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EFFECTS OF THE COMBINED THERAPY WITH USING OF MAGNETIC FIELDS AND MEXICOR FOR REDOX HOMEOSTASIS ON PATIENTS WITH STABLE ANGINA PECTORIS

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Summary: *The article is devoted to the redox homeostasis in 101 patients with stable angina FC I-III.*

Comparative effectiveness analysis was conducted for traditional medical complex for the complex that included of cytoprotector Mexicor, and its combination with magnetic therapy. Mexicor adding to standard therapy results in a significant reduction of radical processes and increased of antioxidant protection. Mexicor sharing with magnetotherapy is even more pronounced antioxidant effect. This effect allows to get the impaired pro-and antioxidant system in balance.

Keywords: stable angina, lipid peroxidation, magnet.

According to statistics data, on the last ten years, the prevalence of ischaemic heart disease (IHD) is rapidly growing in most countries including Ukraine [3, 6, 13, 17]. Every year, the world's recorded more than 32 million cases of atherothrombotic complications - heart attack, myocardial infarction, stroke and others. According to the forecast, if the upward trend of cardiovascular diseases in the world will be continues, the death rate from them will reach at 2020 near the 25 million cases per year [14]. Ukraine currently is the leader in cardiovascular mortality in Europe.

In the last decades of the XX century, concept of the important role of lipid

peroxidation in the pathogenesis of atherosclerosis was scientifically based [16, 18-21].

Oxidative stress is manifested as increasing of prooxidant and decreasing of antioxidant processes. Pathophysiologic factors of oxidative stress are ischemic, inflammatory and stress response [1, 2, 4, 5, 7], which logically occur in patients with angina pectoris. Therefore, correction of impaired antioxidant redox homeostasis in patients with stable IHD is extremely parspective way of therapy.

In this respect, new antioxidant Mexicor is more attracting, because it's fundamental difference is the activation of succinyldehydrogenase way of glucose oxidation, which leads eventually to a rapid resynthesis of ATP [10].

The undoubted benefits of this medication should include the water-soluble of thereof salts, which makes it possible to use not only tablets but also an injectable form. The first results of its positive effects in ischemic heart disease have appeared in the Russia [8, 10], but in Ukraine and abroad this drug is virtually unstudied.

As a one of the ways to optimize drug therapy is the combined use of the physical factors. We proposed the use of Mexicor in combination with magnetic therapy (MT). The rationale for this prescribtion is the data about the positive effects of MT on the cardiovascular system: hypotensive, analgesic, hypocoagulative and improves microcirculation effects.

The purpose of the study - to study the effectiveness of mexicor monotherapy and combining therapy with magnetotherapy on the redox homeostasis for patients with IHD.

Materials and methods

We observed 101 patients with stable angina I-III FC, that were hospitalized in the cardiology department of the Military Medical Clinical Centre of South region. Diagnosis of stable angina were set in accordance with the diagnostic criteria and classification of the European Society of Cardiology (ESC) in 2006. [15]

Inclusion criteria:

- signed informed consent form of the patient;
- I - III FC stable angina.

Exclusion criteria:

- using of metabolic drugs by at least 2 weeks before the start of the study;
- acute coronary syndromes;
- B II-III heart failure.
- severe, life-threatening, illness (septic, oncology, hematology, acute ischemic stroke, etc.).

The patients were divided into three groups:

- **Group I** (control group) - 31 males, 54,42±1,69 y.o. The treatment for this patients included a standard set of cardiovascular drugs that are recommended for the treatment of stable forms of ischemic heart disease (eg, nitrates, ACE inhibitors, antiplatelet agents, beta-blockers, statins). If it necessary, the complex added by antihypertensives and diuretics drugs.
- **Group II** - 35 males, 58,51±1,82 y.o. Standart medication complex was added by the inclusion of Mexicor (at first - parenterally, then - per os during all the observation period. The treatment by Mexicor was on average 24,54 ± 1,67 days.
- **Group III** - 35 males, 56,26±2,01y.o. The standard complex was added by mexicor medical complex and the course of magnetic therapy (MT). For the MT we used two different types of magnetic at the same time in the following procedure: an alternating magnetic field to the heart region (14 mT) and a sinusoidal magnetic field on the reflex area of the heart (the thoracic spine at the level of Th1-Th4) - 20 mT, frequency - 50 Hz. The course of MT started on 2-3 days after the start of mexicor and consisted of 10-12 daily procedures with a single exposure of 20 minutes.

Subjective and objective examination of the patient was given a history of myocardial infarction (MI), hypertension, diabetes, angina functional class, burdened by coronary heart disease heredity and smoking. Clinical characteristics of patients studied groups are presented in Table 1.

The table shows that an overwhelming number of patients have an arterial hypertension, occur in about the same for all groups of patients (77.1% -83.87%).

Analysis of anamnesis significant intergroup differences were found (p> 0.05), except for smoking, are more common in patients in the control group. It is interesting to note that the overall functional status of the cardiovascular system, as measured by functional class of angina and the degree of heart failure (CHF) was more severe in patients of group III, among which there are nearly two times as many patients with angina III FC. and CHF IIA Art. compared to other treatment groups.

Table 1- Clinical characteristics of patients from studied groups

Data	Groups					
	Group I (n=31)		Group II (n=35)		Group III (n=35)	
	абс.	%	абс.	%	абс.	%
MI in anamnesis	5	16,1	5	14,3	7	20,0
Heredity by MI	18	58,1	23	65,7	21	60,0
AH	26	83,87	27	77,1	29	82,9
Diabetis	4	12,9	5	14,3	5	14,3
Smoking	10	32,26	5	14,3	9	25,7
Terms of angina	6,10 ± 1,00		5,40 ± 0,76		5,63 ± 0,95	
AP FC-I	4	12,9	8	22,86	11	31,43
AP FC-II	24	77,42	24	68,57	18	51,43
AP FC-III	3	9,68	3	8,57	6	17,14
CHF-0	10	32,26	11	31,43	9	25,71
CHFI	17	54,84	20	57,14	18	51,43
CHF II A	4	12,9	4	11,43	8	22,86

All patients before and after treatment were studied by redox homeostasis. The analysis was included lipid peroxidation (LPO) - the content of primary (diene conjugates - DC) and the secondary (malondialdehyde - MDA), lipid peroxidation products and indicators of antioxidant system (AOS) - the activity of intracellular antioxidant enzyme glutathione reductase (GAD) and superoxide dismutase (SOD). Non-enzymatic antioxidant system link has been investigated by the number of sulfhydryl and disulfide groups (SH and SS), as calculated tioldisulfidnoe ratio (TAR), which reflects the redox balance, or redox potential. All the obtained data were processed by variation statistics using t-test. Differences were considered reliable in the range of <0.05. Factual material is processed using the statistical program «STATISTICA 6.1».

Results and discussion.

Indicators of redox homeostasis: a significant increase of lipid peroxidation

products in all study groups at baseline (DC - almost 2 times, MD - almost 5 times) due to the increased compensatory antioxidant enzymes (GAD - 1.2 times) and reduced the TAR (1.4-fold), for a total show to strengthen the free-radical oxidation and the formation of compensatory reactions to his removal (Table 2).

Both PAUL products (MD and DC) after the use of a standard medical complex at the end of therapy did not improve, and even demonstrated a slight tendency to increase ($p = 0.60$, $t = 0,53$ and $p = 0.31$, $t = 1, 03$, respectively) (Table 2). Consequently, the initial compensatory increased activity of antioxidant enzymes (GR and SOD) by the end of therapy did not change ($p = 0.51$ at $t = 0,66$ and $p = 0.72$ at $t = 0,36$). The study of non-enzymatic level EPA showed slight tendency ($p = 0.85$, $t = 0,19$) reduced SH-groups on the background of constant SS-groups ($p = 0.99$, $t = 0,003$). As a result, initially reduced the TAR has not increased, but decreased slightly from 1.88 to 1.85 (2.64 - in healthy individuals). This is a testifies to preservation of shift towards oxidation of the redox potential, and combined with the dynamics of the above products of lipid peroxidation and EPA - the absence of a positive impact of the complex processes of free-radical oxidation.

Mexicor inclusion in this medical complex is shown that the number of major markers of lipid peroxidation (MD and DC) at the end of treatment decreased, and significantly ($p = 0.049$ at $t = 2,04$ and $p = 0.026$ at $t = 2,34$, respectively). This phenomenon led to the difference between this and the control group at MD clear trend ($p = 0.12$), and in DC - approaching significance ($p = 0.056$). While reducing the activity of initially high antioxidant enzymes (GR and SOD) ($p = 0.007$ at $t = 2,91$ and $p = 0.22$ at $t = 1,23$, respectively), between-group difference in SOD was noted at the level of the tendency ($p = 0.25$), and for GR - was close to significance ($p = 0.06$).

This indicated about reduction of radical processes and reducing of the EPA"intensity" and coincided with the dynamics of indicators of thiol-disulfide system, where the number of SH-groups demonstrated a tendency to increase ($p = 0.59$ at $t = 0,54$), and SS-groups - significantly decreased ($p = 0.04$ at $t = 2,11$), which led to increasing the TAR of 29.7% and indicated the correct redox potential at the end of therapy in dnnoy group of patients (Table 2). From these results it can be

concluded antioxidant effect mexicor in patients with stable angina pectoris.

The analysis of the therapy with Mexicor at same time use of magnetic therapy (Table 2) showed a further reduction in the processes of free-radical oxidation. So at the end of therapy, the main products of LP - DC and MD were significantly decreased (1.32 and 1.5 times, respectively), and both changes were significant ($p = 0.012$ at $t = 2,67$ and $p = 0.004$ at $t = 2.10$, respectively) and DC with almost reached their reference values. Both figures have changed more pronounced than in the group with only Mexicor ($p = 0.30$ and $p = 0.44$), as compared with control almost reached significant difference ($p = 0.01$ and $p = 0.06$).

Accordingly, in this group activity of antioxidant enzymes GAD decreased more significantly ($p = 0.005$ at $t = 2,99$), and SOD significantly increased in comparison with the control, was almost unchanged ($p = 0.10$ at $t = 1, 70$). Given the antioxidant effect of magneto- Mexicor group significant difference between the two groups were recorded and compared with the control differences were observed at the level of SOD clear trend ($p = 0.14$), and for GR - almost significant ($p = 0.05$). The study of the dynamics of thiol-disulfide system showen tended to increase the level of SH-groups ($p = 0.51$ at $t = 0,67$), and the level of SS-group a significant decrease ($p = 0.04$ at $t = 2,11$), which led to the normalization of the TAR and redox balance, in contrast to the previous two groups. Together, the this findings suggest a strong antioxidant effect of combination therapy with MT and Mexicor, and, in our opinion, MT, with its own anti-oxidant properties, also increase the effects of the Mexicor.

Conclusions

1. The study confirmed that patients with stable angina FC I-III have increase of free radical processes and reduce of antioxidant protection.
2. Application of the standard medical complex, included of hemodynamic drugs, Aspekard, atorvastatin does not affect the enhanced of free radical processes.
3. Metabolic cytoprotector Mexicor has powerful antioxidant effects (decreased malondialdehyde from $5,67 \pm 0,45$ to $4,82 \pm 0,37$ p/l., $p = 0.049$).
4. Simultaneous using of Mexicor with magnetotherapy has significant

antioxidant action, which is expressed in the oppression of free radical oxidation (decrease diene conjugates by 34% and MDA by 26%, $p < 0.05$), respectively, reducing the compensatory increased antioxidant enzyme system ($p < 0.01$) and thiol-disulfide system (increasing thiol-disulfide ratio from 1.83 to 2.62, no change in the control of - 1.88 and 1.85, respectively), resulting in impaired into balance of the pro-and antioxidant system for patients with stable angina.

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Table 2. Сравнительная динамика показателей ПОЛ и АОС у больных исследуемых групп

Группы	Контрольная			Мексикор			Мексикор + МТ			Межгруп.значим-ть		
Показатель	д/леч.	п/леч.	p	д/леч.	п/леч.	p	д/леч.	п/леч.	p	p1-2	p2-3	p1-3
ДК, мкмоль/мл	0,52± 0,06	0,60± 0,06	0,31	0,40± 0,049	0,32± 0,038	**0,026**	0,44± 0,050	0,29± 0,026	**0,012**	**0,05 6**	0,30	**0,01**
МД, мкмоль/мл	6,46± 0,74	6,81± 1,11	0,60	5,67± 0,45	4,82± 0,37	**0,049**	5,80± 0,54	4,30± 0,40	**0,04**	0,12	0,44	0,06
Активность ГР, нмоль/(с ▪ мл)	99,53± 2,66	98,20± 2,82	0,51	106,3± 2,39	98,7± 2,79	**0,007**	100,09± 3,25	91,88± 3,06	**0,005**	0,06	0,89	**0,05**
Активность СОД, у.е.	0,192± 0,002	0,192± 0,002	0,72	0,191± 0,002	0,19± 0,001	0,22	0,191± 0,002	0,194± 0,002	0,10	0,25	0,87	0,14
SH-группы, мкмоль/мл	8,02± 0,62	7,90± 0,64	0,85	8,12± 0,52	8,45± 0,73	0,59	8,15± 0,74	8,86± 0,99	0,50	0,61	0,76	0,52
SS-группы, мкмоль/мл	4,27± 0,40	4,27± 0,50	0,99	4,39± 0,35	3,52± 0,37	**0,04**	4,45± 0,44	3,37± 0,36	**0,04**	0,29	0,76	0,22
Тиолдисульфидное отношение, абс.	1,88	1,85		1,85	2,40		1,83	2,62				

Table 3 -Comparative dynamics of POL and AOC for patientsfrom studied groups

Parameters	Group I			Group II			Group III			p-p		
	before treatment	after treatment	p	before treatment	after treatment	p	before treatment	after treatment	p	p1-2	p2-3	p1-3
DC, umol / ml	0,52± 0,06	0,60± 0,06	0,31	0,40± 0,049	0,32± 0,038	**0,026**	0,44± 0,050	0,29± 0,026	**0,012**	**0,056**	0,30	**0,01**
MD umol / ml	6,46± 0,74	6,81± 1,11	0,60	5,67± 0,45	4,82± 0,37	**0,049**	5,80± 0,54	4,30± 0,40	**0,04**	0,12	0,44	0,06
GR activity, nmol / (s.ml)	99,53± 2,66	98,20± 2,82	0,51	106,3± 2,39	98,7± 2,79	**0,007**	100,09 ± 3,25	91,88± 3,06	**0,005**	0,06	0,89	**0,05**
SOD activity, cu	0,192± 0,002	0,192± 0,002	0,72	0,191± 0,002	0,19± 0,001	0,22	0,191± 0,002	0,194± 0,002	0,10	0,25	0,87	0,14
SH-group umol / ml	8,02± 0,62	7,90± 0,64	0,85	8,12± 0,52	8,45± 0,73	0,59	8,15± 0,74	8,86± 0,99	0,50	0,61	0,76	0,52
SS-group umol / ml	4,27± 0,40	4,27± 0,50	0,99	4,39± 0,35	3,52± 0,37	**0,04**	4,45± 0,44	3,37± 0,36	**0,04**	0,29	0,76	0,22
Thiol-disulfide ratio, abs.	1,88	1,85		1,85	2,40		1,83	2,62				

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