

THE PHARMA INNOVATION

The Effect of A Differential Antihypertensive Therapy on Cardiohaemodynamic and Indicators of A Daily Monitoring of Blood Pressure In Patients With Hypertension, Which Were Under A Prolonged Influence Of The Electromagnetic Fields of High Intensity

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This report analyzes the impact of a differentiated antihypertensive therapy on the echocardiography and daily monitoring of blood pressure rates in the patients who were under a prolonged influence of the electromagnetic fields of high intensity. It is noticed, that monotherapy with bisoprolol or enalapril has lead to a reverse remodeling of the left ventricle and to its myocardium weight reduction. Meanwhile, in patients who were treated with bisoprolol a more pronounced antihypertensive effect is noted, compared with the enalapril group, that was shown by a decrease in average daily levels of systolic and diastolic blood pressure and a higher incidence of achieving the target level of performance. An increase of treatment efficiency through the use of a bisoprolol or enalapril combined therapy; with the addition of herbal sedative drug kardiofit is noted.

Keyword: Hypertension, Electromagnetic Field of High Intensity, Daily Monitoring Of Blood Pressure.

INTRODUCTION:

Problem stating and analysis of recent researches:

The course of arterial hypertension (AH) in a particular patient is largely dependent on the presence of such related diseases as diabetes mellitus, coronary artery disease, heart failure, and chronic kidney disease [2, 5]. The environmental factors play a significant role in the pathogenetic mechanisms of AH development. Among them: noise, vibration, weather conditions, the state of the Earth's magnetosphere [1, 3, 7]. However, the question of peculiarities of an influence of an antihypertensive therapy on

blood pressure rate and processes of left ventricular remodeling in patients with hypertension, which are under a prolonged influence of the electromagnetic fields of high intensity [9]. It is known, that AH, that is associated with the effect of electromagnetic fields, can be characterized by the higher level of hypertension, increased vascular stiffness, severe endothelial dysfunction, activation of the sympathoadrenal system and an increased level of catecholamine metabolites in plasma, that explains a necessity in a special approach to antihypertensive therapy of such patients [4, 6, 8].

THE AIM OF RESEARCH:

To study the influence of differential antihypertensive therapy on the course of hypertension in the patients who were under a prolonged influence of the electromagnetic fields of high intensity.

MATERIALS AND METHODS:

The study involved 120 patients with hypertension who were under a prolonged influence of the electromagnetic fields of high intensity. Among the patients 76,7% were male and 24,4% female. To determine the impact of the proposed antihypertensive therapy schemes on cardiac hemodynamics and blood pressure rates the patients underwent echocardiography and a daily monitoring of blood pressure. According to the purpose and design of the study patients with hypertension who were under the influence of electromagnetic fields of high intensity were divided into four groups: I (n = 30) - received bisoprolol 5 mg per day, II (n = 30) - received enalapril 10 mg, III (n = 29) - received bisoprolol 5 mg and kardiofit 10 ml per day, IV (n = 31) – received a combined antihypertensive therapy with enalapril 10 mg and kardiofit 10 ml per day.

THE RESULTS AND THEIR DISCUSSION:

Under the influence of the proposed schemes of an antihypertensive therapy a positive dynamics of key indicators of echocardiography was observed. In patients of the first group the level of left ventricular ejection fraction (LVEF) before treatment was $58,90 \pm 3,6\%$ and significantly increased after 4 months of treatment with bisoprolol to $68,07 \pm 2,65\%$ ($p < 0.05$). Using bisoprolol and kardiofit for a combined antihypertensive treatment of the patients who belonged to the fourth group a significant improvement of left ventricular systolic function also was noted. LVEF

index in these patients was $57,35 \pm 2,96\%$ before the treatment and increased to $66,11 \pm 3,05\%$ after 4 months of treatment ($p < 0,05$). Analyzing the effect of enalapril as a monotherapy and a combined therapy with this drug in combination with kardiofit on systolic and diastolic function of the left ventricle in patients with hypertension, who were under a prolonged influence of the electromagnetic fields of high intensity for 2 and 4 months a statistically uncertain increase in LVEF is observed (Table 1.).

The influence of the studied drugs on the value of end-systolic (ESV) and end-diastolic volume (EDV) of the left ventricle (LV). As can be seen from Table 1, in all subgroups a significant reduction of ESV of the LV was noticed after 4 months of treatment. In patients, treated with bisoprolol, ESV LV before treatment was $43,79 \pm 2,18$ ml and significantly decreased to $32,25 \pm 2,52$ ml after 4 months of therapy ($p < 0.05$). In the group of patients where enalapril was used as antihypertensive monotherapy the average number of ESV LV had been $47,63 \pm 3,17$ ml prior to the study and significantly decreased to $36,29 \pm 2,21$ ml after the treatment ($p < 0.01$). It should be pointed out, that the combinations of bisoprolol with kardiofit and enalapril with kardiofit proved to be effective in reducing of ESV LV level after 2 months of treatment. Thus, the average level of ESV LV in the patients of the third group before the study had been $47,86 \pm 2,44$ ml and decreased after 2 months of a combined antihypertensive therapy to $38,12 \pm 2,65$ ml ($p < 0.01$). While analyzing the results of the use of a combination of enalapril and kardiofit was found that the average value of ESV LV in this group of patients had been $45,63 \pm 2,04$ ml before treatment. After 2 months of therapy, this index dropped to $36,34 \pm 2,43$ ml ($p < 0.01$), and after 4 months of antihypertensive treatment it was $34,25 \pm 2,4$ ml ($p < 0.01$). The dynamics of

end-diastolic volume of the left ventricle under the influence of studied drugs was analyzed. A statistically significant reduction in EDV LV was observed only after 4 months of a combined treatment with bisoprolol and kardiofit. In other groups the change in EDV LV turned up to be unreliable (Table 1). The results showed that the addition of kardiofit to bisoprolol or enalapril had led to a decrease in the average level of intensive ESV LV in patients with hypertension that were under a prolonged influence of the electromagnetic fields of high intensity compared to monotherapy with these drugs.

The influence of the investigated schemes of an antihypertensive therapy on echocardiographic indices of left ventricular hypertrophy was investigated. The reduction of the above parameters after 2 months of treatment was proved uncertain, which can be explained by an insufficient duration of treatment (Table 2). In patients of the first group who received bisoprolol the meaning of LVMS(left ventricular mass index) had been $122,87 \pm 3,22 \text{ g/m}^2$ before the start of an antihypertensive therapy and decreased significantly under the influence of treatment to the level of $110,9 \pm 4,23 \text{ g/m}^2$ ($p < 0.05$).

Average LVMI of the II group of patients after a course of therapy with enalapril was $112,72 \pm 1,35 \text{ g/m}^2$, which is significantly lower compared with its value before treatment - $123,32 \pm 3,03 \text{ g/m}^2$ ($p < 0, 05$). As shown in Table 2, monotherapy with bisoprolol or enalapril, and the use of a combination of these drugs with kardiofit had led to activation of reverse left ventricular remodeling processes in the patients with hypertension. This is proved by a significant reduction in values of left ventricular mass and left ventricular mass index after 4 months of treatment. After a course of a combined antihypertensive therapy with bisoprolol and kardiofitom that lasted 4 months, average LVMI in these patients was $111,64 \pm 2,10 \text{ g/m}^2$ ($p < 0.01$). The combination of enalapril with kardiofit also led to a significant reduction in left ventricular mass. This is shown by a reduction of LVMI in patients of the fourth group from $123,81 \pm 3,01 \text{ g/m}^2$ to $112,81 \pm 1,64 \text{ g/m}^2$ ($p < 0.01$) (Figure 1).

To study the effect of an antihypertensive therapy of the given combined schemes we have analyzed the figures dynamics of a daily monitoring of blood pressure.

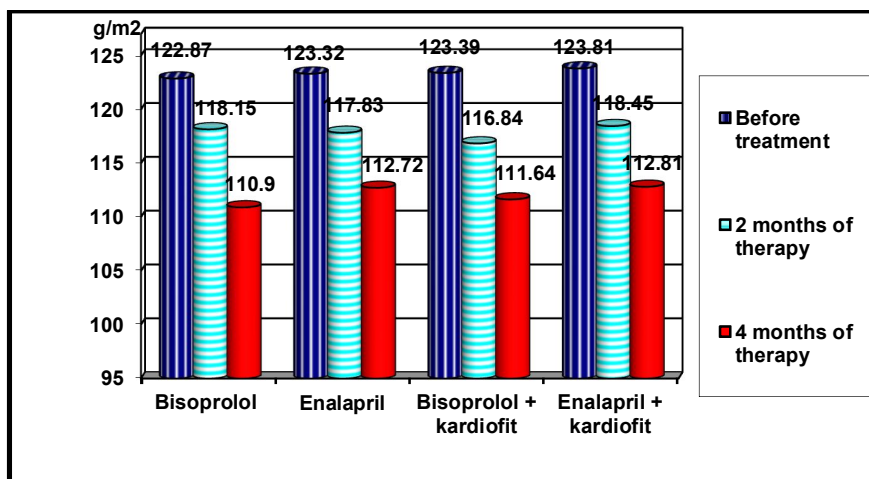


Figure 1. Dynamics of indices of left ventricular mass under the influence of antihypertensive therapy

Table 1: The figures dynamics of the systolic function and sizes of the left ventricle after the conducted antihypertensive therapy in the patients with hypertension who were under a prolonged influence of the electromagnetic fields of high intensity.

Group of patients	EDD, cm	ESD, cm	EDV, ml	ESV, ml	SV, ml	EF, %
Bisoprolol(n=30)						
- before treatment	4,99±0,21	3,56±0,17	104,55±18,7	43,79±2,18	61,19±2,24	58,90±3,6
- in 2 months	4,68±0,18 p>0,05	3,19±0,16 p>0,05	98,96±5,3 p>0,05	39,39±2,95 p>0,05	59,26±2,02 p>0,05	59,74±2,5 p>0,05
- in 4 months	4,53±0,22 p>0,05	3,04±0,17 p<0,05	87,72±4,6 p>0,05	32,25±2,52 p<0,001	60,36±2,07 p>0,05	68,07±2,65 p<0,05
enalapril(n=30)						
- before treatment	5,03±0,24	3,55±0,34	110,7±10,21	47,63±3,17	63,10±2,61	57,39±3,25
- in 2 months	4,7±0,2 p>0,05	3,20±0,15 p>0,05	95,16±3,13 p>0,05	38,86±2,11 p>0,05	56,24±2,32 p>0,05	59,64±2,07 p>0,05
- in 4 months	4,51±0,21 p>0,05	3,06±0,16 p>0,05	94,03±3,55 p>0,05	36,29±2,21 p<0,01	57,96±2,44 p>0,05	61,45±1,98 p>0,05
Bisoprolol+ kardiofit (n=31)						
- before treatment	5,07±0,31	3,53±0,24	109,84±8,54	47,86±2,44	62,26±2,26	57,35±2,96
- in 2 months	4,7±0,2 p>0,05	3,21±0,15 p>0,05	97,19±2,34 p>0,05	38,12±2,65 p<0,01	59,01±2,10 p>0,05	60,42±2,19 p>0,05
- in 4 months	4,53±0,22 p>0,05	3,05±0,17 p>0,05	90,54±2,45 p<0,05	36,21±2,79 p<0,01	59,54±2,09 p>0,05	66,11±3,05 p<0,05
Enalapril+ kardiofit (n=29)						
- before treatment	4,92±0,33	3,51±0,27	113,4±8,77	45,63±2,04	67,46±2,84	59,96±2,03
- in 2 months	4,73±0,21 p>0,05	3,20±0,16 p>0,05	96,44±2,58 p>0,05	36,34±2,43 p<0,01	59,6±1,96 p<0,05	61,11±2,20 p>0,05
- in 4 months	4,52±0,22 p>0,05	3,15±0,17 p>0,05	95,81±4,27 p>0,05	34,25±2,4 p<0,01	61,39±2,66 p>0,05	64,48±1,76 p>0,05

Note: p- the reliability of the difference of average values before and after the treatment

It is noticed that, the addition of bisoprolol to kardiofit was accompanied by a more pronounced antihypertensive effect compared with a monotherapy with bisoprolol. The average daily systolic blood pressure in the third group of patients after 4 months of treatment decreased to 14.38 mm Hg. The decrease rate in the average daily systolic blood pressure in the patients receiving monotherapy with bisoprolol was 13.29 mm Hg. The reduction of the average daily systolic blood pressure in the second group, in which patients had been treated with enalapril

was 8.55 mm Hg, and the addition of kardiofit to the medical scheme led to a decrease in the average daily systolic blood pressure to 9.26 mm Hg.

Analyzing the average daily diastolic pressure a significant decrease of this index in all study groups after 2 months of therapy was not observed. However, treatment for 4 months resulted in a statistically significant reduction in diastolic blood pressure with the use of all investigated schemes of an antihypertensive therapy.

Table 2: The figures dynamics of the ventricular mass and sizes of the left ventricle after the conducted antihypertensive therapy in the patients with hypertension who were under a prolonged influence of the electromagnetic fields of high intensity

Group of patients	PWTd, cm	PWTs, cm	SWTd, cm	SWTs, cm	LVM, g	LVMI (g/m ²)
Bisoprolol (n=30)						
- before treatment	1,29±0,019	1,38±0,046	1,29±0,026	1,42±0,019	235,29±6,18	122,87±3,22
- in 2 months	1,26±0,02 p>0,05	1,34±0,023 p>0,05	1,28±0,026 p>0,05	1,39±0,035 p>0,05	225,9±4,20 p>0,05	118,15±2,13 p>0,05
- in 4 months	1,22±0,02 p<0,05	1,32±0,019 p>0,05	1,22±0,022 p<0,05	1,35±0,023 p<0,05	211,61±7,99 p<0,05	110,9±4,23 p<0,05
enalapril (n=30)						
- before treatment	1,3±0,02	1,43±0,059	1,29±0,027	1,46±0,046	233±5,74	123,32±3,03
- in 2 months	1,26±0,02 p>0,05	1,40±0,03 p>0,05	1,27±0,022 p>0,05	1,43±0,02 p>0,05	222,66±5,02 p>0,05	117,83±2,58 p>0,05
- in 4 months	1,23±0,02 p<0,05	1,38±0,026 p>0,05	1,24±0,035 p>0,05	1,38±0,026 p>0,05	215,09±2,29 p<0,01	112,72±1,35 p<0,01
Bisoprolol+ kardiofit (n=31)						
- before treatment	1,30±0,02	1,41±0,045	1,3±0,022	1,42±0,033	234,06±5,46	123,39±2,82
- in 2 months	1,24±0,02 p<0,05	1,37±0,02 p>0,05	1,27±0,02 p>0,05	1,38±0,023 p>0,05	222,55±5,14 p>0,05	116,84±2,76 p>0,05
- in 4 months	1,22±0,019 p<0,01	1,33±0,026 p>0,05	1,22±0,026 p<0,05	1,34±0,033 p>0,05	211,8±3,97 p<0,01	111,64±2,10 p<0,01
Enalapril+ kardiofit (n=29)						
- before treatment	1,29±0,02	1,42±0,05	1,3±0,04	1,41±0,029	232,52±6,7	123,81±3,01
- in 2 months	1,25±0,018 p>0,05	1,37±0,03 p>0,05	1,26±0,02 p>0,05	1,37±0,044 p>0,05	220,74±4,79 p>0,05	118,45±2,45 p>0,05
- in 4 months	1,22±0,019 p<0,05	1,34±0,02 p>0,05	1,25±0,03 p>0,05	1,35±0,027 p>0,05	211,63±3,55 p<0,01	112,81±1,64 p<0,01

Note: p- the reliability of the difference of average values before and after the treatment.

But, a combined antihypertensive therapy was accompanied by the more intense reduction of DBP. We have noticed that the level of the average daily diastolic pressure after 4 months of bisoprolol therapy decreased on 6.55 mm Hg. A combined treatment with bisoprolol and kardiofit was accompanied by a decrease of this index at 8.82 mm Hg. In the enalapril group the average daily diastolic pressure had been 91,32 ± 3,18 mm Hg and decreased after treatment from 8.52 mm Hg to the level of 82,8 ± 1,78 mm Hg.

In the combined therapy group with enalapril and kardiofit the level of blood pressure decrease reached 9.85 mm Hg. The analysis of heart rate level found that a significant decrease of this

index under the influence of treatment was observed only in patients receiving bisoprolol monotherapy and in combined therapy group with bisoprolol and kardiofit (Group I and III). Treatment with enalapril and use a combination of enalapril with kardiofit isn't accompanied by a significant effect on heart rate. The results of daily monitoring of blood pressure indicate a higher efficiency of bisoprolol compared with enalapril for lowering systolic blood pressure and a more pronounced antihypertensive effect when herbal sedative drug kardiofit is added to bisoprolol, that was shown by a more intense decline in the average daily diastolic pressure and the average daily systolic

pressure This can be explained by the high degree of activation of the sympathoadrenal system in the development and progression of hypertension in patients who are under a prolonged influence of the electromagnetic fields of high intensity.

CONCLUSIONS:

1. Monotherapy with bisoprolol has proved to be more effective for lowering systolic blood pressure compared with enalapril antihypertensive therapy in patients with hypertension who were under a prolonged influence of the electromagnetic fields of high intensity.

2. The addition of herbal sedative drug kardiofit to bisoprolol or enalapril has led to intensive antihypertensive effect, which manifests itself in more rapid normalization of indices of diastolic blood pressure in the groups with a combined treatment.

3. The investigated schemes of antihypertensive therapy turned up to be highly effective for reducing left ventricular mass, that indicates the activation upon their processes of reverse remodeling of the left ventricle.

4. The use of a combined antihypertensive therapy has led to intensification of reverse remodeling of the left ventricle that manifested in faster statistically significant decrease of its weight in comparison with bisoprolol or enalapril.

There was a significant effect of bisoprolol and its combination with kardiofit on systolic function of the left ventricle, which is manifested by the increase of LVEF in the observed patients.

REFERENCE:

1. Bachmakov I. Characterization of beta-adrenoceptor antagonists as substrates and inhibitors of the drug transporter P-glycoprotein / I. Bachmakov, U. Werner, B. Endress, D. Auge, M.F. Fromm. // *Fundam Clin Pharmacol.* – 2006. – Vol.20,№3. – P. 273–82.
2. Chanock S. Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk / S. Chanock // *Nature Genetics.* – 2009. – Vol.41. – P. 765 -766.

3. Conroy R.M. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the Score project / R.M. Conroy, K.Pyorala, A.P. Fitzgerald [et al.] // *Eur. Heart. J.* – 2003. – Vol.24. – P. 987-1003.
4. Carlberg B, Samuelsson O, Lindholm L. Atenolol in hypertension: is it a wise choice? / B. Carlberg, O. Samuelsson, L. Lindholm // *Lancet.* – 2004. – Vol.364. – P. 1684–1689.
5. ESH-ESC Guidelines Committee. 2007 guidelines for the management of arterial hypertension // *J. Hypertension.* – 2007. – Vol.25. – P. 1105–1187.
6. Gradman A.H. Combination therapy in hypertension / A.H. Gradman, J.N. Basile, B.L. Carter [et al.] // *J. Am. Soc. Hypertens.* – 2010. – Vol.4. – P. 42–50.
7. Haffner S.M. Risk constellations in patients with the metabolic syndrome: epidemiology, diagnosis, and treatment patterns / S.M.Haffner // *Amer. J. Med.* – 2006. – Vol. 119 (Suppl 1). – P. 3-9.