hemodynamics. Consequently, a decrease in systemic blood pressure in primary arterial hypotension leads to a change in blood flow in the microcirculatory bed of the periodontium and complicates the course of pathological processes in it [15].

Regulation of systemic and regional blood flow is a complex, multicomponent, interdependent mechanism in which the kallikrein-kinin blood system plays an important role [16]. This is due to the powerful influence of kinins on the functional activity of the heart, kidneys and blood vessels, the close connection of the kallikrein-kinin system with the autonomic nervous system, catecholamines, renin-angiotensin system, prostaglandins, corticosteroids and other

humoral factors regulating blood pressure. As a result of complex relationships involving the kallikrein-kinin system, there is a change in the state of coronary blood flow, functional activity of the myocardium, vascular tone, and rheological properties of blood [17-19].

In the available literature, there are only isolated works [17,18,20-22] devoted to the study of the kallikrein-kinin system of blood in primary arterial hypotension, but its effect on the incidence of soft tissues in the dental system has not been sufficiently studied.

Objective: to clarify the features of the course of chronic inflammatory periodontal diseases and the state of the main components of the kallikrein-kinin blood system in patients with background primary arterial hypotension.

3 Method

The study involved 60 patients with chronic inflammatory periodontal diseases and background primary arterial hypotension (group I), 60 patients with inflammatory periodontal diseases and normal blood pressure indicators (group II), and 40 patients with an intact periodontal condition and normal blood pressure indicators (control).

In the course of the study, the dental status was studied, and a clinical and instrumental examination of patients of two age subgroups was conducted: subgroup A - 20-25 years old and subgroup B – 35-44 years old. Each subgroup of patients with periodontal pathology is formed from 30 research objects (Table 1)

Table 1: Study groups of patients with periodontal pathology.

	subgroup A (20-25 years old)	subgroup B (35-44 years old)
chronic inflammatory periodontal diseases + primary arterial hypertension (group I)	30	30
chronic inflammatory periodontal diseases + normal blood pressure (group II)	30	30
Control	20	20

Patients with catarrhal gingivitis, mild periodontitis, and moderate periodontitis were selected in groups of patients with chronic inflammatory periodontal diseases. In the diagnosis of periodontal diseases, the classification approved at the meeting of the Presidium of the Periodontology Section of the Dental Association of Russia (2001) was used [23].

A comprehensive examination of the periodontal condition included: anamnesis collection, examination and instrumental and functional research methods [24-26].

The assessment of the condition of periodontal tissues was carried out according to the CPITN index using a special button probe in the areas 17, 16, 11, 26, 27, 36, 37, 31, 46, 47 calculations of the PMA index, gingival sulcus bleeding index SBI and periodontal index (PI) were used in the work [27]. The hygienic condition of the oral cavity was assessed using the simplified hygienic index OHI-S [27].

To assess the state of the kallikrein-kinin system, the content of kallikrein, precallikrein, and the activity of plasma protease inhibitors (α1 – antitrypsin (α1-AT) and α2–macroglobulin (α2-MG)) were determined according to the methodology presented by Rzhepakovsky et al. (2022) [28].

Statistical processing of the obtained data was carried out using the standard mathematical software program Statistics for Windows 6.0. For quantitative indicators, the average value of M and the standard error of the average m was calculated. To compare the values of the indicators in the two groups, the methods of parametric and nonparametric statistics were used: the Student's t-test for normally distributed indicators [29,30]. Statistically significant differences were considered corresponding to the estimate of the probability error $p<0.05$.

4 Results and Discussion

Examination of patients with primary arterial hypotension and arterial normotension revealed the existing diseases of the dental system: caries, gingivitis, periodontitis, dental anomalies, etc. Patients of the control groups with normal blood pressure and intact periodontal disease did not present dental complaints. The OHI-S index was 0.56±0.07; the PMA, PI and SBI indices were not determined.

Among 30 patients aged 20-24 years with inflammatory periodontal diseases on the background of systemic arterial hypotension, 63.3% of the examined patients revealed catarrhal gingivitis, 30.0% - mild periodontitis and 6.7% - moderate periodontitis. In 30 patients aged 20-24 years of the clinical group with a normal level of blood pressure, catarrhal gingivitis was detected in 76.7%, periodontitis of only mild severity - in 23.3% of the examined.

In the older group of patients with the presence of inflammatory diseases in periodontal tissues against the background of primary arterial hypotension, catarrhal gingivitis was detected in 40.0%, mild periodontitis - in 46.7% of the examined, moderate periodontitis - in 13.3%, and in patients with arterial normotension - 53.3%, 40.0% and 6.7%, respectively.

Table 2: Features of the inflammatory process in periodontal disease with background primary arterial hypotension (M ± m).

Groups \ Indicators		OHI-S	PMA%	SBI	PI
Intact periodontal		0.56 ± 0.07	0	0	0
Catarrhal gingivitis	Primary arterial hypertension	2.14 ±0.05♦♦*	36.2±1.4*♦	1.56±0.07*♦	1.43±0.09*
	Normal blood pressure	1.89± 0.07*	31.4± 1.5*	1.38± 0.04*	1.27±0.06*
Mild periodontitis	Primary arterial hypertension	2.36 ± 0.08*♦	43.7± 1.2*♦	1.73± 0.06*♦	3.33 ±0.05*♦
	Normal blood pressure	2.13±0.07*	39.1± 1.3*	1.51±0.07*	3.11±0.08*
Moderate periodontitis	Primary arterial hypertension	2.56 ±0.09*♦	51.1± 1.8*♦♦	2.67±0.09*♦♦♦	4.01±0.05*♦♦♦
	Normal blood pressure	2.31± 0.04*	44.2± 0.9*	1.96±0.06*	3.68±0.04*

Note: *** - the reliability of the differences when compared with the control ($p>0,001$), ♦ - reliability of differences between groups ($p>0,05$). ♦♦ - reliability of differences between groups ($p>0,01$), ♦♦♦ - reliability of differences between groups ($p>0,001$).

The indicators of hygiene indices in the age subgroups did not differ statistically significantly, therefore, the values in the groups were calculated depending on the severity of periodontal lesion (Table 2).

The PMA index in patients with catarrhal gingivitis on the background of primary arterial hypotension was 36.2±1.4, the hygiene index ONI-S was 2.14±0.05, the periodontal index PI was 1.43±0.09, bleeding according to the SBI index was 1.56±0.07, which also confirmed the presence of inflammation.

The clinical manifestations of inflammation in catarrhal gingivitis were statistically significantly less pronounced against the background of normal blood pressure values: the PMA index was 31.4±1.5, the hygiene index ONI-S was 1.89±0.07, the periodontal index PI was 1.27±0.06, bleeding according to the SBI index was 1.38±0.04.

With mild periodontitis and background primary arterial hypotension, the OHI-S index was 2.36±0.08, its values were more than 4 times higher than in the control group, the periodontal index PI was 3.33±0.05, the bleeding index SBI was 1.73±0.06.

With mild periodontitis against the background of normal blood pressure, dental indices were significantly lower than in patients with hypotension, so the OHI-S index was 2.13±0.07, and the periodontal index was 3.11±0.08; the SBI bleeding index was 1.51±0.07.

The most significant changes were noted in periodontitis of moderate severity: Thus, with background primary arterial hypotension, the OHI-S index was 2.56±0.09, the periodontal index was 4.01±0.05, the SBI bleeding index was 2.67±0.09, in patients with normal blood pressure levels - 2.31±0.04; 3.68±0.04 and 1.96±0.06, respectively.

Analysis of CPITN index indicators also revealed that the intensity of individual symptoms of periodontal pathology was significantly higher in the group of patients with primary arterial hypotension than in patients with normal blood pressure and in the control (Table 3).

Table 3: Intensity of pathological changes in periodontal tissues (CPITN index) in patients with primary arterial hypertension and normal blood pressure (M±m)

Indicators / Groups		Sextants			
		Healthy	Bleeding	Tartar	Pocket
I	A	0.59±0.06***♦♦♦	1.84±0.05♦♦	2.69±0.03**♦♦♦	0.21±0.004♦♦♦
	B	0.47±0.05***♦♦♦	1.89±0.07	2.78±0.05♦♦♦	0.26±0.005♦♦♦
II	A	1.69±0.03***	1.65±0.04	3.63±0.06***	0.09±0.004
	B	1.58±0.04***	1.79±0.05	3.69±0.09***	0.14±0.005
Control	A	3.79±0.05	-	2.41±0.08	-
	B	3.41±0.06	-	2.79±0.11	-

Note: *** - the reliability of the differences when compared with the control (p>0,001), ♦ - reliability of differences between groups (p>0,05). ♦♦ - reliability of differences between groups (p>0,01), ♦♦♦ - reliability of differences between groups (p>0,001).

The study of the components of the complement system in all groups with periodontal pathology in comparison with the control revealed statistically significant activation of the kallikrein-kinin system of blood. More significant changes were noted in patients with primary arterial hypertension.

Thus, the activity of kallikrein in patients aged 20-24 years with primary arterial hypotension was 34.24±1.62 mmol/BAEE/min/ml, and at normal blood pressure – 28.62±2.12 mmol/BAEE/min/ml (Table 4). In the group of patients aged 35-44 years with periodontal pathology

on the background of primary arterial hypotension, this indicator was 45.21±3.55 mmol/BAEE/min/ml, and with normal blood pressure – 34.11± 3.64 mmol/BAEE/min/ml.

At the same time, in patients with periodontal pathology, there is a decrease in comparison with the control of the content of the precursor of kallikrein – precallikrein, also more pronounced in patients of both age subgroups with primary arterial hypotension (Table 4).

Table 4: Indicators of activity of the kallikrein-kinin blood system in patients with primary arterial hypertension

Groups		Kallikrein micromole /BAEE/min/ml	Precallikrein micromole /BAEE/min/ml
I	A	34.24±1.62***♦	232.16± 5.29***♦♦♦
	B	45.21±3.55**♦	207.29± 6.52***
II	A	28.62±2.12***	256.28± 4.18***♦♦
	B	34.11±3.64	229.88± 5.19**
Control	A	16.12±2.39	279.71± 5.14
	B	28.54±1.71	259.68 ±7.14

Note: *** - the reliability of the differences when compared with the control (p>0,001), ♦ - reliability of differences between groups (p>0,05). ♦♦ - reliability of differences between groups (p>0,01), ♦♦♦ - reliability of differences between groups (p>0,001).

The study of the content of kininogenase inhibitors revealed a significant increase in the activity of α1-AT and a decrease in α2-MG compared with the control. The most pronounced changes in the activity of inhibitors were noted in both age subgroups with primary arterial hypotension. Thus, the activity of α1-AT in adolescents with primary arterial hypotension was 28.36 ± 0.8 IU/ml, which significantly differed from the indicator in the same age subgroup with normal blood pressure - 25.34±0.7 IU/ml. In the older age subgroup of patients with primary arterial hypotension, the value of α1-AT activity was 41.14±1.2 IU/ml, and at normal BLOOD PRESSURE level - 38.47± 0.8 IU/ml (Table 5).

When comparing the activity of α2-MG in patients with different central hemodynamic settings, a significant decrease in the indicator was revealed in patients with primary arterial hypotension in comparison with patients with normal blood pressure in the older age subgroup (Table 5).

Table 5: Activity indicators of kininogenase inhibitors in patients with systemic blood pressure disorders(M±m).

Groups		α 1-AT activity (IE/ml)	α 2- MGactivity (IE/ml)
Group I	A	28.36± ± 0.8***♦♦	4.61 ± 0.11**
	B	41.14± 1.2***	5.74 ± 0.13***
Group II	A	25.34 ± 0.7**	4.78 ± 0.10*
	B	38.47± 0.8***	6.27 ± 0.12***♦♦
Control	A	22.35 ± 0.7	5.29 ± 0.18
	B	31.72 ± 0.6	7.72 ± 0.14

Note: *** - the reliability of the differences when compared with the control (p>0,001), ♦♦ - reliability of differences between groups (p>0,01).

The obtained results on the study of the activity of kallikrein-kinin system in patients with periodontal tissue damage with different indicators of systemic blood pressure reflect the participation of kallikrein-kinin system in the implementation of the inflammatory response, as well as homeostasis in conditions of reduced systemic blood pressure. At the same time, an increase in the activity of the kallikrein-kinin system of blood, apparently, is aimed at ensuring the adequacy of microcirculation processes in the area of inflammation, especially in conditions of systemic arterial hypotension.

The change in the activity of kininogenase inhibitors is, apparently, a compensatory reaction of the body aimed at preventing depletion of kinin reserves and preventing excessive activation of the kallikrein-kinin system in inflammation and systemic disorders of blood pressure.

5 Conclusion

Thus, the characteristic of the dental status of patients with different levels of systemic blood pressure indicates a deterioration in the indicators of hygienic indices with background primary arterial hypotension. The results of the study indicate a higher prevalence and more severe course of chronic inflammatory periodontal diseases in adolescent and young patients with background arterial hypotension.

The revealed features of the functioning of the kallikrein-kinin blood system certainly affect the state of microhemodynamics of the tissues of the dental system and make a significant contribution to the formation of dental pathology, especially in people with arterial hypotension, causing the severity of the clinical course of the disease.

The results obtained dictate the need to develop adequate treatment regimens that take into account the contribution of disorders of systemic and regional hemodynamics, the state of the kallikrein-kinin system in primary arterial hypotension, especially clinical manifestations of periodontal diseases.

6 Availability of Data and Material

Data can be made available by contacting the corresponding author.

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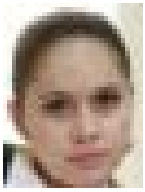

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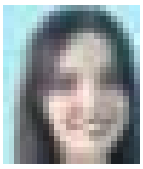

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