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АНТИАТЕРОСКЛЕРОТИЧЕСКАЯ ЭФФЕКТИВНОСТЬ СТАНДАРТНОЙ ТЕРАПИИ ИБС, ЕЕ КОМБИНАЦИИ С ИЗОСОРБИДА ДИНИТРАТОМ И НИКОРАНДИЛОМ У ПАЦИЕНТОВ СО СТЕНОКАРДИЕЙ И ОЖИРЕНИЕМ

Резюме: Антикоагулянты — это лекарственные средства, снижающие свертываемость крови, угнетая образование фибрина. При различных формах ИБС антикоагулянты используются как для профилактики развития коронарных тромбозов и связанных с ними инфаркта и стенокардии, так и для самого лизирования тромба в острейшей стадии - ОИМ.

Ключевые слова: ишемическая болезни сердца, стенокардия, ожирения, атеросклероз, лечения.

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ANTIATEROSCLEROTIC EFFICIENCY OF IHD STANDARD THERAPY, ITS COMBINATIONS WITH ISOSORBIDE DINITRATE AND NICORANDIL IN PATIENTS WITH STENCARDIA AND OBESITY

Resume: Anticoagulants are drugs that reduce blood coagulation, inhibiting the formation of fibrin. In various forms of coronary heart disease, anticoagulants are used both to prevent the development of coronary thrombosis

and related heart attack and angina pectoris, as well as for the lysis of a blood clot in the acute stage of ¬OIM.

Key words: coronary heart disease, angina pectoris, obesity, atherosclerosis, treatment.

Relevance. Ischemic heart disease, according to the definition of WHO experts (1995), is an acute or chronic myocardial dysfunction due to a relative or absolute decrease in the supply of arterial blood to the myocardium, most often associated with a pathological process in the coronary artery system [1,3,4].

Despite the successes achieved in recent decades in the prevention and treatment of coronary heart disease (CHD), it still represents one of the urgent problems of modern cardiology both in the world and in many economically developed countries of the world, due to the high prevalence, disability and mortality, mainly among young people of working age [2,5]. This is due to the importance of adequate pharmacotherapy of this disease.

The purpose of the study. The study of anti-ischemic and anti-atherosclerotic effects of standard CHD therapy with the inclusion of the drug nicorandil of domestic production (Cordinik, PIK-PHARMA company) or isosorbide dinitrate for long-term use in patients with stable angina and obesity.

Materials and methods of research. 107 patients were selected for the study, after screening and initial collection of anamnesis and complaints, 93 patients with stress angina of functional class II-III (FC) were randomized into 3 groups. Informed consent to this study was obtained in all patients. The average age of the patients was 69.9±8.1 years, of which 38 were men and 55 were women. Group 1 included 31 people, group 2 – 30 people, group 3 - 32 people.

The results of the study. The effectiveness of standard therapy in combination with prolonged nitrate was comparable and did not differ statistically from the effectiveness of taking nicorandil in combination with standard therapy. However, with regular intake of isosorbide dinitrate for 6 months. 4 patients (13.3% of group 2) stopped taking the drug due to the

development of headache, and in terms of antianginal efficacy, the indicators of group 2 were almost equal to those of group 1, from which it can be concluded that a possible developed loss of the effectiveness of isosorbide dinitrate in some patients with stable angina pectoris. According to Holter ECG monitoring at the end of the follow-up period, patients of all 3 groups showed a comparable significant decrease in the average daily heart rate, the number of episodes of myocardial ischemia, the duration of daily myocardial ischemia (PSIM) and the depth of ischemic displacement of the ST segment (GIS ST). It is necessary to note a more pronounced decrease in the duration of daily ischemia and GIS ST in patients taking nicorandil, which, according to single-factor analysis of variance, achieved a significant difference compared with that against the background of standard therapy in terms of PSIM (-68.17% vs. -50.81%, respectively, p=0.026) and against the background of taking prolonged nitrates in terms of SMGIS (-59.26% vs. -35%, respectively; p=0.0259).

The same dynamics remained during the load tests. VEM indicators: the maximum load capacity (Max power) and the total load time before the occurrence of clinical and ECG signs of myocardial ischemia significantly increased by the end of the 24th week. therapy in all 3 groups. The increase in physical performance was more pronounced in Group 3 patients compared to group 1 (ΔMax power 40.25% vs. 24.86%; p=0.05 and ΔTotal load time 74.57% vs. 48.14%; p=0.02, respectively), no significant differences were achieved between groups 2 and 3.

When comparing the antianginal efficacy of drug combinations used in the study in patients in the subgroups with and without obesity, a decrease in effects with an increase in BMI was revealed. These results were confirmed by a reliable correlation between BMI and changes in clinical parameters in all 3 groups (Table 2). The data obtained were comparable with the presence in obese patients of higher levels of lipids and glucose, markers of systemic inflammation

and, as a consequence, greater rigidity of the vascular wall, the prevalence of atherosclerosis.

It should also be noted that the doses of drugs in this study were moderate therapeutic, did not take into account the severity of overweight.

After 24 weeks of observation according to the ultrasound of the carotid arteries (Table. 3) in patients of 3 groups, there was a significant decrease in the TIM of the right and left common carotid arteries (POSA and LOSA): TIM POSA and LOSA in group 1 decreased by 6.9 and 7.53% ($p=0.011$ and $p=0.028$, respectively), in group 2 – by 6.79 and 6.63% ($p=0.03$ and $p=0.01$, respectively), in group 3 – by 10.4 and 11.84% ($p<0.001$). The diameter of the brachial artery during the test of reactive hyperemia with temporary occlusion, reflecting the processes of ED, significantly increased in all groups: PPD PA in group 1 – by 46.18% ($p= 0.002$), in group 2 – by 44.49% ($p= 0.02$), in group 3 – by 62.37% ($p= 0.0014$). There was also a decrease in the size of plaques that stenosed the lumen of the brachiocephalic arteries; during the study, the PSP BCA index in groups 1 and 2 decreased by 4.52 and 9.41% ($p= 0.15$ and $p=0.23$, respectively), and in group 3 – by 16.5%, reaching statistical significance ($p=0.028$).

It should be noted that despite the presence of a proven negative effect of nitrates on the processes in the vascular endothelium associated with pro-oxidative effects, statin, which was part of standard therapy together with isosorbide dinitrate, leveled these processes due to its pleiotropic effect and significantly reduced the parameters of TIM POSA and LOSA, as well as increased the PPD of PA in the group 2. In group 3, with the inclusion of nicorandil, there was a greater weakening of the oxidative effect on the endothelium, which was expressed in a more significant decrease in TIM POSA and LOSA, an increase in PPD PA. The proven effect of statins on the lipid spectrum, stabilization of atherosclerotic plaques mediated through inflammatory markers, and possible suppression of angiogenesis in plaques led to a decrease in the percentage of vascular lumen stenosis in all groups. This

effect in group 3 exceeded those in groups 1 and 2 by several times. An additional decrease in the size of plaques in the brachiocephalic arteries was probably caused by the activity of nicorandil against anti-inflammatory and antioxidant mechanisms.

In all 3 groups, there was a decrease in all indicators of the lipid spectrum (total cholesterol, LDL, TG) without significant differences between the groups. This result was provided to a large extent by the hypolipidemic effect of rosuvastatin, which also has a number of pleiotropic effects, such as a decrease in the severity of free radical oxidation, ED, inflammatory processes of the vascular wall. These "non-lipid" properties played a role in the process of reducing the level of Hf-CRP and fibrinogen, reflecting the processes of chronic systemic inflammation accompanying coronary heart disease. However, in the nicorandil group, the decrease in fibrinogen levels exceeded by more than 2 times the indicators of the standard therapy group (-16.46% vs. -8.05%, respectively, p=0.042), and the concentration of Hf-CRP significantly decreased in the 3rd group as compared with the 1st (-37.08% vs. -22.16%, respectively, p=0.003), and with the 2nd (-37.08% vs. -23.38%, respectively, p = 0.04), which may be a confirmation of its positive effect on the processes of reducing oxidative damage and systemic inflammation.

Thus, the data obtained by us indicate a high antianginal and anti-ischemic efficacy of standard therapy of coronary artery disease, including bisoprolol, valsartan, aspirin and statins, in patients with angina pectoris, which increases with the addition of isosorbide dinitrate and the domestic drug nicorandil. These effects were more pronounced in the subgroups of normal and overweight patients than in the subgroups of obese patients, which was confirmed by a significant correlation between BMI and clinical indicators.

The frequency of anginal attacks, the duration of daily myocardial ischemia according to XM ECG data, the maximum power and total load time during VEM significantly improved in group 3 with the addition of nicorandil

compared with those in group 1, who received only bisoprolol, aspirin and statins (standard therapy), and were comparable with those of group 2 (with the addition of isosorbide dinitrate). Also, taking combinations of these drugs in all 3 groups for 6 months. led to a decrease in ED, in groups 1 and 2 there was a tendency to reduce the size of atherosclerotic plaques, which reached statistical significance in group 3. It can be noted that nicorandil, combining the properties of an agonist of ATP-dependent potassium channels and a nitrate-like vasodilating effect, activates the processes of ischemic preconditioning, as part of standard therapy is able to reduce oxidative damage and systemic inflammation more actively than a combination of standard therapy with prolonged nitrates, which ultimately leads to a slowdown in the progression of ED and atherosclerosis, providing anti-ischemic effect and long-term endothelioprotection. The high prevalence of obesity in the population and its role in the pathogenesis of coronary heart disease require a more detailed study of this problem, an integrated approach to the treatment of patients suffering from angina in combination with overweight and obesity.

Conclusion. Thus, the data obtained by us indicate a high antianginal and anti-ischemic efficacy of standard therapy of coronary artery disease, including bisoprolol, valsartan, aspirin and statins, in patients with angina pectoris, which increases with the addition of isosorbide dinitrate and the domestic drug nicorandil.

The high prevalence of obesity in the population and its role in the pathogenesis of coronary heart disease require a more detailed study of this problem, an integrated approach to the treatment of patients suffering from angina in combination with overweight and obesity.

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