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PHARMACODYNAMIC FEATURES OF DRUG TREATMENT OF PATIENTS WITH ISCHEMIC DISEASE

Summary. The development of recommendations based on the results of clinical trials, with a unified approach to treatment, modern drugs for the treatment of coronary artery disease, undoubtedly led to a significant improvement in the quality of life of patients and prognosis, however, the disease is still a poor predictor of drug therapy for coronary artery disease in order to achieve improvement quality of life and prognosis, slowing down the progression of the disease became possible thanks to the creation of a new drug nebivalol. The effective effect of nebivalol on the incidence of outcomes (death or hospitalization for coronary artery disease) was manifested in patients of different sex and age in the early stages of treatment and was maintained throughout the entire follow- up period.

Key words: ischemic heart disease, lipid spectrum, sympathoadrenal system, nebivalol.

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ФАРМАКОДИНАМИЧЕСКИЕ ОСОБЕННОСТИ ЛЕКАРСТВЕННОГО ЛЕЧЕНИЯ БОЛЬНЫХ ИШЕМИЧЕСКОЙ БОЛЕЗНЬЮ

Резюме. Разработка рекомендаций, основанных на результатах клинических исследований, с унифицированным подходом к лечению, современные лекарственные средства для лечения ИБС, несомненно, привели к существенному улучшению качества жизни пациентов и прогнозу, вместе с тем заболевание по прежнему является прогностически неблагоприятным медикаментозной терапии ИБС с целью достижения улучшения качества жизни и прогноза, замедления прогрессирования заболевания стали возможными благодаря созданию нового лекарственного препарата небивалола. Эффективное влияние небивалола на частоту развития исходов (смерть или госпитализация по поводу ИБС) проявлялось у различных по полу и возрасту больных в ранние сроки лечения и поддерживалось в течение всего периода наблюдения.

Ключевые слова: ишемическая болезнь сердца, липидный спектр, симпатоадреналовой система, небивалол.

According to WHO estimates, the annual mortality from all CVDs is 17 million people, the main cause of which is coronary heart disease (CHD). In 2008, the total mortality from coronary artery disease in the world amounted to 7.25 million people, which in the overall structure of mortality was 12.8%. In Russia, coronary artery disease is one of the most common reasons for the population to seek outpatient and inpatient care for all CVDs and is 28%. Among the risk factors for coronary artery disease, a significant role is given to the heart rate (HR). An increase in heart rate leads to the development of myocardial ischemia and is the main indicator of the risk of developing CVD, at least in men. In the general population, the risk of death from CVD increases significantly with a heart rate > 84 bpm and decreases with a heart rate < 60 bpm.

For patients with coronary artery disease, first-line anti-ischemic drugs are B-blockers. By reducing heart rate, prolonging diastole, and improving myocardial perfusion during longer diastole, B-blockers help reduce myocardial oxygen consumption and lead to a decrease in myocardial ischemia. The patients included in our study, at the time of inclusion in the study, most often received bisoprolol (56.09% ± 0.49) and metoprolol tartrate as antianginal therapy.

The rationale for the appointment of beta-blockers was evidence of chronic hyperactivation of the sympathoadrenal system in patients with progressive and severe (FC II-IV) coronary artery disease, as well as the successful use of drugs from the group of beta-blockers, which reduce the risk of sudden death, death from progression of chronic heart failure and reduce the number hospitalizations. The study of the action of beta-blockers showed that a significant effect on the symptoms and prognosis in chronic heart failure has a decrease in heart rate (HR) caused by them as a risk factor for death and complications of cardiovascular diseases [5].

At the same time, in real medical practice, the reduction. Heart rate often does not reach the target values. New approaches to the drug therapy of coronary artery disease in order to achieve an improvement in the quality of life and prognosis, slowing down the progression of the disease have become possible drug beta-blockers.

35 patients were selected for inclusion in the study, including 17 in the nebivalol group, the rest in the placebo group. The average duration of treatment was 3 months.

Nebivalol or placebo was added to standard therapy for chronic heart failure, which included ACE inhibitors or angiotensin II receptor blockers, beta-blockers, diuretics, antagonists aldosterone, digoxin and other drugs (isosorbiddinitrate, etc.) in the same ratio in both groups of patients. Background therapy for CAD reflected the true picture of clinical practice.

After randomization, 89% of patients received beta-blockers and the same number received placebo groups. In each of the study groups in the treatment of

coronary artery disease, the target dose of beta-blockers reached 26% of patients, while at least 50% of the target dose of b-blockers received 56% of patients.

A month after the start of treatment, the heart rate was: in the nebivalol group at an average dose of the drug 6.4 ± 1.6 mg 2 times a day - 64 beats / min, in the placebo group - up to 75 beats / min. After 32 months treatment, the average heart rate was 67 and 75 beats/min, respectively. Primary endpoint events (cardiovascular death or hospitalization for exacerbation of coronary artery disease) were observed in the nebivalol group (24%) and (29%) in the placebo group (hazard ratio 0.82; 95% CI 0.75– 0.90, $p < 0.0001$). Events were mainly due to hospitalization of patients due to worsening heart failure: 16% in the nebivalol group, 21% in the placebo group ($p < 0.0001$); and deaths from heart failure: 3% vs. 5%, respectively ($p = 0.014$).

Thus, in the nebivalol group, there was a lower incidence of death from heart failure (–26%; $p = 0.014$) and hospitalizations due to worsening heart failure (–26%; $p < 0.0001$). Calculations showed that to prevent one death from complications of cardiovascular diseases or one hospitalization for worsening coronary artery disease, 26 patients should take nebivalol for one year.

It is important to note that the positive effect of nebivalol was observed in patients with chronic heart failure of ischemic and non-ischemic origin. The effect in the nebivalol group on cardiovascular mortality compared with the placebo group did not differ significantly, however, mortality from coronary artery disease decreased statistically significantly (hazard ratio 0.74, 95% CI 0.58 to 0.94; $p = 0.014$) .

It should be noted that in the nebivalol group, a decrease in the risk of death and hospitalization due to heart failure was observed in the early stages - after 3 months. from the start of treatment. Despite the complexity and combination of drug treatment of moderate and severe chronic heart failure, patients noted good tolerability of the drug. Changes (decrease) in CHD FC were observed after 6 weeks from the start of treatment with nebivalolam, while patients with severe

heart failure noted a significant improvement: 1 out of 7% of the subgroup with FC IV remained; FC III - 53% of 93%; FC II - 44% previously referred to FC III. Among all patients in the nebivalol group and the placebo group, 28% and 24%, respectively, showed improvement during treatment, 68% and 70%, respectively, and worsened, 5% and 6%, respectively.

Side effects and adverse effects in the nebivalol group developed less frequently compared to the placebo group ($p = 0.02$).

The use of nebivalol resulted in an 18% ($p < 0.0001$) reduction in the risk of mortality from complications of cardiovascular disease and hospitalizations for coronary artery disease. The effective effect of nebivalol on the incidence of outcomes (death or hospitalization for coronary artery disease) was manifested in patients of different gender and age in the early (after 3 months) terms of treatment and was maintained throughout the entire observation period.

Thus, improvement of the clinical condition in patients with chronic coronary artery disease can be achieved with the use of nebivalol. Based on the data obtained in the SHIFT study, nebivalol is included in the National Guidelines for the Diagnosis and Treatment of Chronic IHD. In the treatment of nebivalolam, the quality of life of patients with coronary heart disease (angina pectoris) increases statistically significantly.

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