RESULTS OF USE ANTIOXIDATE THERAPY WITH "ANTOKSID" IN COMPLEX TREATMENT OF CHRONIC GENERALIZED PARODONTITIS OF MODERATE SEVERITY

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Studies have revealed a close relationship between the development of inflammatory changes in the periodontium and the activity of free radical processes (antiparticles) and antioxidant protection (AOP). Objective: to study the effectiveness of antioxidant therapy with "Antoksid" in the complex treatment of patients with chronic periodontitis of moderate severity. The task of the study was also the determination of the antioxidant activity of the developed therapeutic and dental agent "Antoksid" (Patent # 960) by the "in vitro" method. The object of the study was the shade of erythrocytes obtained from peripheral blood taken from 20 adult patients with periodontitis at the age of 30 to 39 years. It was revealed that "Antoksid" possesses antioxidant properties when exposed to pathological biological fluids, in particular, the blood plasma of patients with periodontitis. Comparative clinical studies in evaluating different treatment methods were performed in 30 patients, the control group consisted of 10 healthy people. The results of the treatment were evaluated on the 5th and 10th days of treatment. The evaluation was carried out by biochemical methods on the effect on the state of the processes of LPO, AOP systems in cell membranes (erythrocyte) and blood plasma. It was found that the best effect was achieved by treatment with the introduction of "Antioxidant" by the method of UFF, and the treatment with the traditional method was the least effective. Studies have shown that the use of "Antoksid" in the treatment of chronic generalized periodontitis leads to an increase in cell resistance to oxygen deficiency, activation of enzymatic reactions, and elimination of microcirculation disorders. Activation of the AOZ system, in turn, leads to restriction and breakage of chain radical reactions, normalization of oxidation-reduction reactions in cells and tissues, restriction of the inflammation focus and intensification of proliferative processes in periodontal tissue.

Keywords: Chronic periodontitis, free radical processes, lipid peroxidation, antioxidant protection, "Antoksid" phonophoresis

According to the opinion of many authors the lipid peroxidation processes (LPP), which are of general biological nature and, in opinion of many authors, are the universal mechanism of cell damage the level of membranes and play an important role in periodontitis pathogenesis. LP processes accelerate in case of any inflammatory diseases, cell membrane damage, stress factors effect on the human body, and in carcinogenesis, with a deficiency of vitamins and microelements, as well as in radiation illness, aging [1]. The products offree-radical processes (FRP) are able to damage the endothelia by causing microcirculation disorders, and also the basic components of connective tissue, including disturbance of the synthesis of alveolar bone protein matrix, collagen with disturbance of regeneration processes [2]. Basic representatives are the enzyme antioxidants and low molecular weight species of various chemical nature. When using in gnonenzymatic antioxidants, firstly vitamins, not only their anti-oxidant properties, but also pro-oxidant properties can be observed, which, certainly, is the undesirable property and reduces their antiradical efficiency [3, 4]. The development and introduction in practical stomatology of the medicinal facilities, which have high antioxidant activity, but don't have pro-oxidant properties, is perspective. Such medications include the substances from the group of enzymic antioxidants (superoxide dismutase, catalase and glutathione peroxidase). All the above mentioned enzymes are metalloproteases, i.e. their prosthetic centers include copper, zinc, cobalt and selenium and, accordingly, adequate functioning of these enzymes is possible only in condition of sufficient micronutrient content in the body. This task can be successfully solked by prescribing medicinal preparations consisting of anti-oxidation micronutrient elements, firstly Zn, Cu, Co and Se being basis of antioxidant enzymes [5].

The research goal is to study the efficiency of antioxidant therapy with "Antoksid" in patients with moderate severe chronic periodontitis.

Materials and methods of research

Depending on the treatment methods, the patients are divided into the following groups: first group – 10 patients who received traditional medical treatment; second group – 10 patients, in which treatment "Antoksid" in the form of applications was applied; third group – 10 patients, in which treatment "Antoksid" was introduced by the Ultraphonophoresis method. The treatment results were assessed on the 5th and10nd days of treatment. The control group comprised 10 healthy adults. The assessment was carried out by biochemical methods under effect on the condition of the LP processes, antioxidant defense system in cell membranes (erythrocyte) and blood plasma. Before you can assess the effectiveness of different regimens for treatment of patients periodontitis, one of the research

objectives was to determine the antioxidant activity of "Antoksid" by in vitro method through inhibitory action on free-radical oxidation of the red-cell membranes of patients with periodontitis, in which the free-radical oxidation processes are initiated by UV light. The object of research was the achromacytes produced from peripheral blood (venous), taken from 20 adult patients with periodontitis aged 30 to 39 years.

Results of research and their discussion

As the research have shown, the optical density of samples in the experimental series decreases in proportion to the activity of the investigational medicinal product "Antoksid" (table 1). Thus, the optical density fluctuations in the experimental samples after adding "Antoksid" ranged from 0.016 to 0.044 nm (on average, 0.029 ± 0.005 nm), whereas these fluctuations in the control samples ranged from 0,044 to 0,078 nm, which was on average 0,061 ± 0,09nm. Consequently, the inhibition of free-radical oxidation processes with "Antoksid" initiated by ultraviolet irradiation in experimental samples decreases by 51,9 ± 3,96%.

Thus, "Antoksid" has antioxidant properties on exposure to pathological biological fluids, particularly blood plasma of patients with periodontal disease. Taking into consideration that the "Antoksid" comprises the micronutrients such as zinc, cobalt, copper and selenium, which, in its turn, are the key elements in prosthetic groups of main enzymes of the antioxidant defense system, it is likely that its pharmacological effect will be determined by the activity of main antioxidant enzymes, namely superoxide dismutase, catalase and glutathione peroxidase. As shown by research, the activation of LP processes is observed in patients during the height of disease in comparison with the control group (table 2). So, if the content of primary products of lipid peroxidation in red-cell membrane – Lipid hydroperoxides, increases by 56% ($P < 0.01$), the concentration of end products of peroxidation – valid concentration, increases by more than 3 times ($P < 0.001$). The antioxidant defense system activity is changed in parallel to the change in LP intensity in steady-state functioning of biological membranes and about the role of these processes in the mechanisms of oral mucosa diseases development. Thus, the reference is made to the decrease in the general antioxidative activity of blood plasma lipids ($P < 0.01$), catalase activity ($P < 0.01$) and decreased concentration of ceruloplasmin in blood plasma ($P < 0.001$). Therefore, the intensity of oxidative processes under periodontitis, the indicator of which is the level of lipid peroxidation products content in the body, can give ideas about the stages of changes.

Table 1

Antioxidative activity of the dental agent "Antoksid" in vitro

Sample No.	Optical density of test samples (nm)	Optical density of control samples (nm)	Antioxidative activity, %
1	0,03	0,054	45,5
2	0,022	0,061	64,0
3	0,035	0,067	47,8
4	0,026	0,07	62,9
5	0,4	0,067	40,3
6	0,016	0,048	66,7
7	0,018	0,055	67,3
8	0,037	0,06	38,4
9	0,044	0,071	38,1
10	0,023	0,049	53,1
11	0,04	0,078	48,8
12	0,031	0,068	54,5
13	0,024	0,054	55,6
14	0,028	0,059	52,6
15	0,036	0,071	49,3
16	0,23	0,044	47,8
17	0,042	0,082	48,8
18	0,019	0,054	64,9
19	0,033	0,067	50,8
20	0,026	0,044	41,0
M ± м	0,029 ± 0,005	0,061 ± 0,009	51,9 ± 3,96

Table 2

Indices of LP processes andantioxidant defense system in red-cell membrane and blood plasma in patients with periodontitis

Analyzed indices	Units	Study group		Difference reliability
		Healthy people n = 10,M ± m	Patients with periodontitis, n = 30,M ± m	
Lipid hydroperoxides of red-cell membranes	Optical area	0,111 ± 0,008	0,174 ± 0,011	P < 0,01**
Valid concentration of red-cell membrane	Optical area	0,016 ± 0,003	0,059 ± 0,006	P < 0,001***
Antioxidative activity of blood plasma	%	25,1 ± 0,97	17,1 ± 0,8	P < 0,01**
Blood plasma catalase	μkat/L	22,5 ± 1,03	11,2 ± 0,67	P < 0,01**
Blood plasma ceruloplasmin	mcmol/l	3,07 ± 0,06	1,31 ± 0,03	P < 0,001***

Table 3

Indices of the LP products and the antioxidant defense system in red-cell membrane and blood plasma in the patients with periodontitis receiving traditional treatment

Patient groups and examination periods	Statistical indicators	Analyzedindices				
		LP products optical area		Antioxidative-activity, %	Catalase μkat/L	Ceruloplasmin mcmol/l
		Lipidhydrop-eroxides	Validcon-centration			
1. Healthy(control group), n = 10	M ± m	0,111 0,008	0,016 0,003	25,1 0,097	22,5 1,03	3,07 0,06
2. Patients at the height of the disease, n = 30	M ± m	0,174 0,011	0,059 0,004	17,1 0,084	11,2 0,67	1,31 0,03
3. Patients on the 5th treatment day, n = 10	M ± m P_{3-1} P_{3-2}	0,166 0,008 < 0,01** > 0,05	0,048 0,004 < 0,001*** > 0,05	17,8 0,092 < 0,01** > 0,05	10,3 0,63 < 0,01** > 0,05	1,41 0,06 < 0,001*** > 0,05
4. Patients on the 10th treatment day, n = 10	M ± m P_{4-1} P_{4-2} P_{4-3}	0,159 0,009 < 0,01** < 0,05 < 0,05	0,037 0,003 < 0,01** < 0,05* < 0,05*	17,9 0,074 < 0,01** > 0,05 > 0,05	13,9 0,8 < 0,01** > 0,05 > 0,05	3,2 0,08 > 0,05 < 0,01** < 0,01**

The first group of patients has not shown any significant changes in the analyzed parameters on the 5th day of treatment, that is, the lipid peroxidation intensity and the activity of antioxidant defense system remain at the height of the disease (P > 0.05), and accordingly in relation to the control indicators (P < 0.01- < 0.001) (table 3). On the 10th day of treatment there is a significant decrease in the valid concentration level of the red-cell membrane as compared with the data of previous examination periods (P < 0.05), but still its value remains significantly increased relative to the control index (P < 0.01). Also on the 5th treatment day the concentration of lipid hydroperoxides in red-cell membrane remains at the level of the height of disease and (P > 0.05). On the part of the indicators of the AOSIS system, the following picture is marked: antioxidant defense system indicators: general anti-

oxidative activity and catalase activity remain without significant dynamics compared to the previous examination terms ($P > 0.05$) and, accordingly, significantly reduced as compared to the control group indicators ($P < 0.01$).

The values of ceruloplasmin concentration in blood plasma reach the level of control ($P > 0.05$) and, accordingly, significantly increase in comparison with the data of the period of clinical manifestations and on the 5th day of treatment ($P < 0.01$).

Thus, the studies of the functional state of red-cell membranes and blood plasma in this group of patients at the end of treatment show that the depleted homeostatic potential at the micro level in the treatment process is not fully restored, which can create conditions for the prolongation of clinical disease manifestations in the future. The group of patients, who received "Antoksid" treatment in the form of applications, shows other picture in dynamics of changes in LP processes and antioxidant defense system in red-cell membranes and blood plasma (tab. 4). Thus, on the 5th treatment day as compared with the disease onset period, there was a significant decrease in the content of lipid hydroperoxides of red blood cell membranes ($P < 0.05$), valid concentration ($P < 0.05$), as well as a significant increase in catalase activity ($P < 0.05$) and the content of ceruloplasmin ($P < 0.01$) in blood plasma.

The general antioxidative activity has not changed during this period ($P > 0.05$). Despite the dynamics of changes in the functional state of red-cell membranes and blood plasma, these values do not reach the control indicators ($P < 0.05$- < 0.001) (table. 4).At the end of treatment (10 day) the indicators of lipid hydroperoxides, valid concentration, antioxidative activity, ceruloplasmin reach control values ($P > 0.05$), and the value of catalase activity, despite an increase relative to the period of height and on the 5th treatment day ($P < 0.05$), remains significantly lower ($P < 0.05$) than the control values. Accordingly, as compared with the previous examination periods, the indicators of lipid hydroperoxides, valid significantly reduce ($p < 0.01$), and the indicators of antioxidative activity, catalase and ceruloplasmin are significantly increase ($P < 0.05$- < 0.01).

Thus, in the periodontitis treatment the use of "Antoksid" in the form of applications has a pronounced antioxidant effect provided by the inhibitory effect on lipoperoxidation processes in cell membranes, by increasing the enzymatic system of antioxidant defense in blood plasma and by increasing the general antioxidative activity of blood lipids.

Table 4

Indices of the LP products and the antioxidant defense system in red-cell membranes and blood plasma in the patients with periodontitis receiving treatment with "Antoksid" applications

Patient groups and examination periods	Statisticalindicators	Analyzedindices				
		LP products optical area		Antioxidative activity, %	Catalase, μkat/L	Ceruloplasmin, mcmol/l
		Lipidhydroperoxides	Validconcentration			
1. Healthy (control group), n = 10	M ± m	0,111 0,008	0,016 0,003	25,1 0,097	22,5 1,03	3,07 0,06
2. Patients at the height of the disease, n = 30	M ± m	0,174 0,011	0,059 0,004	17,1 0,084	11,2 0,67	1,31 0,03
3. Patients on the 5th treatment day, n = 10	M ± m P_{3-1} P_{3-2}	0,146 0,009 < 0,01** < 0,05	0,043 0,005 < 0,001*** > 0,05*	19,9 0,10 < 0,05* > 0,05	14,3 0,72 < 0,01** < 0,05*	2,4 0,08 < 0,05* < 0,01*
4. Patients on the 10th treatment day, n = 10	M ± m P_{4-1} P_{4-2} P_{4-3}	0,099 0,01 > 0,05 < 0,01** < 0,01**	0,023 0,003 > 0,05 < 0,01** < 0,01**	24,2 0,11 > 0,05 < 0,01** < 0,05*	18,6 1,09 < 0,05* < 0,01** < 0,05*	2,98 0,06 > 0,05 < 0,01** < 0,05*

Table 5

Indices of the LP products and the antioxidant defense system in red-cell membranes and blood plasma in the patients with periodontitis receiving treatment with "Antoksid" by the ultraphonophoresis method

Patient groups and examination periods	Statisticalindicators	Analyzed indices				
		LP products optical area		Antioxidative activity, %	Catalase, μkat/L	Ceruloplasmin, mcmol/l
		Lipidhydroperoxides	Validconcentration			
1. Healthy (controlgroup), n = 10	M ± m	0,111 0,008	0,016 0,003	25,1 0,097	22,5 1,03	3,07 0,06
2. Patients at the height of the disease, n = 30	M ± m	0,174 0,011	0,059 0,004	17,1 0,084	11,2 0,67	1,31 0,03
3. Patients on the 5th treatment day, n = 10	M ± m P_{3-1} P_{3-2}	0,137 0,007 < 0,05* < 0,01**	0,039 0,004 < 0,01** < 0,05*	18,1 0,09 < 0,05* > 0,05	13,3 0,57 < 0,01** > 0,05	2,54 0,07 < 0,05* < 0,01**
4. Patients on the 10th treatment day, n = 10	M ± m P_{4-1} P_{4-2} P_{4-3}	0,102 0,009 > 0,05 < 0,01*** < 0,05*	0,21 0,003 > 0,05 < 0,01** < 0,05*	26,2 0,121 > 0,05 > 0,05 < 0,01**	20,4 0,98 > 0,05 < 0,01** < 0,05*	3,12 0,08 > 0,05 < 0,01** < 0,05*

In the third group of patients treated with "Antoksid" by the ultraphonophoresis method, the dynamics of change in the functional state of red-cell membranes and blood plasma has a picture almost identical to the second study group (table. 5).

At the end of treatment (10 days) the complete normalization of functional state of red-cell membranes and blood plasma is observed in this patient group. In other words, the analyzed indicators do not have a significant difference with respect to the indicators of the control group ($P > 0.05$) (table. 5). Thus, the conducted studies have shown that the "Antoksid" application in the treatment of chronic generalized periodontitis leads to increased cell resistance to the oxygen deficiency, enzymatic reaction activation, elimination of microcirculatory disorders. The activation of the antioxidant defense system, in its turn, leads to the limitation and breakage of chain radical reactions, normalization of oxidation-reduction reaction in cells and tissues, and to the limitation of inflammation site and enhancing proliferative processes in the periodontal tissue.

Conclusions

1. The determination of "Antoksid" antioxidant activity has revealed that "Antoksid" has antioxidant properties, and its pharmacological action is determined by the activity of the main antioxidant enzymes, namely superoxide dismutase, catalase and glutathione peroxidase.

2. The "Antoksid" administration by the ultraphonophoresis method increases the enzymatic component of antioxidant defense system, which results in the normalization of the main enzymes in the blood plasma, and in more restrictive lipo-pereoxidation processes. All this contributes to the faster recovery of periodontal tissues.

References

1. Elbakyan K.S., Karakov K.G., Markarova G.V. Free-radical oxidation and antioxidant defence with periodontitis // PFUR Bulletin, series Medicine. – 2012. – № 2. – P. 133-136.

2. Kirichek L.T. Comparative evaluation of tissue and hematological parameters of oxidative stress in oral mucosa inflammation in experiment // Successes of modern natural science. – 2014. – № 7. – P. 17-19.

3. Blekanova V.A. Correction of disorders of red-cell membrane lipid composition in chronic generalized periodontitis. Modern problems of science and education. – 2012. – № 5. – P. 21-25.

4. Kulchenko A.A. Pathogenetic mechanisms of antioxidant therapy in chronic periodontitis prevention of: dis. ... Candidate of Medical Science. – Moscow, 2013. – 114 p.

5. Kondyurova E.V. Laser therapy in the correction of lipid metabolism in chronic periodontitis // Bulletin of the Moscow University. – 2016. – Vol. 26. – № 4. – P. 548-560.