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EFFICACY OF CAVERGAL IN PATIENTS WITH CORONARY HEART DISEASE AND METABOLIC SYNDROME

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ABSTRACT

Were examined 50 patients aged 45 - 53 years, suffering from stable exertionangina of the II functional class and metabolic syndrome (MS). Patients were randomized into two groups of 25 people. In the main group, cavergal was added to the basic therapy at a dose of 0.9 g / day. The duration of the study was 12 weeks. It was shown that cavergal as part of the complex therapy of coronary heart disease (CHD) in patients with MS contributes to reducing the number of strokes and improves the quality of life of patients. Inclusion of a cavergal in the combined therapy of CHD on the background of MS has a positive effect on lipid and carbohydrate metabolism, significantly reduces the severity of insulin resistance.

KEY WORDS: metabolic syndrome, coronary heart disease, cavergal, insulin resistance, carbohydrate and lipid metabolism.

INTRODUCTION

Stable exertional angina (SEA) is the most common form of coronary heart disease (CHD), which is often combined with metabolic syndrome (MS). This syndrome is one of the main causes of the development of CHD and a factor complicating its course, therefore, patients with MS are at high risk.[1] Recent studies show that “cytoprotection” is one of the important areas in the treatment of patients with cardiovascular diseases (CVD) and MS, which can be considered not only as optimization of metabolism at the level of cardiomyocytes in myocardial ischemia, but also as an element positively affecting the indices of carbohydrate and lipid metabolism under conditions of insulin resistance (IR).[2,3] So far, there is no clearly formulated and generally accepted classification of myocardial cytoprotectors (MC) that would be effective when included in complex therapy of patients with CVD associated with MS, IR, and hyperinsulinemia. In this regard, the search and study of effective MCs and their rational combinations with the basic means of CVD in patients with MS are still ongoing.[4,5,6]

In recent years, preference has been given in the world to “cytoprotectors” of natural origin, due to their better tolerability, effectiveness, and the absence of side effects. Among these drugs is the drug of local production Cavergal (capsules of 0.3 g), which has a fairly convincing evidence base in the number of antihypoxants and antioxidants, both in experimental and in clinical therapy.[7,8,9,10,11,12] The composition of this preparation, obtained by processing the bark of young oak branches, contains the sum of proanthocyanidins - regulatory polymeric flavonoids with varying degrees of polymerization and a molecular weight of 1500: 10,000 CU (average molecular weight 8278 CU).

As an antihypoxantcavergal, increasing the electron transport along the respiratory chain and the rate of phosphorylation, promotes the formation of energy in the mitochondria of myocytes. As an antioxidant cavergal reduces the concentration of lipoperoxides in the blood. The latter accelerate the degradation of NO and aggravate endothelial dysfunction, which contributes to the reduction of coronary blood flow. Thus, therapy with cavergal indirectly leads to an improvement in coronary blood flow. The lipid-lowering effect of cavergal is manifested by a decrease in the level of total cholesterol (total cholesterol) and an increase in the level of high-density lipoproteins (HDL).[12] Due to its pharmacological properties, cavergal has an impact on the main pathogenesis of various diseases associated with hypoxic conditions and free radical oxidation processes. This explains the breadth of its therapeutic action. However, in the available literature, we have not found data on the possibility of using cavergal in patients with CHD and MS from the point of view of the impact on both components of MS and CHD.

The purpose of our study was to assess the effectiveness of the cavergal in the combination therapy of CHD in combination with MS. Material and methods: The study was prospective, comparative. Were examined 50 patients.

50 patients aged 45–53 years with stable exertion angina pectoris of I-II functional class (FC). All patients included in the study had clinical and laboratory manifestations of MS.[13] All patients received basic therapy of CHD.[14] After randomization into two groups, patients of the 1st main group (25 people), in addition to the basic therapy, received Cavergal 0.9 g peros/ day. The duration of the study was 12 weeks. The main and control (2nd) groups of patients were comparable in age, sex, severity of the disease, the nature of the basic therapy. The average dosages of the basic therapy drugs in the 1st and 2nd group did not differ significantly. The initial characteristics of patient groups are presented in table 1.

Table 1: Clinical and demographic characteristics of patients included in the study.

Indicator	All patients	Main group – basic therapy + Cavergal (n=25)	Control group – basic therapy (n=25)
Number of patients	50	25	25
Average age, years	36,7 ± 5,01	39,1 ± 4,7	38,4 ± 5
Waist	113,7±3,6	114,84 ±3,02	112,5±4,2
Body mass index (BMI), kg/ m2	34,3±1,1	34,6±1,03	34,1±1,2
Stable exertion angina I FC	27 (%)	11	12
Stable exertion angina II FC	23 (%)	14	13

Quality of life (QOL) of patients was assessed using the Seattle Questionnaire (QOL of patients with angina). In a laboratory study, were assessed blood parameters: cholesterol, TG, HDL cholesterol; fasting glucose (FG) and 2 hours after taking 75 gr. of Glu, immunoreactive insulin on an empty stomach (IRI) with the calculation of the index HOMA-IR; LDL cholesterol level according to Friedwald formula. Statistical processing of the data was performed using Microsoft Excel; results are presented as M + m. In order to test the hypothesis of the difference of averages, the Student's t-criteria was used between the groups. The deviations at p <0,05 were considered statistically significant.

RESULTS

The addition of cavergal to the baseline treatment of patients with coronary heart disease and MS was accompanied by an improvement in the clinical condition: a significant decrease in angina attacks requiring nitrates (Ni) (p <0.1) (Table 2).According to the Seattle questionnaire (QOL of patients with angina pectoris) cavergal combination with basic therapy of CHD was associated with a significant increase in the average score - 27.3% in the main group, totaling 64.8 points, and 12.4% in the control group, amounting to 54.4 points. The difference between groups at the trend level (p <0.1).

Table 2: The effect of combined with cavergal basic therapy of coronary heart disease on the clinical condition in patients with metabolic syndrome (M ± m).

Indicator	Main group – basic therapy + cavergal (n=25)		Control group – basic therapy (n=25)	
	initial	after 12 weeks	initial	after 12 weeks
Number of angina attacks per week.	3.5	3	3.4	3.2
No. tab. of Ni per week	3.5	2.9	3.32	3.15

Table 3: The dynamics of biochemical parameters of blood in the background of cavergal inclusion in the basic CHD therapy in patients with metabolic syndrome.

Indicator	Main group – basic therapy+ cavergal (n=25)		Control group–basic therapy (n=25)	
	Initial	After 12 weeks	Initial	After 12 weeks
Blood glucose, mmol/l	5,58±0,12	5,2±0,1*	5,54±0,1	5,51 ±0,14
Blood glucose after 2 hours of 75 gr. Glu taking, mmol/l	8,3±0,2	7,2±0,2#	8,1±0,18	8,3±0,2
Cholesterol, mmol/l	5,5±0,1	5,2±0,1	5.3±0.1	4.98±0.13
Triglycerides, mmol / l	1,8±0,02	1,65±0,03	1,71±0,02	1,62±0,02
Cholesterol LDL, mmol / l	3,7±0,1	3,3±0,1	3,82±0,11	3,87±0,1
CholesterolHDL, mmol / l	1,0±0,03	1,2±0,03*	0,94±0,03	0,9±0,02
Atherogenic index	4,6±0,2	3,5±0,11*	4,63±0,14	4,53±0,2

*Note: * - significance of differences in comparison with baseline indicators (p <0.05); # - significance of differences between groups (p <0.05).*

After 12 weeks of therapy with the use of cavergal and compliance with the recommendations on non-drug measures for the prevention of atherosclerosis, positive metabolic effects were noted (Table 2). In patients with CHD and MS in the main group, the basal insulin level decreased by 14.3%. In the control group, there was a decrease in the basal level of insulin by 1.9%. Differences between groups were at the level of statistical trends ($p < 0.1$). In the main group, there was a significant decrease in the severity of insulin resistance (IR). The Homa index in the group of patients who additionally took cavergal significantly decreased by 19.5%, in the control group this figure decreased only by 1.7% (the difference between the groups is statistically significant).

By the 12th week of the study, the fasting blood glucose level in patients receiving cavergal decreased by 6.4%, compared to that in the control group (by 0.9%), the glucose level 2 hours after exercise decreased by 13.3 % Perhaps the normalization of impaired glucose tolerance with a cavergal is due to a decrease in IR and an increase in the hypoglycemic effect. The positive influence of cavergal in the composition of the combined treatment of coronary heart disease in patients with MS on the lipid profile was primarily reflected in an increase in the level of HDL cholesterol by 16%. A decrease in the level of blood triglycerides (TG) by 9% and LDL - by 10% and a decrease in the atherogenic index by 23.3% in patients of the main group. In the control group, the TG level decreased only by 5.8%, the level of HDL did not tend to increase.

DISCUSSION

Improving the quality of life of patients associated with the antianginal effect of the cavergal may be due to the antioxidant effect of the drug, leveling the pathological effect of hypercatecholaminemia caused by the activation of lipid peroxidation.[8] A decrease in insulin resistance by taking a cavergal is possibly related to its antioxidant property — to reduce the concentration of lipoperoxides in the blood[12], activating the processes of lipolysis in fat depots, i.e., restoring the sensitivity of adipocytes to insulin. In this way, the vicious circle is broken, caused, on the one hand, by the phenomenon of insulin resistance, which promotes the increased flow of free fatty acids into the bloodstream, which blocks oxygenation and glucose transport, which worsen the effects of insulin on liver and muscle cells. On the other hand, an increased content of free fatty acids in the blood contributes to an increase in the production of very low density lipoproteins (VLDL) in the liver, followed by an increase in plasma concentration of triglycerides and a decrease in the content of high atherogenic lipoproteins (HDL), aggravating the severity of IR. It should be noted that the presented results are consistent with the previously obtained data on the positive effect of cavergal on the lipid profile of blood.[12] Thus, the use of cavergal as part of the combined treatment of coronary heart disease in patients with MS has a positive effect on the lipid profile by reducing the level of atherogenic LDL cholesterol fractions, TG and increasing HDL. The noted effect of the cavergal seems to be mediated by the activation of lipolysis processes in the fat depots, as a result of which a decrease in the blood TG level is noted.

CONCLUSION

1. In patients with coronary heart disease and MS, the addition to the basic therapy of cavergal improves the clinical condition and quality of life of patients, which is associated with a significant decrease in angina attacks requiring nitrates. 2. Cavergal as part of complex coronary heart disease has a beneficial effect on lipid and carbohydrate metabolism, reduces the severity of insulin resistance, which is important for CHD patients with metabolic syndrome.

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