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RESEARCH ARTICLE

THE EFFECT OF ORAL SANITATION ON SYSTEMIC INFLAMMATION AND ENDOTHELIAL FUNCTION IN PATIENTS WITH CARDIOVASCULAR DISEASES

Djaneta Ashadovna Sozaeva [1], Laura Anzorovna Bichoeva [2], Aida Ruslanovna Gyaurgieva [3] Aset Adamovna Saidova [4], Aminat Ruslanovna Dagaeva[5], Khava Umarovna Magomedova[6], Tatyana Kharitonovna Timokhina[7]

[1]Kabardino-Balkarian State University named after H. M. Berbekov, 173 Chernyshevskogo St., 360004 , 0009-0007-4587-0543
[2]Kabardino-Balkarian State University named after, H. M. Berbekov, 173 Chernyshevskogo St., 360004, 0009-0007-2697-3571
[3]Kabardino-Balkarian State University named after H. M. Berbekov, 173 Chernyshevskogo St., 360004, 0009-0000-3673-7117
[4]Aset Adamovna Saidova, Kabardino-Balkarian State University named after H. M. Berbekov, 173 Chernyshevskogo St., 360004, s, 0009-0005-7764-4167 ,
[5]Kabardino-Balkarian State University named after H. M. Berbekov, 173 Chernyshevskogo St., 360004, 0009-0009-0342-4347
[6]Kabardino-Balkarian State University named after H. M. Berbekov,173 Chernyshevskogo St., 360004,0009-0007-1696-118X
[7]Tatyana Kharitonovna Timokhina, Tyumen State Medical University, Tyumen, Russia 0000-0003-4479-8280

*Corresponding Author

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Abstract: The article examines the effect of oral cavity sanitation on indicators of systemic inflammation and endothelial function in patients with established cardiovascular diseases. The starting point of the study is the concept of the participation of chronic inflammation in the oral cavity, primarily periodontal diseases, in the formation of endothelial dysfunction and atherosclerotic vascular lesions. The study evaluated the dynamics of high-sensitivity C-reactive protein and interleukin-6 levels, as well as the indicators of endothelial-dependent vasodilation of the brachial artery, before and three months after comprehensive oral cavity sanitation, in 70 patients with coronary heart disease and arterial hypertension. Patients were randomly assigned to the main group, which received comprehensive dental treatment to eliminate chronic infection foci, and the comparison group, which underwent standard cardiological monitoring without targeted dental treatment. It was shown that comprehensive oral cavity treatment was associated with a significant decrease in systemic inflammation markers and improvement in endothelial-dependent vasodilation compared to the comparison group, where no significant changes were observed during the follow-up period. The article discusses the possible pathophysiological mechanisms of the effect of eliminating chronic infection foci on the vascular wall, the clinical significance of integrating dental care into secondary prevention programs for cardiovascular diseases, and the limitations of the study.

Keywords: oral sanitation, chronic periodontal diseases, systemic inflammation, endothelial function, coronary heart disease, cardiovascular diseases.

INTRODUCTION

Cardiovascular diseases remain the leading cause of morbidity, mortality, and disability, necessitating a constant search for additional ways to improve the prognosis for this patient population. Modern understanding of atherosclerosis and coronary artery disease suggests that it is a chronic inflammatory process characterized by endothelial dysfunction, systemic activation of innate and adaptive immunity, and persistent elevation of pro-inflammatory mediators [9]. Against this background, extravascular sources of chronic low-intensity inflammation, including diseases of the respiratory system, digestive system, and oral cavity, are being actively studied [10].

Chronic periodontal inflammatory diseases attract special attention, as they are considered a significant source of systemic inflammatory response. Severe forms of periodontitis have been shown to be accompanied by persistent increases in the levels of high-sensitivity C-reactive protein, interleukin-6, tumor necrosis factor alpha, as well as transient bacteremia that occurs during chewing and hygienic procedures. These systemic changes are accompanied by signs of endothelial dysfunction, including reduced endothelium-dependent vasodilation and increased markers of vascular inflammation. Clinical studies have described associations between periodontal diseases and an increased risk of coronary events, but the effect of oral sanitation on vascular function and cardiovascular outcomes remains controversial [7].

Despite the accumulation of data on the relationship between periodontal status and cardiovascular risk, dental interventions are rarely integrated into comprehensive secondary prevention programs for coronary artery disease. The primary focus has traditionally been on medical therapy, lifestyle modifications, and the control of traditional risk factors. The potential benefits of oral health care for reducing systemic inflammation and improving endothelial function have been primarily explored in theoretical contexts or through small-scale pilot studies. There is a need to obtain additional data on the effect of comprehensive elimination of chronic oral infection foci on markers of systemic inflammation and vascular

dysfunction in patients with established cardiovascular diseases [4].

The study was conducted at the Tyumen Cardiology Research Center (Tyumen), where patients with cardiovascular diseases were selected, and at the Regional Dental Polyclinic (Tyumen), where the patients' oral cavities were comprehensively treated.

The aim of the present study is to evaluate the effect of comprehensive oral cavity sanitation on the levels of high-sensitivity C-reactive protein and interleukin-6, as well as on the indicators of endothelial-dependent brachial artery vasodilation in patients with coronary heart disease and arterial hypertension.

An additional objective is to determine the degree of intergroup differences between patients who underwent sanitation and patients who received standard cardiological treatment without targeted dental intervention.

MATERIAL AND METHODS

The study was conducted in the format of a prospective comparative clinical and laboratory observation involving 70 patients who were under dispensary observation by a cardiologist for stable coronary artery disease in combination with arterial hypertension. The study included men and women aged 40 to 70 years who had a confirmed diagnosis of coronary artery disease and a stable regimen of drug therapy for at least three months prior to inclusion. The exclusion criteria were acute inflammatory diseases in the previous four weeks, decompensation of chronic somatic pathology, recent acute coronary events, and the impossibility of performing dental interventions for medical reasons.

After the initial cardiological and dental examination, the patients were randomly divided into two equal groups. The main group included 35 patients who underwent comprehensive oral rehabilitation, which included professional hygiene, caries treatment, and therapy for chronic periodontitis using non-surgical and, if necessary, minimally invasive surgical methods, as well as the elimination of other chronic oral infections. The comparison group included 35 patients who did not receive a specially organized dental treatment and continued their standard cardiological therapy. If they had acute dental complaints, they received treatment as part of their usual practice, without participating in a structured treatment program.

The dental examination included an assessment of the oral hygiene index, the depth of periodontal pockets, the degree of bleeding on probing, the presence of subgingival tartar, and radiological signs of generalized periodontitis. Based on the combination of these data, an integral periodontal status was formed, which allowed for an assessment of the initial inflammatory load and the dynamics after the treatment.

The cardiological examination was carried out in the standard volume and included the collection of anamneses, physical examination, measurement of blood pressure, registration of electrocardiogram and specification of the regimen of drug therapy. The stratification of cardiovascular risk was carried out taking into account age, gender, smoking, blood pressure and lipid profile, the comparability of groups on these parameters at the initial stage was analyzed.

The laboratory part of the study included the determination of the levels of highly sensitive C-reactive protein and interleukin-6 in the blood serum, as well as the standard lipid profile. Blood samples were taken in the morning on an empty stomach before the start of oral sanitation and three months after the completion of the complex of dental interventions in the main group, in the comparison group the sampling was carried out at the same time.

Endothelial function was assessed by ultrasound Doppler of the brachial artery with measurement of endothelium-dependent vasodilation in reactive hyperemia. The indicator was calculated as a percentage increase in the diameter of the artery after temporary occlusion in relation to the initial value. The study was carried out under the same conditions before the start of the sanation and after three months.

Statistical analysis included calculation of the mean values and standard deviations of quantitative indicators, checking the normality of distribution, comparison of parameters within groups in dynamics using the paired t-test and comparison between groups using the independent t-test. Categorical indicators were analyzed using the chi-square test. The level of statistical significance was set at $p < 0.05$.

RESULTS AND DISCUSSIONS:

The complex of state medical institutions in Tyumen, including the Tyumen Cardiology Research Center and the Regional Dental Polyclinic, was chosen as the clinical base for this study. The Tyumen Cardiology Research Center was used to select patients with various forms of cardiovascular pathology, collect clinical and anamnestic data, register indicators of systemic inflammation, and assess endothelial function. The Center is a specialized state medical, diagnostic, and research institution that provides high-tech assistance to patients with coronary heart disease, arterial hypertension, chronic heart failure, and other cardiovascular diseases. The availability of a well-developed laboratory base, functional and radiological diagnostic departments, as well as the accumulated experience of conducting clinical

and clinical-pathogenetic studies, create favorable conditions for standardized patient examinations and reliable determination of markers of systemic inflammation and endothelial dysfunction.

Oral cavity sanitation, as well as dental monitoring and treatment of patients, was carried out at the Regional Dental Polyclinic (Tyumen), which is the largest state dental institution in the region. The polyclinic's structure includes therapeutic, surgical, orthopedic, and periodontal departments, allowing for a comprehensive range of oral care and prevention, including the elimination of chronic odontogenic infection, treatment of periodontal diseases, and professional hygiene services. A significant advantage of this database is the significant flow of patients, including those with cardiovascular diseases, who are referred from a cardiology hospital, which allows for the formation of a representative sample and the organization of continuous interdisciplinary monitoring.

The choice of these state medical organizations for the study was based on a number of scientific, methodological, organizational, and practical factors. First, the combination of a specialized cardiology center and a large dental institution ensure a comprehensive approach to assessing the impact of oral cavity sanitation on systemic inflammation and endothelial function in patients with cardiovascular diseases, allowing for all stages, from clinical, instrumental, and laboratory diagnostics to comprehensive dental treatment, to be conducted within the framework of a coordinated protocol. Secondly, the state status of both clinics, the availability of approved medical care standards, and local ethics committees increase the reliability and reproducibility of the results obtained and make it easier to comply with regulatory requirements for conducting clinical trials. Thirdly, the geographical and organizational accessibility of these institutions for a research student, their traditional cooperation with educational organizations, and their experience in scientific and dissertation work create real conditions for the systematic recruitment of patients, long-term observation, and subsequent validation of the study results on the basis of clinic data.
The clinical and demographic characteristics of the patients are presented in Table 1.

Table 1 – Initial characteristics of the patients in the main group and the comparison group (n = 70)

Indicator	The main group (sanitation , n=35)	The comparison group (n=35)	p
Age, years (M ± SD)	58,3 ± 6,7	57,9 ± 6,9	0,78
Men, %	57	54	0,80
Body mass index, kg/m² (M ± SD)	29,4 ± 4,1	29,1 ± 4,3	0,82
Active smoking, %	34	37	0,79
Arterial hypertension, %	100	100	–
Stable angina pectoris II–III FC, %	71	69	0,84
Type 2 diabetes, %	24	21	0,77
Total cholesterol, mmol/L (M ± SD)	5,5 ± 0,9	5,6 ± 0,8	0,71
LDL, mmol/L (M ± SD)	3,4 ± 0,8	3,5 ± 0,7	0,64
HDL, mmol/L (M ± SD)	1,11 ± 0,22	1,09 ± 0,20	0,72
Triglycerides, mmol/L (M ± SD)	1,8 ± 0,6	1,9 ± 0,7	0,60
hs-CRP, mg/L (median [25; 75 percentile])	3,6 [2,4; 4,9]	3,4 [2,2; 4,7]	0,68
Interleukin-6, pg/mL (M ± SD)	4,9 ± 1,7	4,7 ± 1,6	0,68
Endothelium-dependent vasodilation, % (M ± SD)	6,8 ± 2,1	7,0 ± 2,0	0,69

The groups did not differ in terms of age, gender, body mass index, smoking frequency, prevalence of concomitant diabetes mellitus, lipid profile parameters, and baseline levels of systemic inflammation markers. The parameters of endothelial-dependent vasodilation were also comparable, which creates conditions for a correct analysis of the effect of oral sanitation on the dynamics of the studied parameters.
After the comprehensive oral cavity sanitation, the main group showed an improvement in their dental status, which was reflected in a decrease in the hygiene index, a reduction in the depth of periodontal pockets, and a high frequency of elimination of chronic infection foci, including complicated caries and chronic periodontitis. In the comparison group, there was no significant positive change in dental indicators during the follow-up period, which was due to the lack of a structured sanitation program.

The dynamics of systemic inflammation markers and endothelial function indicators are presented in Table 2.

Table 2 – Dynamics of systemic inflammation and endothelium-dependent vasodilation indicators over three months of observation

Indicator	The main group (sanation, n=35) before	The main group in 3 months	p (inside the group)	The comparison group (n=35) before	The comparison group in 3 months	p (inside the group)	p (between groups of changes)
hs-CRP, mg/L (median [25; 75])	3,6 [2,4; 4,9]	2,4 [1,6; 3,3]	0,004	3,4 [2,2; 4,7]	3,2 [2,1; 4,5]	0,41	0,01
Interleukin-6, pg/mL (M ± SD)	4,9 ± 1,7	3,8 ± 1,4	0,001	4,7 ± 1,6	4,6 ± 1,7	0,62	0,008
Endothelium-dependent vasodilation, % (M ± SD)	6,8 ± 2,1	9,2 ± 2,3	<0,001	7,0 ± 2,0	7,3 ± 2,2	0,28	0,002

In the main group, three months after the completion of oral cavity sanitation, there was a significant decrease in the median values of high-sensitivity C-reactive protein and the average values of interleukin-6, indicating a reduction in the severity of systemic inflammation. At the same time, there was a significant improvement in endothelial-dependent vasodilation of the brachial artery, reflecting the restoration of endothelial function. In the comparison group, there was no significant change in the markers of inflammation and vasodilation. The intergroup analysis confirmed statistically significant differences in the change of all three key parameters, which indicates the potential contribution of oral cavity sanitation to the reduction of inflammatory load and improvement of vascular function in patients with cardiovascular diseases.

It is advisable to present the graphical representation of the obtained results in the form of a figure reflecting the direction and magnitude of changes in the indicators of systemic inflammation and endothelium-dependent vasodilation in the two groups.

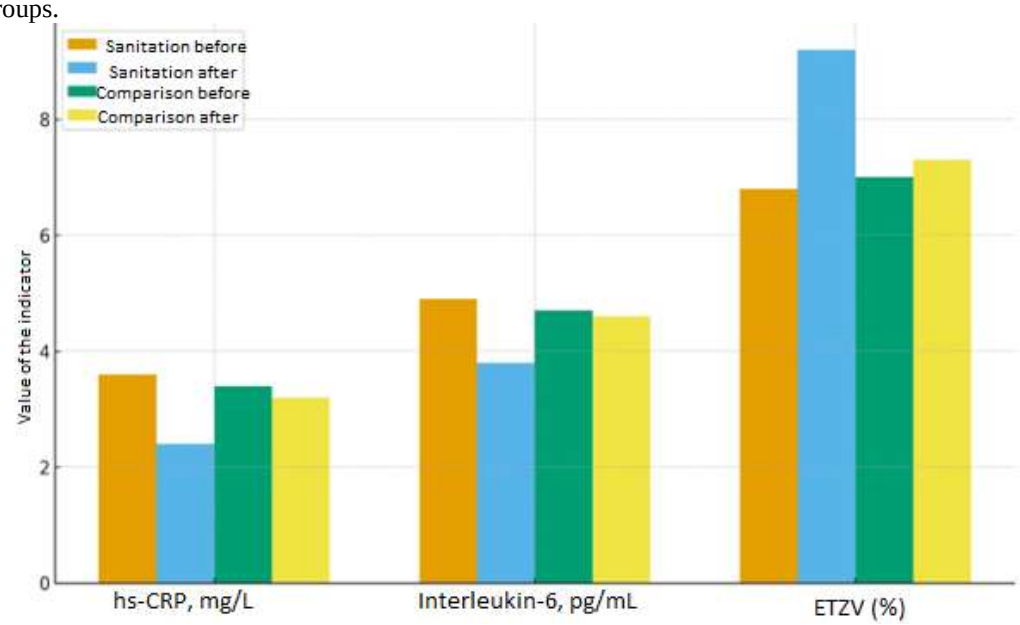

Figure 1 – Comparative dynamics of high-sensitivity C-reactive protein, interleukin-6, and endothelium-dependent vasodilation in patients of the main group and the comparison group over three months of follow-up

Figure 1 shows three blocks corresponding to each of the parameters. For hs-CRP, there is a more pronounced decrease in the median values in the main group compared to the minimal change in the comparison group. For interleukin-6, there is a decrease in the average values in the main group, while the average values in the comparison group remain stable. For endothelium-dependent vasodilation, there is an increase in the average value in the main group from 6.8% to 9.2%, while the average value in the comparison group remains unchanged. This visual representation allows for a clear demonstration of the differences between the groups and facilitates the interpretation of the clinical significance of the results.

Discussion of the results requires reference to the pathophysiological mechanisms linking chronic oral infection foci to systemic inflammation and endothelial function. Chronic periodontitis and other inflammatory periodontal diseases create a long-lasting source of bacterial antigens and proinflammatory mediators that enter the systemic circulation and

sustain low-grade inflammation. Increased levels of highly sensitive C-reactive protein and interleukin-6 as markers of systemic inflammation cause endothelial cell activation, increased expression of adhesion molecules, increased migration of leukocytes into the vascular wall, and a shift in the vasoactive balance towards reduced bioavailability of nitric oxide.

Comprehensive oral cavity sanitation, including the removal of subgingival tartar, reducing the bacterial load and eliminating foci of chronic inflammation, can reduce the frequency of bacteremia episodes and the concentration of circulating bacterial components, as well as reduce the stimulation of the systemic immune response. As a result, the production of pro-inflammatory cytokines decreases, the synthesis of C-reactive protein decreases, and endothelial function is normalized, which is reflected in the improvement of endothelial-dependent vasodilation. The changes in the levels of systemic inflammation markers and vasodilation indicators identified in the study are consistent with this pathophysiological model and support the hypothesis of the potential role of oral sanitation in reducing cardiovascular risk [3].

It should be noted that the observed improvement in endothelium-dependent vasodilation by a few percent may have clinical significance, as this indicator is considered an early marker of atherosclerotic damage and an independent predictor of cardiovascular events. The practical significance of even a moderate improvement in endothelial function in a group of patients with established cardiovascular diseases may manifest itself in a more favorable course of the disease during long-term follow-up.

When interpreting the results, it is important to consider the limitations of the study. The follow-up period was only three months, which allows for the assessment of short-term effects of oral health on systemic inflammation and endothelial function. Longer-term follow-up is necessary to determine the long-term persistence of these changes and their impact on clinical outcomes, such as the frequency of coronary events or the need for repeated hospitalizations. An additional limitation is the impossibility of completely eliminating the influence of concomitant factors, including changes in lifestyle, adherence to drug therapy, and self-treatment of dental problems in the comparison group, although the comparability of the main parameters and the stability of the cardiological therapy regimen partially compensate for this shortcoming.

Despite these limitations, the study demonstrates an important fundamental conclusion that oral sanitation can be considered not only as a local dental intervention, but also as a component of systemic effects on inflammatory burden and vascular function in patients with cardiovascular diseases. Incorporating assessments of dental status into standard cardiological screening can identify patients with severe oral inflammation who require targeted interventions to optimize overall cardiovascular risk.

The data obtained in the study substantiate the need to include oral sanitation and control of periodontal inflammatory diseases in the system of comprehensive management of patients with cardiovascular diseases. It is advisable to consider the dental status as an obligatory component of an extended assessment of cardiovascular risk, along with indicators of the lipid profile, blood pressure and glycemic level. During initial and subsequent visits to a cardiologist or general practitioner, patients with stable coronary artery disease and arterial hypertension should be advised to undergo routine dental examinations to detect signs of chronic periodontitis, generalized gingivitis, and other chronic oral infections. If there are inflammatory periodontal diseases or complicated caries, an individualized treatment plan should be developed based on the severity of the cardiological condition and the patient's existing medical treatment, particularly if they are taking antiplatelet agents or anticoagulants.

It is important to integrate dental interventions into the secondary prevention system, where the assessment of high-sensitivity C-reactive protein and interleukin-6 levels can be used as markers of inflammatory load, and the endothelium-dependent vasodilation index can be used as a sensitive indicator of vascular endothelial function [4]. In the presence of a combination of elevated levels of inflammatory markers, signs of endothelial dysfunction, and clinically significant periodontitis, it is advisable to consider oral sanitation as one of the priority non-pharmacological components of cardiovascular risk reduction. At the same time, the tasks of a dentist and a cardiologist should be considered as complementary: dental treatment helps to reduce systemic inflammation and improve endothelial function, while optimized medical therapy reduces the likelihood of vascular complications that can complicate oral interventions [1].

From an organizational point of view, it is recommended to form interdisciplinary patient routes, providing for the exchange of information between dental and cardiological units. In inpatient and outpatient cardiological institutions, it is possible to introduce a brief dental screening, including a visual assessment of the mucous membrane, gingival margin and the presence of tartar, followed by referral to a dentist in case of active inflammation in the periodontium. In dental institutions, it is advisable to record the presence of coronary heart disease, arterial hypertension, and other cardiovascular diseases in patients, which will allow for a more targeted planning of the intervention, monitoring of the hemodynamic status, and coordination of the treatment with the attending cardiologist [8].

From a clinical perspective, it seems reasonable to regularly monitor markers of systemic inflammation and indicators of endothelial function in patients with severe periodontal inflammatory diseases, especially in the presence of concomitant coronary artery disease [6]. The values of high-sensitivity C-reactive protein, interleukin-6, and the percentage change in the diameter of the brachial artery during endothelium-dependent vasodilation can be used as reference points. In the presence of initially elevated levels of inflammatory markers and reduced values of vasodilation, comprehensive oral cavity sanitation followed by assessment of the dynamics of these indicators allows not only to control the local dental status, but also to indirectly assess the impact of the intervention on the vascular wall [2].

Based on the results of the study, it is possible to propose an approximate monitoring structure that combines dental, laboratory, and functional parameters. This structure is presented in the table, which reflects the recommended frequency of dental examinations, target levels of systemic inflammation markers, and approximate values of endothelium-dependent vasodilation for different patient categories.

Table 3 - Approximate recommendations for monitoring oral health, systemic inflammation, and endothelial function in patients with cardiovascular diseases

Patient category	Characteristics of dental status	Recommended frequency of dental examinations	Target indicators of systemic inflammation (high-sensitivity C-reactive protein, interleukin-6)	Estimated indicators of endothelial function (endothelium-dependent vasodilation of the brachial artery)	Expected clinical and prognostic effect
A patient with coronary artery disease and no active periodontal inflammation	Clinically healthy periodontium or mild gingivitis without bone destruction	Once every 12 months	hs-CRP is less than 3 mg/L, and interleukin-6 is within the reference range	Endothelium-dependent vasodilation is at least 8–9 %	Maintaining a stable vascular status with standard cardiological therapy
Patient with IHD and mild-to-moderate chronic periodontitis (before sanitation)	Presence of periodontal pockets, bleeding, and radiological signs of bone resorption	At least once every 6 months until the sanitation is completed	hs-CRP more than 3 mg/L, moderate increase in interleukin-6	Endothelium-dependent vasodilation of about 6–7 % or less	Identification of increased inflammatory and vascular risk, and planning of comprehensive treatment
A patient with IHD after comprehensive oral sanitation	Treatment of acute infection foci, reduction of pocket depth, and reduction of bleeding	Once every 6-12 months, with monitoring of periodontal status	Reduction of hs-CRP to values less than 3 mg/L, and reduction of interleukin-6 compared to the initial level	Increase in endothelium-dependent vasodilation to 8–9% or more	Reduction of systemic inflammatory load, improvement of endothelial function, and potential reduction of cardiovascular risk

The presented table is indicative and should be adapted to the individual characteristics of the patient, the severity of cardiovascular pathology and concomitant diseases.

Nevertheless, it illustrates the fundamental approach, which is the linking of the dental status, levels of systemic inflammation and indicators of endothelial function into a single monitoring system. With this approach, oral cavity sanitation acquires the value of not only a local dental procedure, but also an element of complex cardiovascular prevention.

CONCLUSION

A prospective study involving 70 patients with coronary heart disease and arterial hypertension showed that comprehensive oral sanitation was associated with a significant decrease in markers of systemic inflammation and improvement in endothelial function compared to standard cardiological monitoring without specially organized dental intervention. In the main group, three months after completing oral sanitation, there was a statistically significant decrease in the levels of high-sensitivity C-reactive protein and interleukin-6,

as well as an increase in the endothelium-dependent vasodilation of the brachial artery, while no significant changes were observed in the comparison group.

The results obtained confirm the pathophysiological concept of the participation of chronic infection foci in the oral cavity in the maintenance of systemic inflammation and the formation of endothelial dysfunction in patients with cardiovascular diseases. Oral sanitation in this context can be considered as an additional tool for modifying cardiovascular risk, along with traditional measures for controlling blood pressure, lipid metabolism, glycemia, and smoking cessation.

The practical significance of the work lies in substantiating the need to integrate dental care into comprehensive secondary prevention programs for cardiovascular diseases. The joint efforts of cardiologists and dentists aimed at assessing and correcting inflammatory periodontal diseases and other dental pathologies can help reduce the inflammatory burden and improve vascular function.

It is recommended that when planning clinical routes for patients with coronary heart disease and arterial hypertension, healthcare facilities should provide information about the role of inflammatory oral diseases in maintaining systemic inflammation and developing endothelial dysfunction. An important task is to raise awareness among patients themselves about the possible link between dental problems and the course of cardiovascular disease, as their commitment to regular dental care and oral hygiene depends largely on their understanding of the systemic consequences of these conditions. Incorporating education about the importance of dental care into school programs for patients with cardiovascular diseases can help foster a more responsible attitude towards dental health as a component of a comprehensive strategy to reduce cardiovascular risk.

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