Evaluation of the cytokine profile and vascular elasticity in middle-aged men with essential hypertension and combined pathology

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The diagnosis and management of patients with polymorbid cardiovascular pathology is a significant challenge. The pathogenesis of many cardiovascular diseases, such as arterial hypertension, coronary heart disease, angina pectoris, as well as diabetes mellitus, obesity and dyslipidemia are associated with systemic inflammation. The inflammatory process, both at the systemic and local levels, can make a significant contribution to the progression of atherosclerosis and endothelial dysfunction, and provoke the destabilization of blood pressure. Therefore, it is important to develop new approaches to the identification of patients with polymorbid pathology and chronic inflammatory processes in the body. It is known that the presence of the oral cavity inflammation increases the risk of cardiovascular disease. Periodontal pathology, leading to an increased expression of pro-inflammatory cytokines, affects the initiation of atherosclerosis, endothelial dysfunction, vasospasm, and blood pressure dysregulation. It can be assumed that the oral cavity inflammatory processes against the arterial hypertension increase the probability of early vascular aging, the overall cardiovascular risk, and also increase the chance of other diseases of the cardiological profile The research subject was to determine the vascular elasticity parameters and the dynamics of blood pressure daily profile, as well as the level of pro-inflammatory and anti-inflammatory cytokines in persons with arterial hypertension, considering the presence of inflammatory processes in the oral cavity. The structure of comorbidity and a number of laboratory and instrumental data of middle-aged men with arterial hypertension in combination with periodontitis were analyzed in comparison with patients with arterial hypertension without periodontitis and healthy volunteers of the same age. A correlation was shown between the periodontal inflammation level in men with arterial hypertension and the polymorbid cardiovascular pathology presence (diabetes mellitus, dyslipidemia, anxiety and depressive disorders, coronary heart disease, signs of left ventricular hypertrophy by ECG, high ankle-brachial index as a marker of peripheral atherosclerosis), significant variability in blood pressure, an altered cytokine profile with a

predominance of pro-inflammatory cytokines, an increase in “vascular age” on the ASCORE scale, and increased vascular stiffness, assessed by 24-hour blood pressure monitoring using the “VasotensOffice” program.

Keywords: blood vessels elasticity, blood pressure variability, arterial hypertension, cytokines, periodontitis, polymorbidity.

WHO considers circulatory system diseases as one of the leading causes of death worldwide [1]. Despite the improvement of non-invasive and invasive diagnostics methods of the cardiovascular system, new laboratory markers development for predicting vascular accidents, as well as new pharmacological agents on the world drug market (hypocholesterolemic, anti-thrombotic, neurohumoral regulators), cardiovascular diseases (CVD) remain the most common non-infectious pathology in our country. One of the probable reasons is the provision of medical care, in most cases, already at the stage of manifest disease.

Currently, a promising approach to solving this problem is preventive cardiology, whereby it is possible to assess various parameters and risk factors for CVD development. One of these indicators distinguishing a high risk of cardiovascular complications is arterial stiffness [2]. This criterion allows us to assess the processes of the vascular wall early aging as a predictor of the general phenomenon of premature aging in humans.

Currently, various diagnostic techniques are being studied for identifying vascular rigidity and parameters of early vascular aging. These methods include: angiological screening using the VaSera-1500 apparatus evaluating the cardio-ankle vascular index CAVI (Fukuda Denshi, Japan), pulse wave velocity (PWV), central BP and augmentation index assessment, ultrasound examination with pulse changes determination in the arteries diameter and the intima-media layer thickness measurement, atherosclerotic plaques visualization in the blood vessels lumen, ankle-brachial index [3; 4]. The authors identify vascular phenotypes associated with individual vascular wall aging rates, for example, a favorable vascular phenotype with preserved elastic potential and a negative vascular phenotype with increased arterial stiffness [2; 5–7].

Blood vessel’s early aging significantly increases the arterial hypertension risk developing (AH), which has been confirmed in a number of studies. A typical clinical example is the arteries early aging observed in young patients with essential hypertension [8]. Currently, in many studies, it is vascular stiffness that is noted as a criterion characterizing the target organs damage in patients with arterial hypertension [9; 10], as well as a predictor of cardiovascular complications [11; 12].

Normal vascular aging can be accelerated by body’s pathological processes such as inflammation, oxidative stress, endothelial dysfunction, vascular ischemia and dyslipidemia. Inflammatory markers — CRP and pro-inflammatory cytokines (TNF-αandIL-6) are apparently associated with morphological changes caused by atherosclerosis and increased arterial stiffness [13]. It has been shown that the presence of chronic infection foci in childhood and adolescence is associated with the early ACS incidence in adulthood, hospitalization for CVD, and signs of subclinical atherosclerosis [7; 14–16].

One of the widespread inflammatory diseases of the adult population is chronic periodontitis. According to the WHO, the prevalence of periodontal disease in the world as a whole average is 94.3 % [17; 18]. Inflammation in the periodontal tissues promotes the

bacterial pathogens migration and their metabolic products into the systemic circulation, which can cause an immune response in the vascular endothelial lesions form, and contribute to early vascular aging. [19; 20].

In this regard, it seems relevant to find pathogenetic relationships in the structure of hypertension and periodontitis, as well as to determine the vascular stiffness level in middle-aged people with arterial hypertension.

Objective: to evaluate the elastic properties of the vascular wall and the spectrum of concomitant diseases in persons with a combination of arterial hypertension and inflammatory periodontal diseases, considering the cytokine profile of patients.

Materials and methods

The study included 120 male subjects 45–60 years old, average age 51.2 ± 6.4 years. Three groups were formed:

Group 1 — patients with hypertension and periodontitis (52 people);

Group 2 — patients with hypertension (48 people);

Group 3 — healthy volunteers (20 people).

Patients of groups 1 and 2 were treated in the therapeutic profile department of the St Petersburg State Budgetary Healthcare Institution "City Hospital No. 15" in the period from 2019–2020. The study did not include patients with secondary (symptomatic) hypertension, stage 3 hypertension with blood pressure above 180/110 mm Hg, cancer, acute inflammatory diseases of internal organs (pneumonia, pancreatitis, cholecystitis, etc.), CVD unstable forms, as well as patients with positive smoking status.

A clinical blood test to determine ESR, a biochemical blood test examining CRP, fibrinogen, glucose, creatinine, lipid profile, prothrombin, homocysteine, albumin/creatinine ratio in urine, glomerular filtration rate — GFR (according to the CKD-EPI formula), ECG were performed.

On the day of hospital admission, patients were taken blood samples to determine serum concentrations of pro-inflammatory (IL-1, IL-2, IL-5, IL-6, IL-8, TNF-alpha) and anti-inflammatory (IL-4, IL-10) cytokines. The samples were processed immediately and stored at a temperature of –70 degrees Celsius until they were analyzed at the Central Research Laboratory of the Central Research Laboratory of the North-Western State Medical University named after I. I. Mechnikov. The concentration was determined by the enzyme-linked immunosorbent assay (ELISA) using BenderMedSystems and ThermoFisher kits.

To assess the state of the vessels, USDG of the carotid arteries was performed with the determination of the carotid intima-media complex thickness (IMT) and visualization of atherosclerotic (AS) plaques, the ankle-brachial index (ABI) was determined by the blood pressure ratio at the ankle and brachial artery. Indicators 1.0–1.3 were considered normal values. When analyzing the data obtained, the mean IMT was used, which is the arithmetic mean between the IMT of the right and left OCA.

The "vascular age" was calculated using the modified Systematic Coronary Risk Evaluation (ASCORE) scale [21–23].

Daily monitoring of blood pressure (BPDM) was performed, with the study of vascular elasticity (model BPLab® V.06.02.00, the diagnostic system "VasotensOffice" ("PetrTelegin")). In the daytime (7:00–23:00) BP was measured every 15 minutes, at night (11:00–7:00) — every 30 minutes. A special cuff was used to measure blood pressure in

obese patients. The following indicators were determined: average heart rate, blood pressure in the daytime and at night, pulse blood pressure, the nighttime decrease level and blood pressure variability, the hypertension time index — load with increased blood pressure, augmentation index in the aorta (AIxao), estimated pulse wave velocity in the aorta (PWVao), reflected wave distribution time (RWTT), arterial stiffness index (ASI), augmentation index (AIx), maximum rate of blood pressure increase (dP / dt) max.

Subjects' psychological testing was carried out using the HADS (Hospital Anxiety and Depression Scale) and SF-36 (Quality of Life Assessment Questionnaire) questionnaires. The HADS score severity measure ranges from 0 to 21 HADS assessment criteria: 0–7 points — no significant symptoms of anxiety/depression, 8–10 points for subclinically severe anxiety/depression, 11 points and higher for clinically expressed anxiety/depression. According to the SF-36 questionnaire, the life quality indicators were assessed in a percent: up to 40 % — a reduced life quality, more than 40 % — a normal or high life quality.

The structure of "PSAF-maladjustment" was carried out to assess the significance of the effect of periodontitis on the life quality and patients' psychological status by analyzing the structure and the internal picture severity of the disease. The total indicator of the auto maladaptation severity was assessed in points and as a percentage to the maximum value (36 points). Values of more than 10 points were regarded as moderate maladaptation and more than 20 points — as pronounced maladaptation.

To diagnose periodontitis, the appearance of the face, dentition, and periodontal tissues was visually studied. The severity of inflammatory changes in the oral cavity was assessed using the The Periodontal Profile Class (PPC) scale. Considering the PPC data, the periodontitis severity was determined. The examination of the gums included: the presence of supra- and subgingival dental deposits, the periodontal pockets depth determination, definition of the tooth mobility degree, the gingival inflammation stage estimation (PMA index in the Parma modification), the gingival sulcus bleeding rate (SBI index (Muhlemann — Cowell)).

Statistical processing of the research results was carried out using the statistical software package Statistica 10.0 (StatSoftInc., USA). Continuous quantitative baseline and demographic traits were tested with a simple t-test for independent samples. In the case of characteristic values distribution, other than usual, the Mann — Whitney test was used. The $\chi 2$ test was used for qualitative signs. Differences were considered statistically significant at $p < 0.05$.

Results

The patients' characteristics included in the study, considering the anamnestic data and the structure of the disease, are presented in Table 1.

To the results of table 1, it turned out that stage 2 hypertension was significantly more often diagnosed in patients with hypertension and concomitant periodontitis. The subjects' obtained characteristics indicate that such diseases as ischemic heart disease, angina pectoris of 2 F.C., moderate anxiety-depressive disorders are significantly more common in persons with the presence of combined pathology in the form of hypertension and periodontitis. Also, in group 1 persons, the incidence of type 2 diabetes mellitus, adjustment disorders on the PSAF test, and a decrease in the life quality on the SF-36 scale were significantly higher.

Table 1. **Structure of morbidity of patients**

Index	1 group (n = 52)	2group (n = 48)	3 group (n = 20)	p
Age	55.2 ± 3.5	51.8 ± 4.1	48.3 ± 3.9	ns
BMI	28.4 ± 4.6	27.5 ± 3.3	23.7 ± 2.6	ns
HD stage 1	17 (33 %)	33 (68 %)*	0	0.001
HD stage 2	35 (67 %)*	15 (32 %)	0	0.001
DM type 2	16 (30 %)*	7 (14.5 %)	0	0.05
IHD Exertional angina 1 F. C.	6 (11.5 %)	8 (16 %)	0	ns
IHD Exertional angina 2 F. C.	15 (29 %)*	4 (8 %)	0	0.009
CHF 1 F. C.	13 (25 %)	10 (20 %)	0	ns
CHF 2 F. C.	7 (13.5 %)	5 (10.5 %)	0	ns
AF	10 (19 %)	7 (14.5 %)	0	ns
Moderate periodontitis	34 (65 %)	0	0	-
Severe periodontitis	18 (35 %)	0	0	-
Depression / anxiety HADS: 0–7 points	15 (29 %)*	23 (48 %)	6 (30 %)	0.05
Depression / anxietyHADS: 8–10 points	24 (46 %)*	10 (20 %)	2 (10 %)	0.008
Depression / Anxiety HADS: more than 11 points	9 (17 %)	4 (8 %)	0	0.1
Scale score SF-36: the reduced life quality (less than 40 %)	25 (48 %)*	14 (29 %)	1 (5 %)	0.05
PSAF scale: moderate maladaptation	23 (44 %)*	2 (4 %)	1 (5 %)	0.001
PSAF scale: pronounced maladaptation	19 (36 %)*	0	0	0.001

BMI — body mass index, HD — hypertensiondisease, IHD — ischemic heart disease, AF — atrial fibrillation, FC — functional class, ns — statistically unreliable, * — $p < 0.05$.

The patients underwent a set of the standard general clinical laboratory (blood and urine tests) and instrumental (ECG, USDG of the carotid arteries, ABI) studies, as well as a consultation with a dentist. The results are shown in Table 2.

When analyzing the data obtained, it turned out that the inflammatory shifts level in ESR, CRP, and fibrinogen parameters were higher in persons with combined pathology of group 1 compared with subjects in groups 2 and 3. At the same time, in patients with hypertension and periodontitis, the gums' indices of inflammation and bleeding were

Table 2. **Laboratory and instrumental data of patients ±**

Index	1 group (n = 52)	2group (n = 48)	3 group (n = 20)	p
ESR (mm/h)	26 ± 4.8*	11 ± 3.6	7 ± 2.9	0.01
CRP (mg/l)	8.4 ± 1.5*	5.2 ± 0.6	2.1 ± 0.7	0.04
CS (mmol/l)	7.1 ± 0.5*	5.8 ± 0.4	4.2 ± 0.6	0.04
LDL (mol/l)	4.8 ± 0.43*	3.7 ± 0.36	2.4 ± 0.21	0.03
HDL (mol/l)	0.8 ± 0.09	1.0 ± 0.07	1.2 ± 0.08	ns
TG (mol/l)	2.3 ± 0.2	2.1 ± 0.07	0.96 ± 0.03	ns
Apolipoprotein A (mg/dl)	95 ± 11.8	122 ± 13.7	146 ± 22.4	0.1
Apolipoprotein B (mg/dl)	180 ± 22.3*	131 ± 12.8	73 ± 9.5	0.05
Homocysteine (μmol/l)	19 ± 2.1	15.5 ± 1.8	7.2 ± 3.5	0.1
Fastingglucose (mmol/l)	6.7 ± 0.45*	5.2 ± 0.6	4.3 ± 0.7	0.04
Fibrinogen (g/L)	6.7 ± 0.9*	3.9 ± 0.6	2.6 ± 1.4	0.01
Al/Cr (mg/g)	167.4 ± 36.3*	88.4 ± 12.6	25.5 ± 4.1	0.03
GFR (ml/min)	63 ± 11.3	79 ± 18.6	118 ± 10.4	ns
Gingivitis Index %	57.9 ± 5.2*	38.2 ± 6.7	27.8 ± 4.1	0.02
SBI index, points	2.4 ± 0.3*	1.63 ± 0.2	1.06 ± 0.04	0.02
ABI	0.71 ± 0.06*	0.92 ± 0.09	1.2 ± 0.07	0.05
LVH on the ECG	38 (73 %)*	26 (54 %)	3 (15 %)	0.05
Extrasystoleon ECG	13 (25 %)	8 (16 %)	0	ns
Repolarization disorders	11 (21 %)	7 (14.5 %)	0	ns
Avarage IMLT, mm	1.2 ± 0.06*	0.96 ± 0.08	0.84 ± 0.05	0.01
AS plaques in the carotid arteries more than 30 %	13 (25 %)	6 (12.5 %)	1 (5 %)	0.1

CRP — C-reactive protein, CS — cholesterol, LDL — low-density lipoproteins, HDL — high density lipoproteins, TG — triglycerides, LVH — left ventricular hypertrophy, ns — statistically unreliable, * — $p < 0.05$.

expected to be significantly increased. More significant cholesterol metabolism disorders were also recorded in group 1 subjects. Examining the lipid profile, it turned out that atherogenic lipoprotein fractions (LDL, Apo B) were statistically higher in these patients. This indicates a high risk of developing cardiovascular complications in persons with hypertension and periodontitis. Fasting homocysteine and glucose were also highest in group 1 subjects, proving a high risk of metabolic disorders and metabolic syndrome. The urine albumin/creatinine ratio, as a marker of glomerular filtration disorders and renal dysfunction, was highest in patients with hypertension and periodontitis.

When instrumental examinations were performed, individuals in group 1 were more likely to have left ventricular hypertrophy on ECG, decreased ABI, and increased thickness of the carotid intima-media complex. Thus, it is in patients with combined pathology, a more aggressive atherosclerotic process and significant target organ damage in hypertension were revealed, due to the influence of both periodontal diseases, the presence of a focus of body's chronic inflammation, and cardiovascular pathology by the type of mutual complication syndrome.

According to the objectives, the level of pro-inflammatory and anti-inflammatory interleukins was determined for all subjects. The analysis results are presented in Table 3.

Table 3. **Interleukin profile of patients**

Index (pg / ml)	1 group (n = 52)	2 group (n = 48)	3group (n = 20)	p
IL-1	6.8 ± 0.2*	4.6 ± 0.4	3.4 ± 0.11	0.00004
IL-2	45.2 ± 11.7*	19.7 ± 8.6	11.6 ± 4.3	0.05
IL-5	24.8 ± 5.6	13.6 ± 4.9	6.8 ± 2.5	0.13
IL-6	15.2 ± 3.3*	6.7 ± 1.2	4.1 ± 1.7	0.01
IL-8	42.7 ± 10.6	23.9 ± 5.8	17.5 ± 3.6	0.09
TNF-alpha	48.3 ± 13.1*	14.8 ± 5.6	7.1 ± 2.2	0.01
IL-4	2.2 ± 0.3*	11.4 ± 3.1	5.6 ± 1.8	0.004
IL-10	19.7 ± 5.2	27.4 ± 14.1	8.5 ± 2.6*	0.04

When assessing the subject's cytokine profile, there was a significant excess of the pro-inflammatory cytokines normal level in patients with comorbid cardiovascular and maxillofacial pathology in such parameters as interleukin-1, interleukin-2, interleukin-6, and TNF-alpha. Estimating the anti-inflammatory response, attention is drawn to a decrease in interleukin-4 levels in individuals of group 1, compared with healthy volunteers and individuals with hypertension, which may indicate the depletion of the body's defense-adaptive mechanisms against the presence of the oral cavity chronic focal infection. Interleukin-10 was elevated in patients with hypertension and periodontitis compared with healthy volunteers, which is probably due to the presence of gum inflammation and systemic atherosclerosis in group 1 patients against the endothelial dysfunction.

To assess the blood pressure dynamics, as well as to determine the parameters of blood vessels arterial stiffness and "vascular age," the vessels age was assessed for all subjects using the ASCORE scale, and blood pressure daily monitoring was performed using the "Vasotens Office" program. The results of the study are presented in Table 4.

According to the presented data, the "vascular age" of patients with hypertension and the oral cavity inflammatory processes significantly exceeded their passport age. Also, these patients had an increased risk of developing cardiovascular complications in the next five years on the ASCORE scale.

The daily blood pressure profile comparison in patients of groups 1 and 2 did not reveal a significant difference in the hypertension degree. However, the group 1 subjects had statistically significantly increased pulse blood pressure, heart rate at night, and blood

pressure variability during the day that also reflects a high cardiovascular risk. Examining the level of nighttime BP reduction, it turned out that persons with periodontitis were significantly more likely to have a "night-peaker" profile, while individuals in group 2 had a "non-dipper" pattern with insufficient BP reduction at night.

Table 4. **Results of daily monitoring of blood pressure in patients with the determination of vascular stiffness**

Index	1 group (n = 52)	2group (n = 48)	3 group (n = 20)	p
Passport age, years	55.2 ± 3.5	51.8 ± 4.1	48.3 ± 3.9	ns
Vascular age, years	64.9 ± 3.4*	56.2 ± 3.2	49.8 ± 3.1	0.05
Five-year CVD risk on the ASCORE scale, %	15.1 ± 1.2*	9.3 ± 2.6	3.7 ± 0.8	0.04
Average daytime BP, mm Hg	156.7 ± 10.2/96 ± 3.3	145.9 ± 6.1/93 ± 2.4	120 ± 4.6/82 ± 2.8	ns
Average SBP / DBP at night	157.1 ± 11/95 ± 4.6	140.7 ± 3.5/90 ± 2.2	109 ± 5.1/71 ± 1.8	ns
Average day time HR, beats/min	90 ± 6.8	84 ± 5.7	79.2 ± 7.1	ns
Average HR, at night, beats/min	76 ± 4.7*	62 ± 4.1	60.3 ± 3.5	0.02
Average pulse blood pressure, mm Hg	59 ± 4.2*	47 ± 3.9	42.4 ± 2.7	0.03
Level of nighttime blood pressure reduction, %	↑4.8 ± 1.6*	5.6 ± 1.3	14.7 ± 3.5	0.05
Daytime SBP / DBP variability, mm Hg	25 ± 2.3/16 ± 2.6*	17 ± 2.8/13 ± 1.5	13.5 ± 2.6/10.1 ± 1.8	0.02
Nighttime SBP / DBP variability, mm Hg	17.9 ± 3.3/13.7 ± 2.1	15.5 ± 2.2/10 ± 1.7	11.6 ± 2.7/9.8 ± 2.2	ns
BP time index, %	47 ± 6.4	34 ± 8.1	13.4 ± 2.1	ns
AIxao, %	7.4 ± 3.5	4.06 ± 5.4	2.2 ± 7.9	ns
PWVao, m/s	12.2 ± 2.1	10.7 ± 1.6	9.4 ± 2.2	ns
RWTT, m/s	125.3 ± 5.4	143.4 ± 7.1*	150.5 ± 9.2	0.05
ASI, mm Hg	179.7 ± 13.2*	147.1 ± 10.5	128.3 ± 6.6	0.05
AIx, %	1.1 ± 15.3*	–24.8 ± 13.6	–46.7 ± 8.4	0.01
(dP/dt)max, mm Hg/s	665.3 ± 92.5	611.9 ± 77.8	507.4 ± 62.1	ns

When studying the arterial stiffness daily indicators in patients of group 1, statistically significant differences with the comparison groups in the AIx augmentation index were revealed, which indicates an increase in arterial stiffness in patients with comorbid

pathology and may be due to chronic inflammation. Also, these patients showed an increase in the pulse wave speed in PWVaoaorta (12.2 m/s versus 10.7 m/s). Accordingly, a significant decrease in the propagation time of the reflected RWTT wave was detected. The specified parameters — augmentation index, pulse wave velocity in the aorta, reflected wave propagation time — describe, first of all, a decrease in the elastic properties of the aorta in persons with a combination of hypertension and periodontitis.

At the same time, the subjects of group 1 showed an increase in the stiffness parameters measured in the brachial artery. A statistically significant increase in arterial stiffness index (ASI) was determined. Also, the group 1 person had the highest rate of increase in the brachial artery blood pressure (665 versus 611 and 507 mm Hg/s, respectively). This indicator — (dP / dt) max shows the maximum rate of blood pressure increase and indirectly reflects the main arteries' total stiffness and the "dynamic" load on the vessels' walls during the pulse wave passage. The results obtained confirm the arterial stiffness increase in persons with periodontitis, regardless of the blood pressure increase.

Discussion

The concept of early vascular aging (EVA — early vascular aging) was proposed by Peter Nilson in 2008 [24]. In 2015, at the Congress of the Russian Cardiological Society, the document "The agreed opinion of Russian experts on the arterial stiffness assessment in clinical practice" was formed and published [25]; it identified the basic concepts of arterial stiffness as a risk factor for CVD and distinguished the most popular in actual clinical practice diagnostic techniques for determining vascular elasticity and rigidity. The wider introduction into clinical practice of methods for diagnosing early vascular aging as a component of preclinical atherosclerosis in combination with the analysis of the subject's cytokine profile is the most acceptable preventive method for identifying a cohort of patients who need to slow down the atherogenesis processes and aging of the organism. Premature vascular aging in individuals with altered cytokine balance increases the risk of CVD. It can be assumed that in the presence of the body's chronic inflammation focus, avascular damage vicious circle develops: mechanical and chemical effects through bacterial aggression and oxidative stress, endotoxemia, secondary endothelial dysfunction, which in case of comorbid pathology and bad habits (dyslipidemia, hypertension, insulin resistance, metabolic syndrome, obesity, albuminuria, arteriolosclerosis, etc.) leads to the syndrome of premature vascular aging EVA in genetically predisposed individuals.

The data obtained in our study allowed establishing a close correlation between the presence of periodontitis in persons with arterial hypertension and the risk of such diseases and pathological processes as ischemic heart disease, type 2 diabetes mellitus, atherosclerosis, depressive and anxiety disorders.

The presence of chronic inflammation focus in the oral cavity led to a more severe course of arterial hypertension and increased the cardiovascular complications risk and target organ damage. Thus, in patients with a focal inflammatory process of the oral cavity and arterial hypertension, higher levels of atherogenic fractions of cholesterol, fasting glucose, and the albumin/creatinine ratio in urine were recorded. Also, in the examined individuals with polymorbid pathology, indirect signs of left ventricular hypertrophy were recorded on the ECG . There was a significant increase in the ankle-brachial index and the thickness of the intima-media complex the carotid arteries in ultrasound examination. The fact that

individuals in group 1 were significantly more likely to have type 2 diabetes mellitus and fasting hyperglycemia may partly explain the more severe periodontitis in this cohort of subjects. It is known that the presence of diabetes mellitus aggravates the course of purulent-inflammatory processes of any localization due to glucose toxicity and oxidative stress. Thus, we observe an interdependent aggravation syndrome of polymorbid pathology.

According to the literature, the inflammatory process, whether it be systemic or local inflammation, makes a significant contribution to atherosclerosis progression and increases the likelihood of cardiovascular disease [20; 26]. It turned out that periodontal bacteria are able to diffuse into the vascular endothelium and initiate atherosclerosis processes by activating macrophages and maintaining systemic inflammation [27].

The investigating data reported, in comorbid pathology combining hypertension and periodontitis, the level of inflammatory markers (ESR, CRP, fibrinogen, IL-1, IL-2, IL-5, IL-6, IL-8, TNF alpha) was significantly increased. The level of anti-inflammatory cytokines — IL-4, IL-10, on the contrary, was reduced and can testify to the immune system depletion with an insufficient increase in the anti-inflammatory cytokines pool in the infectious process of the oral cavity.

Examining the blood pressure daily profile and arterial stiffness, increased blood pressure variability, changes in the night profile with a predominance of the "nightpeaker" pattern, and excess pulse pressure in persons with comorbid pathology, including periodontitis and hypertension, were found. In addition, an increase in the number of arterial vascular stiffness indicators and a decrease in their elasticity was noted in persons with an inflammatory process in the oral cavity. This fact is reflected in significant excess of the passport age over the "vascular age" in persons of group 1, which indicates a high risk of premature aging, and especially blood vessels accelerated aging in patients with polymorbid pathology.

Thus, it can be assumed that arterial stiffness, atherosclerosis, and systemic inflammation mutually condition each other, leading to a more unfavorable course of hypertension and increasing the risk of CVC.

Conclusions

In patients with polymorbid pathology with a combination of periodontitis and arterial hypertension, the risk of developing cardiovascular diseases and complications is increased.

The presence of chronic focal inflammation of the oral cavity in persons with arterial hypertension is associated with higher levels of markers of systemic inflammation and an imbalance in the patient's cytokine profile.

In patients with focal infection of the oral cavity and arterial hypertension, in comparison with healthy volunteers and individuals with isolated hypertension, the elastic properties of blood vessels are reduced and there is an excess of the "vascular age" over the passport age according to the ASCORE criteria. This may be due to more severe hypertensive syndrome in periodontitis, exposure of the vascular endothelium to bacterial toxins of the oral cavity during their translocation into the bloodstream, interleukin imbalance, anxiety-depressive disorders, as well as the syndrome of mutual addiction

In persons with arterial hypertension and polymorbid pathology, according to the indicators of daily monitoring of blood pressure with an assessment of vascular rigidity, its increase was revealed, which strengthen in increasing severity of the periodontitis degree.

It can be assumed that vascular stiffness against the early vascular aging is associated not only with hypertension, obesity, renal dysfunction, type 2 diabetes mellitus, dyslipidemia, but also periodontitis, against the imbalance in the interleukin system.

To optimize preventive measures in persons with arterial hypertension, the existing methods of clinical examination can be supplemented by angiographic screening to identify signs of blood vessels early aging, as well as to assess the state of the periodontium and cytokine profile

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