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Peculiarities of Medical Use of Korvazan in Rehabilitation Treatment of Patients After Myocardial Infarction Regarding Risk Factors

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Risk factors of cardiovascular events made the largest contribution to mortality rate from cardiovascular diseases. In order to determine the effectiveness of rehabilitation there were examined 240 patients with myocardial infarction with concomitant risk factors. The study found that the inclusion in the standard therapy of beta-blocker carvedilol in individually selected dose and depending on the risk factor of cardiovascular events helps to increase myocardial functional reserves and tolerance to physical exertion.

Keyword: Myocardial Infarction, Heart Failure, Hypertension, Obesity, Carvedilol.

1. Introduction

Cardiovascular diseases – are the main causes of patients' death of middle and old age in many countries. Annual losses, according to WHO, are more than 17,500,000 lives. In Ukraine, in 2010 the number of adults who have diseases of the circulatory system is about 25.9 million. Meanwhile in Ukraine over the past 30 years the prevalence of cardiovascular diseases among the population increased by 3.5 times, and the death rate from them - at 46.0 %. In this context, cardiovascular diseases, with their universal influence on people's important functions continue to occupy stably the first place in the structure of the primary causes of death and disability of the Ukrainian adult population [2]. One of the most actual social and medical problems of our time is ischemic heart disease (IHD). The peculiarity of IHD is not only a high morbidity rate, but a high percentage of disability and mortality of working age people. Key problems of patients with IHD is the timely and

accurate diagnosis, risk assessment and prognosis of the disease, the prescription of adequate treatment algorithm. The largest contribution to mortality rate from ischemic heart disease, in particular myocardial infarction is owned by factors such as systolic blood pressure (50%), body overweight, increased cholesterol and LDL (21% and 32 % respectively), impaired carbohydrate metabolism and cardiac failure; it's also proved that the longer effect of any factor on the human body, the higher risk of cardiovascular events [1, 3]. One of the invincible obstacles in reducing cardiovascular risk is time, the more we defers diagnosis and treatment, the fewer opportunities to realize the full potential. It is important for the specialists to focus on the importance of risk stratification of acute coronary syndrome and to determine the most appropriate treatment scheme of patients, who belong to different risk groups. So, to make a sure step forward in reducing cardiovascular risk, it is necessary to evaluate the impact of various

factors on the choice of doctor tactics of examination and treatment of patients with high cardiovascular risk [4]. The most informative diagnostic methods are loading tests (treadmill test and test of 6 minutes walk), that fairly accurately characterize risk prediction of patients with myocardial infarction. Today, one of the group of drugs used in the treatment of virtually all cardiovascular diseases are the beta-blockers [5].

The aim of the work is to improve the rehabilitation of patients with acute coronary syndrome based on clinical and pathogenetic evaluation and medical correction of physical activity in recovery period after myocardial infarction.

2. Materials and Methods

During the study there were examined 240 patients aged 40 to 75 years, who underwent Q- and Non-Q-myocardial infarction with concomitant diseases: heart failure, obesity, hypertension, and a set of risk factors. Each group is divided into four subgroups of 60 persons, of which - 30 patients compose the control subgroup and 30 patients – experimental one. Patients received standard treatment: statins, aspirin, anticoagulants, ACE inhibitors, the control subgroup received beta-blocker metoprolol, experimental subgroup - carvedilol, which was administered in the dosage of 3,125 mg/d; with the method of titration the dose was brought up to 25-50-100 mg/d depending on risk factors of cardiovascular events. In the future, the need for the appointment of additional drugs did not arise. The period of observation lasted 12 months. Patients were examined at the beginning of treatment, in 1, 3, 6 and 12 months. Dosed physical activity was performed on the apparatus treadmill Full Vision Ins. (TMX 425, USA); patients of all groups were evaluated after the following parameters: duration of exercise, the amount of oxygen consumed during exercise (VO_2), after the formula $\text{VO}_2=2,68\times V+0,483\times V\times G+3,5$, where V - velocity of treadmill movement, G - the treadmill

angle, the maximum oxygen demand (MOD) after the formula $\text{MOD}=14,8-(1,379\times T)+(0,451\times T^2)-(0,012\times T^3)$, where T - total duration of exercise, metabolic units (MET) after the formula $\text{MET}=\text{VO}_2/3,5$ and ST segment depression in abductions V4, V5; criteria to achieve the threshold stress were: the appearance of anginal pain and/or horizontal or slanting ascending depression of segment $\text{ST}>1$ mm of at least 008 sec. Exclusion criteria were absolute or relative contraindications to performance of loading tests, complex arrhythmias, chronic obstructive pulmonary disease, atherosclerosis and varicose veins of the lower limbs, cancer. Statistical analysis of the research results were performed in the programme «Microsoft Excel Access». Average values of their percentage share and Student's test were calculated. The values of the personal data of experimental and control subgroups, and the values within each group at different stages of the study were compared. The difference in values at $p<0.05$ was considered statistically significant.

3. Results and Discussion

Analysis of the results showed that the average value of the index MET in patients of all groups to treatment hardly differed and were significantly reduced in comparison with healthy individuals (Table 1). After treatment, the level of MET has significantly increased in all groups of patients ($p<0,05$) and the more expressed tendency was observed in the group with the addition of carvedilol ($7,15\pm0,46$) if compared with metoprolol ($4,86\pm0,43$), especially during the third month of treatment, when almost in all patients the maximum therapeutic effect was achieved by titration method of the drug. Thus, in the group of patients with myocardial infarction in combination with hypertension with addition of carvedilol to standard therapy a significant increase in VO_2 ($41,95\pm0,78$) was observed in comparison with the standard group ($28,75\pm0,92$).

Table 1: Indicators of treadmill-test in patients after myocardial infarction taking into account risk factors ($M \pm m$)

Indicator, units of measurement	Healthy (n=30)	Patients after MI			
		HF (n=75)	AH (n=75)	Obesity (n=75)	All risk factors (n=75)
VO2	77,69±0,14*	14,76±0,42*	13,53±0,58*	24,40±0,75*	10,62±0,37*
MET	22,19±0,11*	4,44±0,14*	3,72±0,15*	7,03±0,18*	3,02±0,12*
MOD	71,93±0,21*	21,60±0,61*	17,37±0,71*	35,31±0,75*	17,62±0,58*
Depression ST V4	0±0,01*	1,26±0,03*	0,73±0,04*	1,10±0,02*	1,33±0,03*
Depression ST V5	0±0,01*	1,16±0,02*	0,58±0,03*	1,06±0,03*	1,25±0,04*

Note: Probability of differences in comparison: * – $p < 0,05$; ** – $p > 0,05$.

Most patients of this group before treatment had tallied to III FC IHD, but up to 12th month of treatment most of them have achieved the I FC IHD. MET level testifies about it - (3,77±0,34) and (22,40±0,42) respectively. The use of beta-adrenoblocker carvedilol in complex of medical support during recovery period after myocardial infarction gives the possibility to control the level of blood pressure and heart rate, impedes the development of tachyarrhythmias, has anti-ischemic effect. In addition, carvedilol has a mild alpha-blocking effect and antioxidant effect, which in its turn promotes a positive impact on the peripheral microcirculation and metabolism. Indirectly carvedilol adjusts, due to the influence on renin synthesis, the activity of the renin-angiotensin system. The average daily dose of carvedilol after our results is 20.2 mg a day. As for the patients with heart failure after myocardial infarction, the recommended therapeutic dose of carvedilol is 37,5-50 mg per day, the achievement of which in almost all patients was observed also during the third month of treatment, the effectiveness of this therapy was noted during the treadmill test with the significant increase in VO₂, MET and the reduce of depression of segment ST V4, V5 in comparison with basic data (Table 2). The use of carvedilol, which blocks unwanted effects in heart failure the hyperactivation of sympathoadrenal system and its simultaneous peripheral vasodilation and antioxidant effects provide a favorable course of the recovery period after myocardial infarction and increase of tolerance to physical activity, reducing the risk of progression of heart failure. Carvedilol helps to prevent life-threatening arrhythmias, has antianginal effects, normalizes heart rhythm, controls blood pressure, and endothelial function.

Analyzing the results of treadmill test in patients with obesity who had myocardial infarction, we observed a significant increase in physical loading in patients, who were added beta-blocker carvedilol to standard therapy; that corresponded to the number of passed steps: before treatment (3,86±0,24), on the 3^d month (5,73±0,17), on the 12th month (8,00±0,22); it was not observed in patients who were added beta-blocker metoprolol to standard therapy: before treatment (3,93±0,13), on the 3rd month (4,42±0,21) and on the 12th month (5,90±0,13), respectively. Patients, whose dose of carvedilol was 75-100 mg per day, have achieved therapeutic effect; on the basis of this dose, due to antiatherogenic action the risk of repeated adverse reactions reduces, and the tolerance to exercises increases. Particular attention is attracted by the group of patients with a combination of risk factors listed above with myocardial infarction. Observing the negative effect of each of these factors on the course of rehabilitation of patients after myocardial infarction, interesting thing was the impact of risk factors totality on the recovery period, and tolerance to physical activity in these patients during treatment with beta-blockers: carvedilol and metoprolol. Analyzing the received data, we observed a clear tendency to increased tolerance to physical activity by increasing the performance of MET with (3,24±0,22) before treatment, (7,15±0,46) on the 3^d and (16,89±0,64) on the 12th months of treatment that meets II and I FC IHD respectively, in contrast to the group of patients who were on standard therapy. Average daily dose of carvedilol for patients with high cardiovascular risk with myocardial infarction in conjunction with the totality of all risk factors was 50 mg per day and is therapeutically

effective due to the reduce of cardiac output, the decrease of myocardial oxygen inhibition of excitability and conductivity, ensuring hypotensive, anti-ischemic, antiarrhythmic, and

antiatherogenic effects on the recovery period after myocardial infarction.

Table 2: Dynamics of treadmill test indexes in patients with MI and in patients of the general group in the process of restorative treatment with carvedilol ($M \pm m$)

Index	Before treatment	1 st month	3 ^d month	6 th month	12 th month
Standard therapy in patients with HF (n=30)					
VO2, mm/min/kg	14,58±0,96*	17,33±0,92*	19,97±1,20*	22,65±1,04*	28,12±1,10*
MET	4,16±0,26*	4,90±0,34*	5,70±0,56*	6,40±0,23*	8,03±0,34*
Depression ST V4, mm	1,40±0,058*	1,30±0,04*	1,10±0,03*	1,00±0,04*	0,80±0,02*
Standard therapy and carvedilol in patients with CH (n=30)					
VO2, mm/min/kg	15,72±0,84*	19,78±0,92*	28,02±1,10*	36,30±0,90*	46,47±1,09*
MET	4,49±0,62*	5,65±0,51*	8,00±0,23*	10,37±0,34*	13,27±0,42*
Depression ST V4, mm	1,30±0,06*	1,00±0,04*	0,50±0,05*	0,30±0,02*	0,20±0,02*
Standard therapy in patients with AH (n=30)					
VO2, mm/min/kg	13,93±0,75*	20,05±1,10*	28,75±0,92*	29,83±1,10*	42,69±1,09*
MET	3,98±0,29*	5,73±0,31*	8,21±0,56*	8,52±0,21*	12,19±0,62*
Depression ST V4, mm	1,16±0,09*	1,00±0,08*	0,80±0,08*	0,73±0,06*	0,52±0,05*
Standard therapy and carvedilol in patients with AH (n=30)					
VO2, mm/min/kg	13,22±0,84*	20,78±0,92*	41,95±0,78*	62,52±0,96*	78,43±1,01*
MET	3,77±0,34*	5,93±0,55*	11,98±0,23*	17,86±0,35*	22,40±0,42*
Depression ST V4, mm	1,21±0,09*	1,09±0,09*	0,60±0,08*	0,22±0,06*	0,01±0,06*
Standard therapy in patients with obesity (n=30)					
VO2, mm/min/kg	24,26±0,88*	26,20±0,94*	28,84±1,10*	35,22±1,05*	45,77±1,14*
MET	6,93±0,42*	7,48±0,54*	8,24±0,56*	10,06±0,38*	13,07±0,66*
Depression ST V4, mm	1,20±0,06*	1,10±0,04*	1,00±0,05*	0,90±0,04*	0,60±0,02*
Standard therapy and carvedilol in patients with obesity (n=30)					
VO2, mm/min/kg	24,94±0,92*	28,84±0,98*	43,68±0,84*	60,11±0,96*	71,37±1,11*
MET	7,12±0,58*	8,24±0,61*	12,48±0,24*	17,17±0,35*	20,39±0,46*
Depression ST V4, mm	1,10±0,08*	1,00±0,06*	0,60±0,03*	0,20±0,02*	0,10±0,02*
Standard therapy in patients with totality of risk factors (n=30)					
VO2, mm/min/kg	0,41±0,58*	14,47±0,75*	17,02±1,12*	26,26±1,31*	33,18±1,22*
MET	2,97±0,24*	4,11±0,33*	4,86±0,43*	7,48±0,52*	9,48±0,61*
Depression ST V4, mm	1,84±0,08*	1,75±0,08*	1,53±0,07*	1,32±0,08*	1,15±0,06*
Standard therapy and carvedilol in patients with totality of risk factors (n=30)					
VO2, mm/min/kg	11,34±1,03*	16,85±1,35*	25,05±1,85*	40,53±2,55*	59,14±3,01*
MET	3,24±0,22*	4,81±0,39*	7,15±0,46*	11,58±0,51*	16,89±0,64*
Depression ST V4, mm	2,15±0,08*	1,52±0,07*	1,26±0,06*	0,75±0,05*	0,22±0,07*

Note. * - differences in accuracy compared with the values before treatment.

4. Conclusions

The results of this study are: 1. Inclusion of beta-blocker carvedilol in individually selected dose into the standard therapy and depending on the risk factor of cardiovascular events improves myocardial functional reserves. 2. The use of carvedilol contributes to a significant increase in exercise tolerance due to a pronounced tendency to VO₂ increase and significant growth of the MOD and MET values compared with standard therapy.

5. References

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