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LIPID PEROXIDATION AND THE ANTIOXIDANT SYSTEM IN ACUTE CORONARY SYNDROME

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Annotation: The involvement of reactive oxygen species in metabolism under conditions of insufficiency (depletion) of antioxidant activity system AOS enzymes has a direct damaging effect on cardiomyocytes, activates the procoagulant system, accelerates the degradation of endothelial NO, which ensures vasodilation. In patients with ACS (acute coronary syndrome) there is a significant increase in LPO (Lipid peroxidation) activity and a decrease in AOS, which is accompanied by oxidative modification of lipids in platelet membranes and blood plasma.

Key words: acute coronary syndrome, lipid peroxidation, antioxidant system, thrombolysis, MDA, catalase, superoxide dismutase

Purpose of the study: to study free-radical oxidation status in patients with acute coronary syndrome (ACS) with and without ST-segment elevation.
Materials and Methods: 109 ACS patients with and without ST-segment elevation. LPO activity was determined by the content of a secondary metabolite of lipid peroxidation - malone dialdehyde - in the blood platelets of patients. AOS was assessed by the activity of intracellular antioxidant enzymes in platelets: superoxide dismutase and catalase.
Results of the study: in ACS patients there is an increase of LPO activity and decrease of AOS activity in platelet membranes with the most pronounced changes in ACS patients without ST elevation. Streptokinase application for systemic thrombolysis in ACS patients with ST-segment elevation is accompanied by significant activation of LPO, AOS parameters.

Despite the pronounced progress in medicine associated with scientific discoveries in recent decades, cardiovascular mortality continues to occupy the first place among the causes of death among adults in developed and developing countries (20-42%) according to epidemiological studies). Statistics show that coronary heart disease (CHD) as a cause of death is far ahead of all other cardiovascular nosologies (more than half of all cardiovascular deaths are related to CHD). Cardiovascular mortality in the Central Asian republics exceeds the average European level by more than 2.5 times, and in the older age group by almost 5 times. The worsening course of CHD is usually associated with the development of acute coronary syndrome (ACS). This clinical syndrome combines unstable angina and myocardial infarction in the first hours and days of their development. Pathogenetically, both these diseases are associated with intracoronary thrombosis at the sites of destabilization of lipid-rich atherosclerotic plaque coats. Destabilization of the cap and accumulation of lipids in it lead to cap rupture, release of biologically active substances, blood aggregation and coagulation, and eventually to vessel lumen narrowing.

After widespread introduction of systemic thrombolysis into clinical practice it was revealed that after thrombolysis there is activation of free-radical oxidation (reperfusion injury phenomenon) in patients. In the process of reperfusion injury there are various rhythm disturbances, which is

associated with free radical damage to cell biomembranes and mitochondria, disruption of transmembrane ion transport. The same mechanism is associated with the phenomenon of development of subacute forms of DIC syndrome (consumption coagulopathies) on day 1-3. In addition, the mechanism of free-radical lipid oxidation activation can change myocardial metabolism with the formation of hibernation zones and ischemic apoptosis of cardiomyocytes.

The aim of this study was to investigate free-radical oxidation in ACS patients with and without ST-segment elevation.

The study involved 109 ACS patients, of whom 54 patients (49.5%) had ECG-examination revealed ST-segment elevation (the 1st group), the remaining 55 patients (50.5%) had no significant ECG changes (the 2nd group). 1(o)-group with systemic thrombolysis. 1(k)-group without systemic thrombolysis.

In platelet membranes of ACS patients without ST elevation there was significantly more pronounced activation of LPO, indirectly estimated by the level of MDA and inhibition of AOS, which was manifested by decreased activity of SOD and CAT. In ACS patients with ST elevation a significant increase of MDA and decrease of CAT activity was observed compared to healthy subjects, while SOD activity slightly exceeded parameters typical for healthy subjects. Thus, in ACS patients there is an increase in LPO activity and a decrease in AOS activity in platelet membranes with the most pronounced changes in ACS patients without ST elevation (Table 1).

Table 1.
The state of LPO/ANS system in ACS patients

Indicator	Index PL (n=20)	Group 1 (n=54)	Group 2 (n=55)
MDA, nmol/mg protein	6,87±0,62	10,17±1,27***	19,80±1,93***^^^
SOD, units act/mg protein	2,22±0,52	2,50±0,43*	1,83±0,32**^^^
CAT, μmol/min/mg protein	1,55±0,20	1,23±0,39***	0,96±0,35***^^^

Note: Significance of difference with healthy person group * $p<0.05$; ** $p<0.01$; p*** $p<0.001$, between ACS patient groups - ^^^ $p<0.001$.

It is known that ACS without ST elevation is associated with the formation of the so-called platelet thrombus. The pathogenesis of this process consists in the increase of platelet aggregation activity, which is based on the increase of LPO activity and decrease of AOS activity in the membranes. This leads to peroxide modification of membrane PL, an increase in their cholesterol content and an increase in membrane stiffness. In ST-elevation ACS patients a more pronounced peroxide modification of lipid structure of platelet membranes is observed, probably due to plasma LPO activation.

Parameters of free-radical oxidation demonstrated unidirectional dynamics in both subgroups of group 1 (Table 2). By the 3rd day of observation, MDA concentration increased in group 1o by 41.84±23.57% and in group 1k by 24.94±17.18% ($p<0.01$), SOD activity in group 1o increased by 18, 76±24.12%, and in group 1k decreased by 7.59±17.93% ($p<0.001$), CT activity increased in groups 1o and 1k by 103.91±75.92% and 19.14±43.14% ($p<0.001$), respectively. By day 7-10, SOD and CT activity (AOS enzymes) increased (SOD by 38.49±32.66%, $p<0.001$, and 21.74±21.89%, $p<0.05$, in groups 1o and 1k, respectively, differences in dynamics between groups - $p<0.05$; CT by 113.86±78.20%, $p<0.001$, and 108.87±69.99%, rd, respectively, differences in dynamics between groups - rd). The concentration of MDA (a secondary product of LPO) slightly decreased by day 7-

10 of observation (overall dynamics by day 7-10 were 42.34±25.51%, p<0.001 and 37.36±17.16%, p<0.001, respectively, differences in dynamics between groups 1o and 1k - rnd). Increase of MDA activity against the background of AOS activity increase confirms the phenomenon of oxidative stress, which is observed after systemic or spontaneous thrombolysis with maximal intensity on the 1-3rd day after disease development and adaptive activation of AOS.

Table 2.

Dynamics of LPO/ANS system activity in ACS patients with ST-segment elevation

Indicator	baseline	3-days	7-10 days
MDA, nmol/mg protein	10,21±1,27 10,17±1,27	14,31±1,98*** 12,58±0,46***^^^	14,25±1,36*** 13,77±0,62***
SOD, units act/mg protein	2,54±0,42 2,50±0,43	2,93±0,19*** 2,25±0,22*^^^	3,40±0,34*** 2,96±0,17***^^^
CT, μmol/min/mg protein	1,28±0,40 1,23±0,39	2,35±0,30*** 1,32±0,23^^^	2,45±0,24*** 2,32±0,15***^^

Note: Numerator is the experimental group, denominator is the control group. Significance of difference with baseline parameters * p<0.05; *** p<0.001, between patient groups -^^^ p<0.01; ^^^^ p<0.001.

The activity of LPO increased, which contributed to an increase in the content of cholesterol in platelet membranes. AOS activity also increased. The increase in LPO activity is a reflection of the oxidative stress observed during thrombus recanalization. In patients who did not receive streptokinase, the same processes were also observed, but significantly less pronounced, which probably indicates the processes of spontaneous recanalization in this group of patients. By 7-10 days of observation there was a decrease in the concentration of stable nitric oxide metabolites in platelets, against the background of a decrease in LPO activity and activation of AOS.

MDA concentration in blood plasma of ACS patients was significantly higher than in the group of healthy subjects, but there was no significant difference between the groups of patients. Antioxidant defense, assessed by the content of SOD and CAT in erythrocytes, was suppressed in ACS patients, with significantly lower AOS activity in the 1st group of patients.

Thus, in ACS patients with ST-segment elevation activation of LPO and decreased AOS activity, and as a consequence, oxidative modification of lipids in platelet membranes is more pronounced. The use of streptokinase for systemic thrombolysis in ST-segment elevation ACS patients is accompanied by significant activation of LPO and AOS parameters. The results of this study indicate the need for additional research on the use of antioxidant therapy to prevent reperfusion injuries.

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