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Ω-3 POLYUNSATURATED FATTY ACIDS AND MAGNETOTHERAPY COMBINED IMPACT ON FREE RADICAL PROCESSES IN PATIENTS WITH STABLE EXERTIONAL ANGINA

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ABSTRACT

Aim: To research the comparative effectiveness of a protocol-based drug complex for angina pectoris and combination therapy using ω-3 polyunsaturated fatty acids and magnetotherapy on the lipid peroxidation and antioxidant system activity dynamics.

Materials and Methods: The clinical examination included 97 patients who were randomized into three group of observation depending the variants of treatment. 50 practically healthy persons were involved into the control group. Lipid peroxidation end-products and antioxidant enzymes activities were determined in blood of the examined patients.

Results: Our results revealed the expressed efficacy of the original method of patients with stable exertional angina pectoris physiotherapeutic treatment. The scheme, which we prove to be effective for patients with stable exertional angina pectoris includes, combined used of ω-3 PUFAs and magnetotherapy. Our data allowed to indicate that the therapeutic benefits of our original physiotherapy complex developed faster and were expressed in more effective lipid peroxidation prevention and inhibition of the blood antioxidant system activity compared to those parameters in case of other used therapeutic complexes.

Conclusions: We determined an antioxidant efficacy of ω-3 PUFAs and magnetotherapy combined use patients with stable exertional angina pectoris. Continuing a series of similar courses of physiotherapy treatment in these patients with the expressed antioxidant effect, we are confident in its effectiveness, safety, and the absence of side effects, which justifies the expediency of its widespread use in physiotherapy clinics.

KEY WORDS: stable exertional angina, magnetotherapy, lipid peroxidation, antioxidant system, physiotherapeutic treatment

INTRODUCTION

The pathogenetic importance of lipid peroxidation (LP) intensification in the atherosclerotic process, which is the basis of coronary heart disease (CHD) and, in particular, exertional angina, is generally recognized [1]. The well-known is the relationship between the intensity of oxidative processes and both cardiac hypertrophy development and remodeling of the heart [2, 3].

The concept about the pathogenetic importance of LP in patients with CHD is unequivocal and boils down to peroxidative processes enhancement [4-6]. The ideas about the antioxidant system (AOS) are contradictory: some authors report a compensatory increase in AOS enzymes [7, 8], and some report a weakening of antioxidant protection [9].

Concerning the angina pectoris protocol therapy impact on LP and AOS, the issue has been studied insufficiently, and there are even isolated opinions about the negative influence, expressed in antioxidants level decrease and low density lipopolysaccharides resistance to oxidation decrease [10]. In this regard, the search for dosage forms that can effectively influence this link of CHD pathogenesis is relevant. Attention is drawn to ω-3 polyunsaturated fatty acids (ω-3 PUFAs), since their competitive ability to partially replace ω-6 PUFAs in cell membranes, which are prooxidants, theoretically contributes to positive changes in LP and AOS functional activities.

It should be taken into account that patients with CHD, according to protocol therapy, have more than a sufficient set of drugs, which increases not only the cost of treatment, but also the possibility of side effects development. We believe that physiotherapy is especially relevant for this contingent of patients, especially magnetotherapy (MT), known for its positive effects on the cardiovascular system (analgesic, hypotensive, hypocoagulant) [11].

AIM

The aim of the present work was to research the comparative effectiveness of a protocol-based drug complex for angina pectoris and combination therapy using ω-3 PUFAs and magnetotherapy on the lipid peroxidation and antioxidant system activity dynamics.

MATERIALS AND METHODS

The clinical examination included 97 patients (52 men and 45 women) aged from 41 till 80 years (the average

age 63.39±0.88 years). 50 practically healthy persons were involved into the control group for LP and AOS system indexes verification. The examined patients were hospitalized at the cardiology clinic of the Military Medical Clinical Center of the Southern Region (Odesa).

We used the following criteria of patients' inclusion into the clinical investigation: the patient's informed agree to the study and the presence of the exertional angina pectoris of the I-III functional classes. Exclusion criteria were the following: unstable angina pectoris, myocardial infarction during the last month, cardiac arrhythmias, heart failure stage of the IIB-III stages and severe somatic pathology (tumors, sepsis, etc.).

All patients were randomized into 3 groups. Group 1 consisted of 32 patients. The following protocol treatment was prescribed to patients with angina pectoris: nitrates, β-blockers, ACE inhibitors, antiplatelet drugs, statins (atorvastatin at a daily dose of 20 mg).

Group 2 consisted of 32 patients. Additionally to the protocol treatment these patients were prescribed with Vitrum Cardio Omega-3 (daily dosage of 2000 mg), divided into 2 doses. The daily dose of atorvastatin was reduced to 10 mg.

Group 3 consisted of 33 patients. Vitrum Cardio Omega-3 and a course of MT were added to the protocol treatment (atorvastatin 10 mg/day) according to the following method: two inductors were simultaneously placed on the heart area (alternating magnetic field, 14 mT) and the liver area (sinusoidal magnetic field, 20 mT). The course of treatment consisted of 10 daily procedures with 20 min exposure starting from 5-7 days from the drug therapy beginning. This MT technique was chosen due to fact that these two types of magnetic fields revealed number of cardiotropic properties, and their simultaneous use could provide a greater effect with less inductance [12].

The period of observation was 61.7±2.0 days. The LP and AOS indicators level - malonic dialdehyde (MDA, μmol/l), diene conjugates (DC), activities of glutathione reductase (GTR), superoxide dismutase (SOD), SH- & SS-groups and thiol-disulfide ratio (TDR) - were determined in all patients' blood before and after the treatment.

The results are presented as M±m, where M is the arithmetic mean, m is the error of the mean. Assuming tthat the obtained distribution was normal, further statistical calculation was performed using One Way Analysis of Variance (ANOVA-test). The minimum statistical probability was determined at $p<0.05$.

RESULTS

The results of patients' treatment under the influence of the used medical complexes are summarized in Table 1.

The LP intensification was registered in patients with stable angina pectoris, which was expressed in peroxidation products of MDA and DC significant increase in by 4 and 3 times, respectively ($p<0.001$), while the AOS activity was suppressed in the form of a tendency of SOD activity to be decreased ($p>0.05$) and a significant decrease in GTR activity ($p<0.05$). The LP enhancement against the background of AOS depletion was also evidenced by the starting indicators of the thioldisulfide system, which was expressed in a significant decrease in SH-gropus ($p<0.05$) and a significant increase in SS-groups ($p<0.05$) which led to a TDR decrease and showed the shift of the redox potential towards oxidation. The absence of a compensatory increase in AOS parameters and the resulting decrease in the activity of its enzymatic and non-enzymatic link is due, in our opinion, to the duration of angina pectoris in patients of the studied groups (on average, about 10 years).

After the treatment using the protocol complex, none of the studied LP and AOS indexes underwent changes, although the overall trend was positive ($p>0.05$).

The greatest antioxidant effect was demonstrated by the complex with the use of ώ-3 PUFAs and a course of MT simultaneously additionally to the protocol therapy. Thus, after treatment, the LP end-products underwent positive changes (MDA, $p<0.01$ and DC $p<0.01$), while in the group using only ώ-3 PUFAs, these indexes changed less ($p<0.05$ in both cases), and in the group with the protocol complex of therapy, they did not change at all ($p>0.05$).

This indicates an intrinsic antioxidant effect of both ώ-3 PUFA and MT, but it should be emphasized that the effect of ώ-3 PUFA on the concentration of radicals was somewhat greater than that of MT, which is confirmed by the presence of an intergroup difference in MD and DC at the level of approximation to reliability and a pronounced trend ($p_{1-2}=0.06$ and $p_{1-2}=0.15$, respectively) against the background of the absence of such a significant difference in groups 2-3 ($p=0.41$ and $p=0.25$, respectively).

A significant intergroup difference between the 3rd group and the 1st group (MDA p1-3=0.02 and DC p1-3=0.03) led to the conclusion about its maximum antioxidant effect, which is confirmed by a decrease in the group with "omega" of the levels of MDA by 26.3% and DC - by 25.6%, and with the addition of MT - by 34.4% and 40.5%, respectively.

The level of LP end-products still did not reach their reference values, then the AOS indexes practically returned to normal. So, despite the absence of intergroup difference in the parameters of the enzymatic link after treatment (with the exception of GTR in the group using combination therapy, where $p_{1-3}=0.12$ is a level approaching a pronounced trend), the concentrations of "depleted" SOD and GTR in the 1st group did not change after treatment, in the 2nd group there was a tendency to increase ($p=0.55$ and $p=0.29$, respectively), and with the addition of MT they normalized, and the difference before and after therapy was in SOD in the form of a noticeable trend ($p=0.15$), and according to GTR it was significant ($p<0.05$).

DISCUSSION

The data obtained showed that the expressed efficacy of the original method of patients with stable exertional angina pectoris physiotherapeutic treatment. The scheme which we prove to be effective for patients with stable exertional angina pectoris includes combined used of ω-3 PUFAs and magnetotherapy.

It should be noted that the therapeutic benefits of our original physiotherapy complex developed faster and were expressed

Table 1. The comparative dynamic of lipid peroxidation and antioxidant system indexes in the investigated patients

INDEXES		Control	Group 1	Group 2	Group 3	P, vs groups
MDA, μmole/l	Before	1.26±0.10	5.26±0.39***	5.39±0.40*	5.32±0.39*	P_{1-2}=0.06
	After	-	5.05±0.37	3.97±0.53#	3.49±0.27##	P_{2-3}=0.41 P_{1-3}=0.02
DC, μmole/l	Before	0.25±0.01	0.79±0.06***	0.78±0.07*	0.79±0.06*	P_{1-2}=0.15
	After	-	0.72±0.08#	0.58±0.07#	0.47±0.05##	P_{2-3}=0.25 P_{1-3}=0.03
SOD, rel. units	Before	0.18±0.04	0.16±0.01	0.15±0.01	0.16±0.01	P_{1-2}=0.51
	After	-	0.16±0.01	0.17±0.01	0.18±0.01	P_{2-3}=0.45 P_{1-3}=0.34
GTR, nmole/s•ml	Before	84.22±2.98	71.22±3.19*	72.22±3.79*	72.53±3.24*	P_{1-2}=0.34
	After	-	71.06±3.08	75.75±3.87#	80.94±3.47#	P_{2-3}=0.30 P_{1-3}=0.12
SH-groups, μmole/l	Before	9.23±0.03	7.54±0.57*	7.37±0.58*	7.27±0.62*	P_{1-2}=0.06
	After	-	8.09±0.35#	9.09±0.38##	9.53±0.41##	P_{2-3}=0.40 P_{1-3}=0.02
SS-groups, μmole/l	Before	3.54±0.08	5.42±0.57*	5.87±0.67*	5.78±0.55*	P_{1-2}=0.09
	After	-	4.95±0.51	4.00±0.35##	3.66±0.27##	P_{2-3}=0.54 P_{1-3}=0.054
TDR	Before	2.61	1.94±0.28	1.94±0.27	1.69±0.24	P_{1-2}=0.19
	After	-	2.17± 0.23#	2.54±0.16#	2.96±0.20##	P_{2-3}=0.14 P_{1-3}=0.02

*Notes: * – p<0.05 and *** – p<0.001 – significant differences in the studied parameters compared to those in the control observations*
 # – p<0.05 and ## – p<0.01 – significant differences in the studied parameters compared to those before the treatment (ANOVA + Newman-Keuls test used in all calculations)

in more effective lipid peroxidation prevention and inhibition of the blood antioxidant system activity compared to those parameters in case of other used therapeutic complexes.

Our data indicate the absence of a positive effect on the processes of peroxidation of the standard drug complex with the inclusion of atorvastatin at a dose of 20 mg/day.

Analyzing the data obtained it should be mentioned that the effect on the enzymatic unit of AOS was somewhat greater for MT than for ώ-3 PUFAs. The effect of combination therapy on the dynamics of indicators of the non-enzymatic link of AOS was also optimal, in which normalization of reduced SH-groups was noted even slightly more than normal against the background of slightly increased oxidized SS-groups (p=0.04 and p=0.04), while in the 1st group after treatment, their significant changes were not observed.

The absence of an intergroup difference in groups 2-3 and its significant difference between groups 1-3 also testifies to their own influence on the glutathione-dependent link of both MT and ώ-3 PUFA. Considering that the thiol disulfide system is the most sensitive and quickly reacting AOS link, the presented evidence indicates that after treatment, not only its balance initially disturbed towards oxidation is restored, but also some compensatory reactions of the AOS are outlined, aimed at significantly reduced, but still persisting, processes intensification of LPO. This is also evidenced by normalization and even a slight increase in comparison with the TDO norm (2.96 ± 0.20 at a rate of 2.61), initially reduced in these patients by almost 1.5 times.

From the point of view of data analysis, the effective use of magnetic therapy in patients with exertional angina is interesting and promising. On the one hand, our initial premise was the shown cardiotropic effects of magnetotherapy. But it should be noted that its effect on lipid peroxidation, according to researchers, is also not unequivocal. In the literature, there are data both on the corrective effect of MT on LP, in particular, on an increase in the levels of antioxidant enzymes [13], and on the stimulation of free radical oxidation processes [14, 15].

Therefore, the data obtained indicate an expressed antioxidant effect of the presented combination therapy, while there is a slightly greater effect of ώ-3PUFA on the normalization of peroxidation processes, and MT on the restoration of inhibited AOS processes, as well as their equivalent effect on the normalization of the disturbed balance of the non-enzymatic link of the antioxidant protection. Continuing a series of similar courses of physiotherapy treatment in these patients, we are confident in its effectiveness, safety, and the absence of side effects, which justifies the expediency of its widespread use in physiotherapy clinics.

CONCLUSIONS

We revealed the expressed efficacy of the original method of patients with stable exertional angina pectoris physiotherapeutic treatment.

The scheme, which we prove to be effective for patients with stable exertional angina pectoris includes, combined used of ω-3 PUFAs and magnetotherapy.

The therapeutic benefits of our original physiotherapy complex developed faster and were expressed in more

effective lipid peroxidation prevention and inhibition of the blood antioxidant system activity compared to those parameters in case of other used therapeutic complexes.

The effective use of magnetic therapy in patients with exertional angina is interesting and promising.

Continuing a series of similar courses of physiotherapy treatment in these patients with the expressed antioxidant effect, we are confident in its effectiveness, safety, and the absence of side effects, which justifies the expediency of its widespread use in physiotherapy clinics.

REFERENCES

1. Incalza MA, D'Oria R, Natalicchio A et al. Oxidative stress and reactive oxygen species in endothelial dysfunction associated with cardiovascular and metabolic diseases. Vascul Pharmacol. 2018;100:1-19. doi: 10.1016/j.vph.2017.05.005.
2. Gál R, Halmosi R. The role of oxidative stress in heart failure. Orv Hetil. 2015;156(47):1916-1920. doi: 10.1556/650.2015.30301.
3. Xu S, Ilyas I, Little PJ et al. Endothelial Dysfunction in Atherosclerotic Cardiovascular Diseases and Beyond: From Mechanism to Pharmacotherapies. Pharmacol Rev. 2021;73(3):924-967. doi: 10.1124/pharmrev.120.000096.
4. Kapustnik VA, Kucherenko OD, Brek VV et al. Perekisnoye okisleniye lipidov, antioksidantnayai gipolipidemicheskaya terapiya bol'nykh ishemicheskoy bolezn'yu serdtsa i sakharnym diabetom [Lipid peroxidation, antioxidant and lipid-lowering therapy in patients with coronary heart disease and diabetes mellitus]. Eksperymental'na klinichna medytsyna. 2014;1(62):64-68. (Russian)
5. Moroz VM, Shandra OA, Vastyanov RS et al. Physiology. Vinnytsia : Nova Knyha. 2016, p.722.
6. Zhang Z, Li X, He J et al. Molecular mechanisms of endothelial dysfunction in coronary microcirculation dysfunction. J Thromb Thrombolysis. 2023;56(3):388-397. doi: 10.1007/s11239-023-02862-2.
7. Li S, Chen H, Zhou L et al. Neutrophil-to-lymphocyte ratio predicts coronary artery lesion severity and long-term cardiovascular mortality in patients with unstable angina pectoris. Acta Cardiol. 2022;77(8):708-715. doi: 10.1080/00015385.2021.1963564.
8. Liu X, Zhang Y, Jin F et al. Correlation between GPR, MHR and elderly essential hypertension with unstable angina pectoris. Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2021;46(4):373-378. doi: 10.11817/j.issn.1672-7347.2021.200222.
9. Baselet B, Sonveaux P, Baatout S et al. Pathological effects of ionizing radiation: endothelial activation and dysfunction. Cell Mol Life Sci. 2019;76(4):699-728. doi: 10.1007/s00018-018-2956-z.
10. Gradinaru D, Borsa C, Ionescu C et al. Oxidized LDL and NO synthesis--Biomarkers of endothelial dysfunction and ageing. Mech Ageing Dev. 2015;151:101-113. doi: 10.1016/j.mad.2015.03.003.
11. Zolotareva NA, Petrosyan AP. Biologicheskiye effekty razlichnykh vidov magnitnykh poley i ikh ispol'zovaniye v lechenii IBS i degenerativnykh zabolevaniy sustavov [Biological effects of various types of magnetic fields and their use in the treatment of coronary artery disease and degenerative joint diseases]. Medychna reabilitatsiya, kurortolohiya, fizioterapiya. 2004;3(39):41-43. (Russian)
12. Hessling G. Arrhythmia in adults with congenital heart disease : Acute and long-term management. Herzschrittmacherther Elektrophysiol. 2016;27(2):81-87. doi: 10.1007/s00399-016-0430-x.
13. Podgornova NA, Grechkanov GO. Vliyaniye obshchey magnitoterapii na klinicheskuyu kartinu i pokazateli perekisnogo okisleniya lipidov u bol'nykh s klimaktericheskim sindromom [The influence of general magnetic therapy on the clinical picture and indicators of lipid peroxidation in patients with menopausal syndrome]. Medychnyy al'manakh. 2009;4(9):159-162. (Russian)
14. Elbaz-Greener G, Sud M, Tzuman O et al. Adjunctive laser-stimulated stem-cells therapy to primary reperfusion in acute myocardial infarction in humans: Safety and feasibility study. J Interv Cardiol. 2018;31(6):711-716. doi: 10.1111/joic.12539.
15. Ganipineni VDP, Gutlapalli SD, Kumar IASK et al. Exploring the Potential of Energy-Based Therapeutics (Photobiomodulation/Low-Level Laser Light Therapy) in Cardiovascular Disorders: A Review and Perspective. Cureus. 2023;15(4):e37880. doi: 10.7759/cureus.37880.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest.

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