IMPACT ASSESSMENT OF PHYSICAL EXERCISE ON THE FACTORS FOR PROGRESSION OF ATHEROSCLEROSIS IN PATIENTS AFTER SUSTAINED MYOCARDIAL INFARCTION: A THREE-YEAR FOLLOW-UP

HODNOTENIE VPLYVU POHYBOVÝCH CVIČENÍ NA PROGRESNÉ FAKTORY ATEROSKLEROTICKÉHO PROCESU U PACIENTOV PO PREKONANÍ INFARKTU MYOKARDU: 3-ROČNÝ VÝSKUM

KUCHMENKO Olena[2], TERESHCHENKO Nataliia[1], MALYNOVSKA Iryna[1], BABII Liana[1], SHUMAKOV Valentyn[1], SHEIKO Vitalii[2], DEREKA Tetiana[3]

[1] *Department of Myocardial Infarction and Cardiorehabilitation, "National Scientific Center "Institute of Cardiology, Clinical and Regenerative Medicine named after Academician M.D. Strazheska of the National Academy of Medical Sciences of Ukraine", Kyiv, Ukraine*
[2] *Department of Biology, Nizhyn Gogol State University, Nizhyn, Ukraine*
[3] *Faculty of Healthcare, Alexander Dubcek University of Trenčín, Trenčín, Slovak republic*

ABSTRACT

Theoretical background: Cardiac rehabilitation is important in the treatment of patients who have suffered from an acute myocardial infarction.

Objective: To verify the dynamics of changes in protein and lipid factors progression of atherosclerosis in patients who sustained acute myocardial infarction (AMI) and were included in a physical exercise program for 3 years of follow-up.

Research sample and method: A total of 91 patients with AMI hospitalized within the "therapeutic window" for revascularization were included in the study. In the first group there were 47 patients who worked out for three months starting at an early post-hospital stage; the second group 44 patients who did not exercise. In year one, two and three coronary angiography was performed to assess the atherosclerotic process activity. Subsequently, the first and second group of patients were rearranged according to the data obtained.

Results: The PON-1 activity was significantly reduced after AMI and during the three-year period, its growth was observed. After AMI the MPO activity was significantly increased and during the three-year period its decrease was observed. The dynamics of changes in the PCG content in serum, and the LDL + VLDL and HDL fraction is consistent with the dynamics of changes in the PON-1 activity. The lack of progression of atherosclerotic plaques on the background of statin therapy was not accompanied by the achievement of LDL-C target level, as in patients with progression of the atherosclerotic process.

Conclusions: Reduce oxidative stress and increase antioxidant activity in the group without the signs of the atherosclerotic progression makes assume that qualitative changes in lipoprotein particles are as important as their quantitative properties.

Key words: Physical exercise. Myocardial infarction. Atherosclerosis progression. Lipoproteins. Oxidative stress.

ABSTRAKT

Východiská: Osobitné miesto v liečbe pacientov, ktorí prekonali akútny infarkt myokardu zaujíma kardiorehabilitácia

Cieľ: Skúmať dynamiku zmien proteínových a lipidových faktorov progresie aterosklerotického procesu u pacientov, ktorí prekonali akútny infarkt myokardu a zúčastnili sa 3-ročného kardiorehabilitačného programu (vykonávali fyzické cvičenia).

Materiály a metódy: Do štúdie bolo celkovo zaradených 91 pacientov s akútnym infarktom myokardu, ktorí boli hospitalizovaní počas „terapeutického okna" s následnou revaskularizáciou. Prvú skupinu tvorilo 47 pacientov, ktorí sa zaoberali komplexom fyzických cvičení počas troch mesiacov začínajúc od skorého ponemocničného obdobia; druhú skupinu tvorilo 44 pacientov, ktorí vôbec necvičili. Po prvom, druhom a treťom roku pozorovania sa všetci pacienti podrobili koronárnej angiografii na posúdenie aktivity aterosklerotického procesu. Potom bola prvá a druhá skupina pacientov reorganizovaná podľa získaných výsledkov štúdie.

Výsledky: Aktivita paraoxonázy-1 výrazne klesá po akútnom infarkte myokardu a jej rast je pozorovaný počas 3-ročného obdobia. Po akútnom infarkte myokardu sa aktivita myeloperoxidázy počas 3-ročného obdobia pozorovania zvyšuje a znižuje. Dynamika zmien obsahu karbonylových produktov oxidácie proteínov v krvnom sére, frakcií LNH (lipoproteíny s nízkou hustotou)+LPVNH (lipoproteíny s veľmi nízkou hustotou) a LVH (lipoproteíny s vysokou hustotou) koreluje s dynamikou zmien aktivity paraoxonázy-1. Absencia progresie aterosklerotického procesu na pozadí liečby statínmi nebola sprevádzaná dosiahnutím cieľovej hladiny cholesterolu v LNH, ako u pacientov s progresiou aterosklerotického procesu.

Záver: Pokles intenzity oxidačného stresu a zvýšenie antioxidačnej aktivity u pacientov v skupine bez progresie aterosklerotického procesu naznačuje, že kvalitatívne zmeny v lipoproteínových frakciách sú oveľa dôležitejšie v porovnaní s kvantitatívnymi zmenami.

Kľúčové slová: Fyzické cvičenia. Infarkt myokardu. Progresia aterosklerotického procesu. Lipoproteíny. Oxidačný stres.

INTRODUCTION

Despite the considerable progress in the treatment of acute coronary syndrome (ACS), coronary heart disease (CHD) remains the main cause of death worldwide. Cardiac rehabilitation has a special place in treating patients who have suffered from an acute myocardial infarction (AMI) (Cowie

et al., 2019). Among the versatile and multidisciplinary cardiac rehabilitation programs for this category of patients, physical rehabilitation is largely perceived as the most important one (Winnige et al., 2021). The authors maintain that in the early post-infarction period, the most prominent ro le should be long to physical training amongst multifarious treatment components (Al Quait et al., 2018) Exercise lays the groundwork for patients in re-evaluating their lifestyle, helps comprehend the chronicity of their disease; it is conducive to making patients take care of weight control, break bad habits that include smoking, control blood pressure and LDL levels. As well as it is contributive to patients' adherence to treatment diets and regular physical activity (The BACPR Standards, 2017). Patients with MI, coronary artery bypass grafting or percutaneous intervention with stable angina or chronic heart failure should exercise at a medium-intensity aerobic workout for 30 minutes at least three times a week (Benjamin et al., 2017). All these factors determine the possibility of widespread physical training in cardiac rehabilitation programs at the post-hospital stage.

Today, lipoprotein particles that role in atherogenesis processes are well-documented, whereas the HDL has not been studied sufficiently when compared with VLDL and LDL. According to current studies, the qualitative characteristics of HDL that are attributed to their associated protein and lipid molecules are much more critical than their circulation numbers. Among the HDL-associated enzymes, an essential role is played by paraoxonase-1 (PON-1) (Gordon et al., 2017). Also, in inflammatory vascular diseases, a significant contribution is made to the enzyme myelo-peroxidase (MPO) to leukocyte-mediated tissue damage that interacts with the vascular wall by binding and penetrating through endothelial cells, and strong oxidants are produced (Kargapolova et al., 2021).

The modern medical care, owing to the timely non-invasive diagnosis of the structure of the atherosclerotic plaque which considers the bioche-mical components of atherogenesis, establishes substantial *grounds to believe* that the above-mentioned developments will allow for preventing recurrent coronary catastrophes and will improve the quality of life of patients with different conditions.

OBJECTIVE

To investigate the dynamics of changes in protein and lipid factors of atherosclerosis progression in patients who sustained AMI and were enrolled in a physical exercise program for 3 years of follow-up.

RESEARCH SAMPLE

The verification included 91 patients (the mean age 52.8 ± 6.7 years) with AMI, hospitalized within the "therapeutic window" for revascularization (Table 1).

An occlusion of the infarction-related coronary artery was revealed on angiography in all patients. When included in the study, patients underwent 4 examinations at discharge from the hospital (12–15 days after the development of AMI), 4, 6, and 12 months after AMI. In addition, a test for bicycle ergometry test was performed during the examination 2.5 months after the AMI (the period that corresponded to the half-course of physical therapy).

Table 1 Baseline characteristics of patients included in the study

Indexes	1st group (n = 47)	2nd group (n = 44)	p
Age, years (Me (IQR))	52.2 (44.0; 60.0)	53.1 (46.5; 60.0)	0.98
Size of myocardial infarction: Q-IM (%) Non Q-IM (%)	 44 (93.6) 3 (6.4)	 41 (93.2) 3 (6.8)	 0.98 0.99
Localization of myocardial infarction: - front (%) - back (%)	 24 (51.1) 23 (48.9)	 22 (50.0) 22 (50.0)	 0.97 0.98
Hypertension (%)	31 (65.9)	32 (72.7)	0.99
Diabetes mellitus (%)	9 (19.1)	6 (13.6)	0.99
Heart Failure: stage I (%) stage IIA (%)	24 (51.1) 23 (48.9)	28 (63.6) 16 (36.3)	0.96 0.90
Smoking (%)	30 (63.8)	33 (75.0)	0.97

Over time, the patients were consistently examined one, two and three years after the AMI onset. All patients received basic therapy according to the existing guidelines, protocols and recommendations. The patients were assigned to two groups depending on the type of cardiac rehabilitation. The first group consisted of 47 patients who worked out for three months starting at an early post-hospital stage. Patients of the 1st group (cardiac rehabilitation program), in addition to distance walking and physical therapy classes, did physical training on a cycle ergometer three times a week for 30 sessions (3 months). The training regime was calculated based on the results of bicycle ergometry, individually and was 75% of the threshold load. After 15 classes, an additional test on bicycle ergometry was conducted with an increase in the level of the training regimen for the next 15classes and other. The second group consisted of 44 patients. In patients of the 2nd group, the rehabilitation program consisted of long-distance walking and physical exercises according to the Myocardial Infarction term and was carried out without the supervision of a doctor and correction of loads, completely independently. They were examined at the same time as the first group. They received all the drug treatment, were given recommendations for exercise therapy and were advised to increase their movements the same way as the patients of the first group. In year one, two and three coronary angiography was performed to assess the atherosclerotic process activity. Subsequently, the first and second group of patients were rearranged according to the data obtained. The group without progression of the atherosclerotic process consisted predominantly of patients who performed physical exercises and complied with the drug treatment. The rehabilitation exclusion criteria were the following: heart failure above stage IIA, large left ventricular aneurysm, intracavitary thrombosis, reduced ejection fraction to less than 45 %, severe ventricular arrhythmias, and severe disorders of the musculoskeletal system interfering with bicycle ergometry exercise. All patients underwent general clinical and instrumental evaluation; including echocardiography and bicycle ergometry with a thorough study of the clinical course of the disease.

METHODOLOGY

Biochemical blood tests were performed according to the generally accepted methods. The content of low-density lipoprotein cholesterol (Ch-LDL), high-density lipoprotein cholesterol (Ch-HDL), triglycerides (TG), total cholesterol (Ch), and atherogenic coefficient (CA) were determined with an automatic biochemical analyzer A-25 (Spain) using appropriate kits. Blood biochemistry assays were performed in all subjects. The protein carbonyl groups (PCG) content in blood serum, HDL and LDL + VLDL fractions, the serum TBARP content and MPO activity were determined by (Vasylchenko et al., 2020). The catalase activity in serum was examined spectrophotometrically (Aebi, 1984). The PON-1 activity was determined by (Manolescu et al., 2013). Leukocyte elastase (LE) and macrophage elastase activity in blood serum was evaluated by (Kubyshkin et al., 2008). The Kolmogorov-Smirnov test for normality distri-bution and Student's t-test, nonparametric Mann-Whitney (U-test) and Pearson rank correlation test were used in the statistical analysis. Different values were considered statistically significant at $p<0.05$. The results were expressed as the mean and standard deviation of the mean (M±SD).

RESULTS

In our research, no significant differences were identified in lipid indices between the groups. Moreover, neither group was able to achieve the target Ch-LDL nor total cholesterol levels.

It was found that in the 2nd group, the PON-1 activity after AMI tended to decrease as compared with the patients of 1st group. A year later, the same trend persisted. The patients in the 1st group manifested a higher level of PON1 activity than those in the 2nd group. But in three-year time, the patients of 2nd group showed an intensive increase in the PON1 activity which became significantly higher when compared to the patients of 1st group. The PON-1 activity trend was the same in both groups. One year after the AMI onset, in both groups the TBARP content was the same, with a slight decrease after three years of observation. The changes in TBARP content in both groups were statistically insignificant. The TBARP content trend was almost the same in both groups. After three years, there was an increase in the catalase activity in the 1st and 2nd groups. In the 2nd group, catalase activity was higher than in the 1st group. Three years after AMI, the 1st group showed an increased catalase activity, and in the 2nd group the progression was comparable (Table 2).

Table 2 PON1 activity, TBARP content and catalase activity in patients of both groups in the dynamics of three years (Med; Q1-Q3)

Parameter	1 group - with atherosclerosis progression					2 group - without atherosclerosis progression					
	Med	p1-3	Q1	Q2	Q3	Med	p1-3	Q1	Q2	Q3	p1gr-p2gr
PON1,after AMI, kU/l	3.33	0.65	0.86	3.33	5.37	2.35	0.66	1.63	2.35	2.99	0.85
PON1, 1 year after AMI	2.18		1.46	2.18	6.19	1.49		1.26	1.49	2.18	0.23
PON1, 3 years after AMI	2.93		0.46	2.93	-	6.21		2.04	6.21	12.33	0.00
TBARP, after AMI, U/l	10,92	0.18	8,97	10.92	11.99	10.92	0.29	10.14	10.92	11.50	0.85
TBARP, 1 year after AMI	10.14		9.36	10.14	11.20	10.92		10.14	10.92	11.70	0.18
TBARP, 3 years after AMI	8.97		7.80	8.97	-	9.36		9.04	9.36	10.92	0.51
Catalase, after AMI,U/l	5.45	0.18	4.48	5.485	7.90	5.71	0.59	5.26	5.71	9.39	0.43
Catalase, 1 year after AMI	6.21		5.48	6.215	8.58	8.44		7.02	5.44	8.50	0.60
Catalase, 3 years after AMI	7.35		6.40	7.350	-	10.45		8.75	7.45	9.29	0.03

Legend: * - p <0.05 compared to the values after AMI, # -p <0.05 compared between groups.

Table 3 The content of the protein carbonyl groups (PCG) in blood serum, HDL and LDL + VLDL fractions in patients of both groups in the dynamics of three years (Med; Q1-Q3)

Parameter	1 group - with atherosclerosis progression					2 group - without atherosclerosis progression					
	Med	p_{1-3}	Q1	Q2	Q3	Med	p_{1-3}	Q1	Q2	Q3	p_{1gr}-p_{2gr}
PCG in blood serum, after AMI, U/ml	5.25	0.18	4.58	5.25	5.93	5.00	0.31	4.73	5.00	5.53	0.76
PCG in blood serum, 1 year after AMI	4.75		3.90	4.75	5.75	5.40		4.70	5.40	5.60	0.36
PCG in blood serum, 3 years after AMI	5.05		3.20	3.75	-	3.75		4.53	5.00	5.25	0.00#
PCG in LDL + VLDL fraction, after AMI, U/mg of lipids	0.87	0.18	0.66	0.87	0.98	0.70	0.37	0.58	0.70	0.80	0.10
PCG in LDL + VLDL fraction,1 year after AMI	0.81		0.60	0.71	0.96	0.90		0.70	0.90	1.00	0.26
PCG in LDL + VLDL fraction, 3 years after AMI	0.86		0.45	0.68	-	0.68		0.55	0.85	1.00	0.002#
PCG in HDL fraction, after AMI, U/ml	2.55	0.66	1.78	2.55	3.48	2.70	0.17	1.80	2.70	3.28	0.95
PCG in HDL fraction,1 year after AMI	2.75		2.13	2.75	3.53	2.10		2.10	3.10	3.40	0.90
PCG in HDL fraction, 3 years after AMI	2.28		1.85	2.18	-	2.01		1.76	2.25	2.75	0.05#

Legend: * - p <0.05 compared to the values after AMI, # -p <0.05 compared between groups.

During the three-year follow-up, in the 1st group the PCG content in blood serum decreased. An increased PCG content was observed in the lipoprotein fractions. There were multidirectional shifts in the 2nd group; a year after AMI, the PCG content in blood serum was higher than the group's initial data. In a three-year time, the PCG content in LDL+VLDL fraction almost approached the reference values. Three years after the AMI onset, the PCG content in HDL fraction of the patients of 1st group differed slightly from the first examination results (after AMI). In three years, the PCG content in the HDL fraction of the 2nd group fluctuated in different directions. The patients of 2nd group

Table 4 The myeloperoxidase, macrophage elastase and leukocyte elastase activity in patients of both groups in the dynamics of three years (Med; Q1-Q3)

Parameter	1st group – with atherosclerotic progression					2nd group - without atherosclerotic progression					
	Med	p_{1-3}	Q1	Q2	Q3	Med	P_{1-3}	Q1	Q2	Q3	p_{1gr}-p_{2gr}
MPO, after AMI, U/min	0.009	0.180	0.004	0.009	0.013	0.004	0.590	0.002	0.004	0.005	0.090
MPO, 1 year after AMI	0.002		0.001	0.002	0.003	0.003		0.001	0.003	0.007	0.513
MPO, 3 years after AMI	0.001		0.000	0.001	-	0.001		0.000	0.001	0.003	0.591
ME, after AMI, nmol/ml·min	0.109	0.180	0.109	0.109	-	0.109	0.110	0.109	0.109	0.218	1.000
ME, 1 year after AMI	0.034		0.004	0.034	0.096	0.055		0.055	0.055	0.109	0.215
ME,3 years after AMI	0.158		0.157	0.158		0.214		0.138	0.214	0.258	0.667
LE, after AMI, nmol/ml·min	0.546	0.180	0.491	0.546	-	0.519	0.114	0.396	0.519	0.587	0.342
LE,1 year after AMI	0.491		0.410	0.491	0.614	0.328		0.218	0.328	0.491	0.055
LE, 1 year after AMI	0.316		0.314	0.316	-	0.428		0.276	0.428	0.516	0.667

Legend: * - p <0.05 compared to the values after AMI, # -p <0.05 compared between groups

showed a decreased PCG content in the DL fraction that became significantly lower than in the patients of 1st group (Table 3).

In a 3-year time, the MPO significantly decreased in patients who had sustained AMI in both groups. One year after AMI, the LE activity decreased by 10% and 37 %, respectively, in the both groups. Three years after MI, the LE activity in the 1st group decreased by 42 % when compared with the results obtained immediately after the AMI onset. Three years after AMI, the LE activity slightly increased, but it was 18% lower than the values after AMI in the 2nd group. One year after AMI, the ME activity in both groups decreased by 50 – 70 % as compared with the values after AMI, to increase later on, in three-year time after the onset of AMI (Table 4).

DISCUSSION

Under normal conditions, the intracellular content of reactive oxygen species (ROS) is maintained at a low level by various enzyme systems involved in the redox homeostasis. Oxidative stress is one of the crucial factors in developing cardiovascular pathologies (Senoner et al., 2019).

One of the aims of our study is to improve the early and delayed course of the 3-year post infarction period through the comprehensive assessment of individual biochemical enzymes in the course of time. These enzymes characterize both the stability of the atheromatous process (PON-1, metalloproteinase) protection, and exercise tolerance against the background of the analysis of the progression of atherosclerotic lesions of the coronary arteries defined according to coronary angiography.

As an enzyme, PON-1 is closely associated with the HDL complex. In case-control studies, it was found that patients with familial hypercholesterolemia and patients with MI had a reduced PON-1 level in blood plasma when compared with healthy individuals (Ayub et al., 1999). Many authors believe that HDL's antiatherogenic properties depend in part on the antioxidant activity of PON-1 associated with HDL apoproteins (apo A-I and apo J) (Aviram et al., 2000). The dynamics of PON-1 in patients of the 1st group differs from that in patients of 2nd group.

A study (Henein et al., 2022) found that lower levels of PON-1 in patients who had survived AMI were associated with an increased risk of recurrent cardiovascular events. PON-1 activity is typically reduced in several atherosclerosis-associated pathologies. There is an inverse relationship between the level of PON-1 activity and the risk of cardiovascular disease (Li et al., 2005), which indicates to the clinical significance of the enzyme.

In terms of TBARP, its augmented blood level indicates to an increased supply of H_2O_2 and lipoperoxides in the blood, which is confirmed by an increase in catalase activity.

The post-infarction period was characterized by activation of free radical oxidation of protein molecules, as evidenced by the growth of carbonyl products of free radical oxidation of proteins in the serum.

The obtained results testified to the peroxidized state of lipoprotein particles. Together with the

TBARP accumulation in lipoprotein particles, these changes underlie the increased blood atherogenicity. These changes are observed in parallel with a long-term change in enzyme activity of the antioxidant defense system.

Qualitative changes in LDL, HDL, and individual enzyme activity were studied to determine the proatherogenic component at different stages of the post-infarction period. According to contemporary ideas, these are the qualitative characteristics of HDL associated with their protein molecules (apoproteins, enzymes, etc.) that are much more important than their numbers in the bloodstream and the amount of cholesterol in them (Al Quait et al., 2018). Some studies testify to the positive effect of exercise on atherogenic lipoprotein levels in patients with CHD (Winnige et al., 2021). The studies have shown that despite high-tech interventions and advanced drug therapy from the first hours of the disease onset, AMI development is characterized by oxidative stress formation. This condition is associated with an increased content of lipid peroxidation products, particularly TBARP products, and a marked activation of free radical oxidation of protein molecules. As evidenced by a higher content of carbonyl products of free radical oxidation of proteins in serum. The increased content of these products in lipoprotein fractions also attract attention. Thus, the dynamics of changes in the content of carbonyl products of free radical oxidation of proteins in the fraction of LDL + VLDL is similar to that for these products content in the serum. An even greater accumulation of carbonyl products of free radical oxidation of proteins is observed in the HDL fraction. The results obtained may indicate to a peroxidized state of lipoprotein particles due to the accumulation in them of lipid oxidation products, which may be the basis of the increased atherogenic potential of the blood. This is confirmed by the index of peroxide modification of atherogenic lipoproteins.

These changes occur against the background of a long-term decrease in the enzyme unit activity of the antioxidant defense system. The established changes are indicative of the oxidative stress formation and inhibition of antioxidant defense mechanisms which can reduce the level of ROS and products of free radical oxidation of macromolecules.

To date, there is more evidence of the important role leukocytes play in vascular damage. It is suggested that leukocyte activation may be an alternative risk factor for atherosclerosis (Henein et al., 2022). The demonstrated increase in MPO activity in patients after the AMI onset is attributed to the stimulation of leukocyte functional activity and increased infiltration of neutrophils and ischemic myocardial tissue. In the bloodstream, MPO forms a complex with HDL-associated enzyme PON-1. PON-1 partially inhibits the activity of MPO, while the latter can inactivate PON-1, oxidizing the tyrosine-71 residue, which leads to a violation of the binding of the enzyme molecule to HDL. As a result of the MPO activation, several ROS are formed that can damage macromolecules and lipoproteins. In the case of binding MPO to the endothelium and its activation, local exacerbation of vascular inflammation is possible (Golwala et al., 2015). Several studies have shown that in patients with acute coronary syndrome there is an increase in the MPO/PON-1ratio, which can be used as a predictor of the development of this pathological condition (Kargapolova et al., 2021). As a result of our own research, we have shown a 4 to 6-fold elevated ratio of MPO to PON-1 after AMI. During the three-year follow-up the MPO/PON-1 ratio decreased. After the 3rd year of observation, it remains higher than at the beginning by 50-70%. The MPO enzyme role in the destabilization of atherosclerotic plaque is well-known: a key part in this process is the thinning and rupture of the fibrous cap due to activation of metalloproteinases, which can occur due to hypochlorite formed by activated MPO (Kargapolova et al., 2021; Vasylchenko et al., 2020).

Analyzing the results, it is worthwhile mentioning that in terms of the lipid metabolism which is within physiologically acceptable range for healthy individuals but slightly higher than the values for patients at very high cardiovascular risk, the quality of lipoproteins is altered, as evidenced by the decrease in PON-1 activity. The increased MPO activity and the content of products of free radical oxidation of proteins and lipids are very likely to contribute to the progression of the atherosclerotic process.

The above metabolic changes can exacerbate atherosclerotic vascular damage and affect the contractile function of the heart muscle. The MPO activation indicates high cytotoxicity of polymorphonuclear leukocytes. Together with a decreased activity of PON-1 and enzymes of antioxidant protection (catalase), these changes can help maintain a high level of oxidation of lipoproteins, primarily their protein components. In turn, oxidized lipoproteins

can enhance cell adhesion to the endothelium, induce the expression of growth factors in smooth muscle cells, inhibit NO synthase expression, and reduce vascular relaxation.

CONCLUSIONS

During the first year of the study, the PON-1 activity was significantly reduced in both groups. During the three-year period, its growth was observed. The activity of the enzyme unit components of antioxidant protection, catalase, during the entire observation period in both groups kept going down. Still, a relative increase in catalase activity was observed until the third year of the follow-up in the patients of 2nd group. Such changes may indicate that the intensity of oxidative stress remains at the appropriate level, but the antioxidant link is also activated. The decreased MPO activity is probably due to the depletion of the depot of azurophilic granules against the background of chronic inflammation. The dynamics of changes in the PCG content in serum, and the LDL+VLDL and HDL fraction is consistent with the dynamics of changes in the PON-1 activity, which is associated with lipoproteins. Thereby indicating an improvement in the functional properties of lipoprotein particles. The lack of progression of atherosclerotic plaques against the background of statin therapy was not accompanied by the achievement of LDL-C target level, as in patients of 1st group. Failure to achieve the LDL targets, reduce oxidative stress and increase antioxidant activity in the group without signs of the atherosclerotic progression makes one assume that qualitative changes in lipoprotein particles are as important as their quantitative properties.

REFERENCES

AEBI H. Catalase in vitro. *Methods in Enzymology*. 1984; 105: 121-126.

AL QUAIT A., DOHERTY P. Overview of Cardiac Rehabilitation Evidence, Benefits and Utilisation. *Global Journal of Health Science*. 2018; 10 (2): 38-48.

AVIRAM M., DORNFELD L., ROSENBLAT M. et al. Pomegranate juice consumption reduces oxidative stress, atherogenic modifications to LDL, and platelet aggregation: studies in humans and in atherosclerotic apolipoprotein E-deficient mice. *Am J Clin Nutr.* 2000; 71: 1062-1076.

AYUB A., MACKNESS M.I., ARROL S. et al. Serum paraoxonase after myocardial infarction. *Arterioscler Thromb Vasc Biol*. 1999; 19 (2): 330-335.

BENJAMIN E.J., BLAHA M.J., CHIUVE S.E. et al. Heart disease and stroke statistics —2017 update: a report from the American Heart Association. *Circulation*. 2017; 135: e146-e603.

COWIE A., BUCKLEY J., DOHERTY P. et al. Standards and core components for cardiovascular disease prevention and rehabilitation. *Heart*. 2019; 105: 510-515.

GOLWALA H., PANDEY A., JU C. et al. Temporal trends and factors associated with cardiac rehabilitation referral among patients hospitalized with heart failure: findings from Get With The Guidelines-Heart Failure Registry. *J. Am. Coll. Cardiol*. 2015; 66: 917-926.

GORDON S.M., REMALRY A.T. High density lipoproteins are modulators of protease activity: Implications in inflammation, complement activation, and atherothrombosis. *Atherosclerosis*. 2017; 259: 104-113.

HENEIN M.Y., VANCHERI S., LONGO G. et al. The Role of Inflammation in Cardiovascular Disease. *Int J Mol Sci.* 2022; 23(21): 12906.

KARGAPOLOVA Y., GEISEN S., ZHENG R. et al. The enzymatic and on-enzymatic function of myeloperoxidase (MPO) in inflammatory communication. *Antioxidants*. 2021; 10: 562.

KUBYSHKIN A.V., FOMOCHKINA I.I. Elastolytic activity of bronchoalveolar lavage in modeling the inflammatory process in the lungs. *Ukr Biochem J*. 2008; 80 (1): 89-95.

LI B., SEDLACEK M., MANOHARAN I. et al. Butyrylcholinesterase, paraoxonase, and albumin esterase, but not carboxylesterase, are present in human plasma. *Biochem. Pharmacol*. 2005; 70 (11): 1673-1684.

MANOLESCU B.N., BERTEANU M., CINTEZÃ D. Effect of the nutritional supplement ALAnerv® on the serum PON1 activity in post-acute stroke patients. *Pharmacol rep.* 2013; 65 (3): 743-750.

SENONER T., DICHTL W. Oxidative Stress in Cardiovascular Diseases: Still a Therapeutic Target? *Nutrients*. 2019; 11 (9): 2090.

THE BACPR Standards and Core Components for Cardiovascular Disease Prevention and Rehabilitation, 3rd ed. Retrieved 29 June 2017, from

http://www.bacpr.com/resources/AC6_BACPRStandards&CoreComponents2017.pdf. (02 September, 2021)

VASYLCHENKO V.S., KOROL L.V., KUCHMENKO O.B. et al. The oxidative status in patients with chronic kidney disease. *Ukrainian Biochemical Journal*. 2020; 92 (5): 70-77.

WINNIGE P., VYSOKY R., DOSBABA F. et al. Cardiac rehabilitation and its essential role in the secondary prevention of cardiovascular diseases. *World J Clin Cases*. 2021; 9 (8): 1761-1784.