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The Place of Colchicine in the Treatment of Chronic Periodontitis in Patients with Coronary Artery Atherosclerosis

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Abstract The aim of this work was to study the pleiotropic and lipid-lowering effects of colchicine in patients with chronic ischemic heart disease against the background of severe periodontitis. We examined 80 patients with moderate periodontitis against the background of chronic ischemic heart disease (CIHD). **Materials and methods**: 80 patients with moderate periodontitis on the background of chronic coronary heart disease (HIBS) were examined. The first group included 40 patients with HIBS who underwent a thorough examination and were prescribed basic therapy using double antiplatelet therapy, rosuvastatin at a dose of 10 mg was prescribed on a regular basis, as well as rosuvastatin at a dose of 10 mg in the form of gum applications for 15 minutes for two weeks, then every other day for 3 months. The second group included 40 patients with diagnosed atherosclerosis – corresponding changes on the ECG or after coronary angiography. The following results were obtained: After 6 months of monitoring the indicators of the first and second groups, the differences in them changed even more in favor of the first group, whose patients received rosuvastatin at a dose of 10 mg orally and 10 mg in the form of gum applications under strict control. Almost all blood counts and changes in periodontal tissue once again confirm a decrease in the level of inflammation around the periodontium, a decrease in the level of plaque, the bleeding index, and the depth of the periodontal pocket. The analysis of the obtained data confirms the connection between atherosclerosis of the coronary arteries and chronic periodontitis. Against the background of taking statins, the level of OH, LDL decreases, and the level of HDL increases. Monitoring the intake of statins in elderly patients with moderate periodontitis with its use in the form of applications significantly reduces the level of C-reactive protein, which once again proves the pleiotropic effect of statins in the elderly against the background of chronic periodontitis.

Keywords Atherosclerosis, Periodontitis, Lipid spectrum, Interleukins

1. Introduction

Currently, cardiovascular diseases occupy the first place in the structure of mortality among all diseases in Uzbekistan [4]. The main disease that ultimately leads to disability and mortality is atherosclerosis. First of all, we are talking about atherosclerosis of the coronary arteries - chronic ischemic heart disease (CIHD), atherosclerosis of the cerebral arteries and atherosclerosis of the peripheral arteries. It has already been proven that inflammation plays a decisive role in the occurrence and development of atherosclerosis. Periodontitis is also a common chronic inflammatory disease associated with other chronic inflammatory diseases, such as atherosclerotic cardiovascular diseases. The mechanisms underlying this association are yet to be fully understood. However, periodontitis and its various manifestations, ranging from aggressive to severe loss of up to several teeth at once, especially in patients with atherosclerosis, are also important, given the quality of life of people. Common factors that contribute to the development of both cardiovascular diseases and chronic periodontitis include aging, smoking, alcohol abuse, ethnicity, education and socioeconomic status, male gender, diabetes mellitus and overweight or obesity [1,5]. Periodontitis is a potential risk factor that can initiate the development, maturation and instability of atheromas in the arteries. A mechanism has been proposed to explain this association: periodontal pathogens directly enter the bloodstream and cause inflammation or indirectly by increasing the systemic levels of inflammatory mediators. Our study focuses on the anti-inflammatory effects of colchicine used in the treatment of CIHD and their impact on reducing inflammation in chronic periodontitis.

Coronary atherosclerosis and periodontitis, given their prevalence, represent a serious epidemiological problem. Pathophysiological data indicate a possible common inflammatory etiopathogenetic origin of these diseases.

Atherosclerosis is a chronic inflammatory process affecting

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mainly the intima of large and medium-sized arteries, resulting in the formation of lipid deposits due to the accumulation of inflammatory cells and the formation of a fibrolipid structure known as an atherosclerotic plaque [1]. Theories of the pathogenesis of atherosclerosis have changed over time [2,4]. Currently, the role of autoimmune and inflammatory conditions in the onset and development of atherosclerosis and in the development of its complications is emphasized [3]. Endothelial dysfunction, resulting from immune and inflammatory reactions in the vessel wall, is the earliest and most important process in the development of atherosclerosis [10]. Periodontitis is preceded by gum inflammation (gingivitis), which is reversible with appropriate treatment. As a result of periodontal inflammation, the tissues surrounding the tooth are permeated with neutrophils, macrophages and, subsequently, activated lymphocytes, which secrete, for example, interleukin-1, prostaglandin E 2 and tumor necrosis factor-alpha [8]. The large area of periodontal tissue, as well as its dense vascularization, allow bacteria, bacterial metabolic products and inflammatory mediators to enter the bloodstream and thus contribute to endothelial dysfunction [9].

It is known that periodontitis itself is an independent risk factor contributing to the development of atherosclerotic vascular disease, and the main mechanism is systemic inflammation [10].

Objective: To study the anti-inflammatory effect of colchicine in patients with chronic ischemic heart disease against the background of periodontitis.

2. Material and Methods

80 patients with moderate periodontitis associated with chronic ischemic heart disease (CIHD) were examined.

The first group included 40 patients with CIHD, who underwent a thorough examination and were prescribed basic therapy using dual antiplatelet therapy, rosuvastatin was prescribed at a dose of 10 mg on a permanent basis, as well as colchicine at a dose of 0.5 mg in tablets once a day for 6 months.

The second group included 40 patients with diagnosed atherosclerosis – corresponding changes on the ECG or after coronary angiography, who received basic therapy for coronary heart disease.

Inclusion criteria of the research:

- Age >45 years;
- Atherosclerotic lesion of the coronary arteries (confirmed by coronary angiography);
- Availability periodontitis stage II gravity;
- Stable symptoms and hemodynamics;
- Those who provided informed consent.

Exclusion criteria of the research:

- patients under 45 years of age,
- planned revascularization of an artery related to infarction or stroke more than 120 days after the qualifying/index event;
- a recent cardiovascular event was probably an embolism, according to a neurologist or cardiologist;
- severe LV dysfunction (LVEF severe valve disease requiring intervention;
- decompensated cardiac heart failure;
- active infection (e.g. pneumonia, active skin infections and antibiotic use);
- chronic diarrhea;
- pregnancy;
- the patient has a history of clinically significant active liver or kidney disease;
- the presence of data on oncological diseases;
- patients with traumatic brain injury;
- acute myocardial infarction less than 30 days old;
- cannot provide informed consent.

To verify the diagnosis of moderate periodontitis, the patient was examined by a dentist according to the generally accepted scheme with determination of the gingival sulcus bleeding index (SBI) and periodontal index (PI) according to Russell (1956). The lipid spectrum was assessed in saliva using the FP -910 (M) analyzer from Labsystems (Finland). Studies were conducted on the level of total cholesterol (TC), low-density lipoproteins (LDL), high-density lipoproteins (HDL), and triglycerides (TG). The diagnosis of coronary artery atherosclerosis was made based on the clinical presence or absence of angina confirmed by ECG and echocardiography or after coronary angiography with the presence of stenosis of the main arteries up to 50%.

Table 1. Comparative analysis of admission indicators

No.	Indicator	1 group (n=40)		2 group (n=40)		P	Index
		M	m	M	m		
1	BMI	31.69	3.50	30.88	3.45	>0.2	BMI
2	ALT	49.25	22.98	43.36	20.39	>0.2	ALT
3	AST	36.10	15.01	38,48	18.12	>0.5	AST
4	LDL	2.98	1.07	3.74	0.96	<0.01	LDL
5	HDL	1.76	0.57	1.38	0.24	<0.01	HDL
6	Triglycerides,	1.98	0.93	1.41	0.60	<0.01	Triglycerides,
7	Glucose	5.47	0.43	5.94	0.67	<0.01	Glucose
8	C-reactive protein	8.03	2.62	8.98	2.47	>0.05	C-reactive protein
9	IL-6	12.20	0.46	12.51	0.46	>0.05	IL-6

No.	Indicator	1 group (n=40)		2 group (n=40)		P	Index
		M	m	M	m		
10	Gum recession	5.14	0.27	5.24	0.34	>0.1	Gum recession
11	Periodontal pocket depth	4.92	0.21	4.84	0.34	>0.1	Periodontal pocket depth
12	Clinical gingival attachment	3.92	0.26	3.89	0.29	>0.5	Clinical gingival attachment
13	Plaque index	2.01	0.29	1.93	0.25	>0.2	Plaque index
14	Bleeding index	2.21	0.27	2.13	0.28	>0.1	Bleeding index
15	Periodontal index	3.48	0.26	3.74	0.20	<0.1	Periodontal index

Note: P – significance of differences in indicators of groups I and II

Table 2. Comparative analysis of indicators after 3 months

No.	Indicator	1 group (n=40)		2 group (n=40)		P	Index
		M	m	M	m		
1	BMI	30.42	3.38	30.77	3.61	>0.5	BMI
2	ALT	33.05	11.42	39.43	19.74	<0.05	ALT
3	AST	25.85	8.16	33.65	16.92	<0.05	AST
4	LDL	2.74	0.96	3.45	0.90	<0.001	LDL
5	HDL	1.99	0.53	1.45	0.20	<0.001	HDL
6	Triglycerides,	1.71	0.79	1.18	0.46	<0.001	Triglycerides,
7	Glucose	5.24	0.36	5.57	0.56	<0.01	Glucose
8	C-reactive protein	5.33	1.95	8.95	1.92	<0.01	C-reactive protein
9	IL-6	7.53	0.30	8.37	0.38	<0.01	IL-6
10	Gum recession	4.93	0.27	5.10	0.37	<0.05	Gum recession
11	Periodontal pocket depth	3.9	0.21	4.71	0.34	<0.05	Periodontal pocket depth
12	Clinical gingival attachment	3.0	0.26	3.79	0.27	<0.1	Clinical gingival attachment
13	Plaque index	1.0	0.29	1.82	0.22	<0.01	Plaque index
14	Bleeding index	1.00	0.29	1.70	0.28	<0.05	Bleeding index
15	Periodontal index	3.32	0.25	3.60	0.21	<0.001	Periodontal index

Note: P – significance of differences in indicators of groups I and II

Table 3. Comparative analysis of indicators after 6 months

No.	Indicator	1 group (n=40)		2 group (n=40)		P	Index
		M	m	M	m		
1	BMI	27.19	2.90	30.92	4.5	<0.001	BMI
2	ALT	21.18	4.68	34.88	16.43	<0.001	ALT
3	AST	19.25	4.58	29.35	13.27	<0.001	AST
4	LDL	2.22	0.58	3.09	0.89	<0.001	LDL
5	HDL	1.91	0.18	1.57	0.17	<0.001	HDL
6	Triglycerides,	1.31	0.54	1.70	0.39	<0.1	Triglycerides,
7	Glucose	4.97	0.27	5.63	0.49	<0.01	Glucose
8	C-reactive protein	1.15	1.23	2.53	1.54	<0.001	C-reactive protein
9	IL-6	4.88	0.22	5.04	0.24	<0.01	IL-6
	Gum recession	4.37	0.30	4.59	0.38	<0.01	Gum recession
10	Periodontal pocket depth	3.60	0.26	4.30	0.36	<0.001	Periodontal pocket depth
11	Clinical gingival attachment	3.21	0.31	3.36	0.32	<0.05	Clinical gingival attachment
12	Plaque index	0.9	0.25	1.48	0.24	<0.01	Plaque index
13	Bleeding index	0.90	0.29	1.60	0.31	<0.05	Bleeding index
14	Periodontal index	2.94	0.25	3.21	0.27	<0.001	Periodontal index

Note: P – significance of differences in indicators of groups I and II

As can be seen from the table 1, patients of groups I and II had practically same BMI, liver ALT and AST levels enzymes, lipoproteins low and high density, triglycerides, glucose, C- reactive protein (CRP), and also changes in periodontal tissue: gum recession, periodontal pocket depth, plaque reading, bleeding index, and periodontal index.

The results of laboratory and instrumental studies were compared between the groups. The first group received 0.5 mg of colchicine once a day. The second group did not receive colchicine. All studies were simultaneously conducted before the administration of colchicine at a dose of 0.5 mg orally, as well as after 1 month, 3 months, and 6 months.

Statistical processing of the obtained data was carried out on an AMD personal computer. Sempron mobile x86 using Microsoft application packages Exel version XP for MS Windows XP Professional using the Biostat library of statistical functions. The mathematical apparatus included traditional methods for calculating relative (P) and average values (M) with the determination of their errors (± m). The difference counts reliable at $p<0.05$.

3. Results and Discussion

All patients were relatively the same age, which was 62.0±3.5 years in both groups.

As can be seen from Table 2, in the first group of patients who received colchicine orally under strict medical supervision, the levels of ALT and AST significantly decreased. Similarly, the level of C – reactive protein and IL-6 decreased reliably.

As for changes in periodontal tissue, after 3 months of observation, gum recession, periodontal pocket depth, plaque index, bleeding index, and periodontal index decreased reliably. This proves one more time the ant-inflammatory effect of colchicine [2,3].

After 6 months of observation of the parameters of the first and second groups, the differences in them changed even more in favor of the first group, whose patients received colchicine at a dose of 0.5 mg orally under strict control. Almost all blood parameters and changes in periodontal tissue once again confirm a decrease in the level of inflammation around the periodontium, a decrease in the plaque index, bleeding index, and periodontal pocket depth. Recently, scientists have increasingly paid attention to the relationship between periodontal diseases and the clinical course of coronary artery atherosclerosis. Analysis of the results of one study showed that the levels of various inflammatory markers, in particular IL-6 and CRP, were elevated in patients with periodontitis and atherosclerosis. An increase in the level of neutrophils was also indicated in both atherosclerosis and periodontitis [10]. These results of this systematic review suggest that endothelial dysfunction may be a link between periodontal diseases, particularly chronic moderate periodontitis, and coronary artery atherosclerosis [7]. Furthermore, atherosclerosis was found to be associated with more severe periodontitis, and this was indicated by higher serum levels of high-sensitivity C-reactive protein (hs-CRP) [6]. Elevated hs-CRP levels due to periodontitis place an additional burden on the pre-existing inflammatory activity of atherosclerotic lesions, and therefore increase the risk of clinically significant severe manifestations of atherosclerosis, such as acute myocardial infarction, sudden cardiac death, and chronic heart failure [2,3].

4. Conclusions

1. The analysis of the obtained data confirms the relationship between coronary artery atherosclerosis and chronic periodontitis.
2. When taking colchicine at a dose of 0.5 mg, the level of CRP, IL-6, TNF-a decreases in the studied saliva and blood, and the level of periodontal pocket depth, clinical gingival attachment, plaque index, bleeding index and periodontal index, as well as significant gingival recession, statistically significantly decreases.

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