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Heart Failure Treatment In Patients With Recurrent Myocardial Infarction

Ruslana Denina [1*]

1. State Higher Educational Establishment, Department of Internal Medicine No 2 "Ivano-Frankivsk National Medical University", 2, Halytska Str., 76000 Ukraine
[E-mail: roksolana.dog@rambler.ru]

160 patients with heart failure classes II and III with recurrent myocardial infarction have undergone treatment by means of cardioprotector - isosorbide mononitrate – mononitrosid and metabolitotropic drug 5-lipoxygenase inhibitor corvitin/quercetin. All the suggested treatment regimens of heart failure in patients with recurrent myocardial infarction had high antagonistic effectiveness, resulted in the decrease of blood pressure, pulse pressure, improved structural and functional characteristics of the myocardium (including the increase in ejection fraction (EF), and significant decrease of left ventricular end-diastolic dimension (LVEDd), end-diastolic volume (EDV), left ventricular mass index (LVMI), reduced NT-proBNP levels, Total NO and improved heart rate variability.

Keyword: Heart Failure, Recurrent Myocardial Infarction, Treatment, 5-Lipoxygenase Inhibitor, Isosorbide Mononitrate.

1. Problem stating and analysis of recent researches:

The leading factors causing heart failure in patients with ischemic heart disease (IHD), including myocardial infarction (MI) are the increase in the workload on the myocardium of the left ventricle, volume overload, overload of surviving cardiomyocytes, that occurs after the death of some of them (after acute MI) [4,5,7,8]. All these factors lead to reduced exercise tolerance in post-infarction period, and are prognostically unfavorable factors for survival rate and sudden cardiac death [1,2,3,6].

With the aim of prevention and treatment of heart failure in patients with myocardial infarction, it is important to inhibit the progression of post-infarction cardiac remodeling [4,5,9].

2. Aim of research:

Improvement of the effectiveness of heart failure treatment in patients with recurrent myocardial infarction based on the study of central hemodynamics, dynamics of NT-proBNP, nitric oxide, heart rate variability.

3. Materials and methods of research:

The study involved the examination of 160 patients with heart failure due to recurrent myocardial infarction, aged 40 to 70 years, the average age of which was (61,16±,788) years, among them women made up - 22,5%, and men -

77,5%. 15 healthy individuals of the same age and sex were also examined to control normal ranges of the studied parameters.

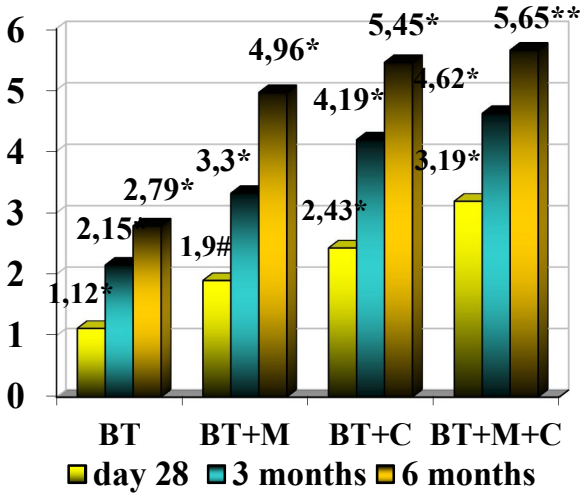
The patients were randomized into 2 groups according to the treatment modalities. Patients of the control group - 40 persons, received the standard treatment of MI with concomitant heart failure (basic therapy-BT). Patients of the basic group - 120 persons, were divided into 3 subgroups. The first subgroup (BT+ mononitrosid) included 40 patients treated with BT, but they received isosorbide mononitrate – mononitrosid (in doses of 20 mg 2-3 times per day) instead of dinitrate. The second subgroup (BT+ corvitin/quercetin) included 40 patients which received basic treatment (BT) in conjunction with 5-lipoxygenase inhibitor corvitin/quercetin that was administered in the dose of 500 mg in 100 ml of isotonic sodium chloride solution intravenously at a rate of 30-40 drops per 1 minute (first day: 500 mg at the time of admission, 500 mg -after 2 and 12 hours; second and third days: 500 mg, twice, every 12 hours; the fourth and fifth days: 250 mg, once a day) with subsequent change to «Quercetin granules» - 1g twice a day, taken orally 30 minutes before a meal after dissolving the granules in ½ cup of warm water. The third subgroup included 40 patients receiving BT in combination with isosorbide mononitrate and corvitin/quercetin (BT+Mnt+C/Q).

The efficacy of treatment was assessed on the 28th day, after 3 and 6 months of ambulatory monitoring.

On admission all the patients have undergone general clinical examination (analysis of the pain syndrome, anamnesis, and objective characteristics) along with clinico-instrumental (electrocardiography) and laboratory tests (cardiac injury markers – cardiac troponin I - cTn-I, NT-proBNP).

Indices of hemodynamics and left ventricular myocardial contractility were evaluated by means of echocardiography performed at PHILIPS HD 11XE apparatus.

The level of brain natriuretic peptide in blood was determined by means of immune-fermentation method (NT-proBNP, "Peninsula Laboratories", USA). NT-proBNP 45,14 fmol/ml level was considered to be normal. The level of nitrogen oxide (Total NO) in blood plasma was determined using R&D Systems GmbH reagents (Germany). The study of heart rate variability was performed by 5- minute recording with the help of «Cardiolab» system of «XAI-MEDICA» production (Kharkiv, Ukraine). Statistical processing of study materials was performed using the methods of biostatistics in software packages EXCEL-2003, STATISTICA 7.0 (Statsoft Inc., USA) [9].

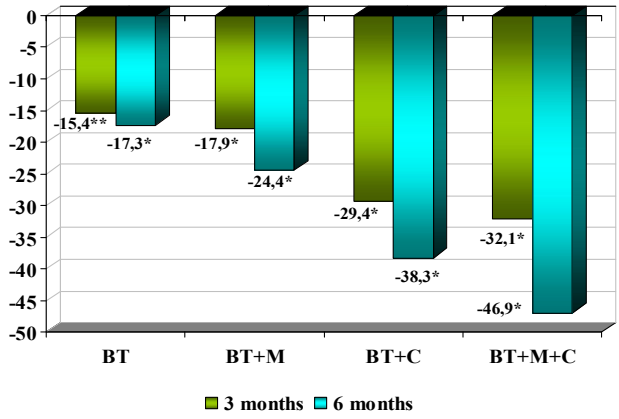


Picture 1. Influence of different treatment methods on the levels of ejection fraction after 28 days, 3 and 6 months of monitoring in patients of the studied groups.

Notes. Probable deviation of the levels to indices for the period of hospitalization *<0,05; ** <0,01; #>0,1.

4. Results of research and their discussion. Evaluating the effectiveness of the above mentioned treatment regimens some positive clinical, instrumental and biochemical changes were observed in all groups of patients.

Thus, the treatment of heart failure in patients with recurrent myocardial infarction with the use of basic therapy showed that the need for further additional use of nitroglycerin tablets (p <0.0001) decreased, exercise tolerance (p>0,1) increased, according to the Rating Scale of Clinical State (RSCS) - clinical symptomatology improved (p<0,001), the indices of systolic blood pressure (SBP), diastolic blood pressure (DBP), partial blood pressure (PBP), and aortal stiffness decreased, the indices of central hemodynamics such as the end-diastolic dimension (EDD), end-diastolic volume (EDV), stroke volume (SV) and left ventricular mass index (LVMI) normalized. Left ventricular ejection fraction (LVEF) increased to +2,79% (p<0,05), and the function of the left ventricular cardiac muscle improved (Picture 1). Under the influence of basic therapy the level of NT-proBNP decreased to the "gray zone" level only after 6 months (Picture 2) and made up 346,698±20,00 fmol/ml (-17,4; p <0,001) as compared to the condition prior to the treatment which was (459,64 ±40,74 fmol/ml), and the Total NO (p<0,0001) normalized.



Picture 2. Dynamics of NT- proBNP level after 3 and 6 month of monitoring.

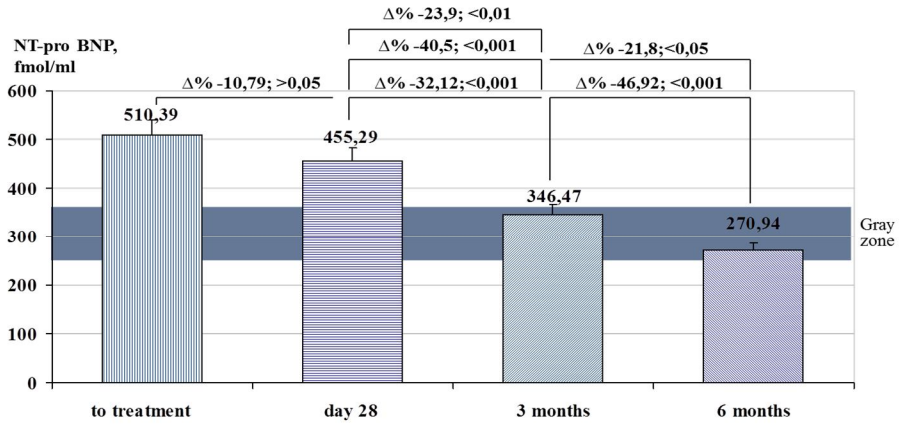
Notes. Probable deviation of the levels to indices for the period of hospitalization p * <0,001; **>0,5.

The indices of heart rate variability in patients with recurrent myocardial infarction with concomitant chronic heart failure haven't significantly changed after the course of basic therapy. The SDNN index at the time of hospitalization was 48,23±5,10 ms, and made up 49,13±4,1 ms (+1,86%; p >0,1) after 28 days, while the level of LF/ HF decreased from 2,8±0,32 to 2,3±0,14 (17,86%; p >0,1), that is the indices haven't significantly changed and were characterized as sympathicotonia.

The clinical state of heart failure in group of patients taking isosorbide mononitrate improved, as evidenced by the reduction in the number of patients with HF class III by 4.8% (p <0.05) after 28 days of treatment and by 14,3% (p<0,05) after 6 months, and the exercise tolerance level increased as proved by the 6-minute walk test (306,04±13,87 m, Δ 7,98%; p< 0,05 in 6 months). The use of isosorbide mononitrate significantly reduced the need for additional administration of nitroglycerin (p<0,001) in only 28 days of treatment. The indices of central hemodynamics

and transmitral flow became normal. The left ventricular ejection fraction (LVEF) increased from 45,78±0,98% to 48,05±0,76 % after 6 months (Δ+4,96%; p < 0,05) – Picture 1. It has also been proved that the use of isosorbide mononitrate has positive influence on the NT-proBNP level to 347,69±29,23 fmol/ml (-24,4%; p <0,001) - Picture 2. The normalization of Total NO release to 24,67±0,36 mkmol/l (p<0,001) was also observed after 6 months of treatment.

The indices of heart rate variability haven't also undergone any significant changes under the influence of the basic therapy in conjunction with mononitrosid. The vegetative tonus kept to be reduced with the tendency for predominance of sympathetic influences, as evidenced by the LF/ HF index that made up 2,4±0,69 at the time of hospitalization, and 1,8±0,49 (-20,83%;p >0,1) after 28 days.



Picture 3. Dynamics of NT -proBNP level in BT+M+C group depending on the treatment period.

The results of treatment with the use of basic therapy in conjunction with 5-lipoxygenase inhibitor turned out to be rather interesting. The number of patients with HF class III in this group decreased by 18,2 % (p<0,05), clinical symptomatology improved and the exercise tolerance level increased.

Under the influence of 5-lipoxygenase inhibitor left ventricular ejection fraction tended to increase by 5,45% (p<0,05), evidences of systolic and diastolic LV dysfunction decreased (Picture 1).

Under the influence of basic treatment in conjunction with corvitin/quercetin the NT-proBNP level decreased by -29,4% (p <0,0001) after 3 months, and by 38,28% (p <0,001) after 6 months.

In response to corvitin/quercetin general vegetative tonus increases, sympathetic influence of the nervous system on the heart decreases. LF/HF levels decreased by 16,16% (p >0,05) under the influence of the suggested therapy.

The introduction of corvitin/quercetin to basic therapy showed positive effect on the production of Total NO, leading to normalization of this anion (p <0.001).

Clinical effectiveness of complex therapy with isosorbide mononitrate and 5-lipoxygenase inhibitor turned out to be much higher as compared to their separate use. The best effects as for the supplementary administration of nitroglycerin and sustained antihypertensive effects were observed with the use of basic therapy in conjunction with isosorbide mononitrate and 5-lipoxygenase inhibitor, as evidenced by the achievement of target indices of

systolic blood pressure (SBP), diastolic blood pressure (DBP) and partial blood pressure (PBP) ($p<0,001$).

The dynamics of aortal stiffness index proved positive influence of treatment, which in these cases was reduced by 20.33% ($P <0.01$) after 28 days and 30.08% ($P <0.001$) after 6 months of ambulatory monitoring. At the same time the functional class of HF increased by 30,0% ($p<0,01$). While assessing the dynamics according to the Rating Scale of Clinical State (RSCS) the number of points decreased by 37,3% ($p<0,001$).

End-diastolic dimension of the left ventricle decreased by 6,84% ($p<0,01$) after 28 days and by 10,26% ($p<0,001$) after 6 months of ambulatory monitoring in patients using isosorbide mononitrate combined with 5-lipoxygenase inhibitor. The similar dynamics was noticed in the indices of end-diastolic volume, which decreased by 3,55% ($p>0,1$) after 28 days, by 6,27% ($p>0,1$) after 3 months and by 7,89% ($p<0,05$) after 6 months of observation. Stroke volume decreased by 12,49% ($p<0,02$), 14,27% ($p<0,01$) and by 15,43% ($p<0,01$) after 28 days, 3 and 6 months of observation respectively.

NT-pro BNP level decreased by 32,1% after 3 months of treatment and made up 346,47 fmol/ml ($p <0,001$), and after 6 months – by 47,0% ($p <0,0001$) and its level was 270,94 fmol/ml. The above mentioned shows that the NT-proBNP level reached the lower values of the "gray zone" (Picture 3) under the influence of basic therapy in conjunction with corvitin/quercetin.

Treatment by means of basic therapy in combination with mononitrosid and corvitin/quercetin normalizes the production of Total NO anions ($p <0.05$).

Treatment with the use of basic therapy, mononitrosid and corvitin/quercetin (BT+Mnt+C/Q) has positive influence on the heart rate variability, as the correlation of LF/HF decreased from 2,79±0,21 to 1,75±0,17 ($p<0,01$). Hz

5. Conclusion

All the suggested treatment regimens of heart failure in patients with recurrent myocardial infarction had high antianginal effectiveness, resulted in the decrease of blood pressure, pulse pressure and NT-proBNP levels, improved endothelial function, structural and functional characteristics of the myocardium, decreased diastolic dysfunction of the left ventricle and normalized heart rate variability.

These effects diminished the signs of heart failure: increased tolerance to physical exertion (according to the six-minute walk test) and decreased functional class of heart failure. The combination of mononitrosid with corvitin turned out to be the most effective when associated with the basic therapy.

Based on the analysis of the data we advanced the principles of treatment of heart failure with repeated MI:

- Antianginal therapy, that reduces symptoms of ischemia and signs of left ventricular diastolic dysfunction;
- Improvement of the structural and functional parameters of the heart (decrease in end-diastolic dimension (LVEDd), end-diastolic volume (EDV) and stroke volume, increase in ejection fraction);
- Improvement of the endothelial dysfunction (decrease in index of aortal stiffness and Total NO);
- Reduction of NT pro BNP level.

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