THE IMPORTANCE OF CARVELAND IN THE TREATMENT OF MAJOR CARDIAC DISEASES

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Abstract. The article is devoted to β-blockers, classification, features of mechanisms of action, indications. The place of carvedilol in the treatment of cardiac patients is highlighted.

Keywords: β-blockers, method, mechanisms of action, carvedilol, cardiovascular diseases.

INTRODUCTION

Beta-blockers (BB) are one of the classes of drugs that have made the most significant contribution to the fight to reduce morbidity and reduce the risk of death from various cardiac pathologies: arterial hypertension (AH), myocardial infarction (MI), chronic heart failure (CHF).

MATERIALS AND METHODS

BBs are highly sensitive to the corresponding receptors, block adrenergic receptors from the effects of endogenous catecholamines and do not cause conformational changes in protein receptors (their sensitivity). The main therapeutic effects of BB are determined by the ability to block the effect of mediators on the β1-adrenergic receptors of the myocardium and the weakening of the effect of catecholamines on membrane adenylate cyclase of cardiomyocytes with a decrease in the formation of cAMP.

The most famous classification of BD is based on the fact that β-adrenergic receptors are heterogeneous. β 1 receptors are mainly present in the heart muscle, and β 2 receptors are present in the lungs and peripheral vessels. When blocking

β1-adrenergic receptors of the myocardium, the excitability of the pacemaker is inhibited, heart rate decreases, the speed of impulse transmission through the conduction system of the heart slows down, and contractility decreases. Blockade of extracardiac β2-adrenergic receptors is associated with undesirable effects of treatment: spasm of peripheral vessels, increased tone of bronchial muscles, deterioration of blood lipid composition, hypoglycemia, increased insulin resistance.

RESULTS AND DISCUSSION

BBs are similar in structure, but differ in cardioselectivity, the presence or absence of internal sympathomimetic activity, lipophilicity, and membrane-stabilizing effect. Selectivity is determined by the affinity for β 1- or β 2-adrenergic receptors. Non-selective BBs act equally on both types of β-adrenergic receptors. Selective blockade of β-adrenergic receptors, causing a decrease in cardiac output, is not accompanied by a significant increase in peripheral vascular resistance and deterioration of bronchial patency. Cardioselectivity provides a slightly more pronounced effect of BB on diastolic blood pressure (BP). At the same time, the negative chronotropic effect at rest and during physical activity, as well as the decrease in cardiac output with selective and non-selective blockade of β-adrenergic receptors are expressed to approximately the same extent. The subgroup of non-selective BBs includes propranolol, nadolol, sotalol, timolol [1].

Some BBs are characterized by internal (intrinsic) sympathomimetic activity (ISA). BBs with ICA cause a decrease in heart rate to a lesser extent, mainly at rest, but partly also during exercise. This property was initially regarded as an advantage of this subgroup of BAB. However, it was subsequently shown that the ability to improve the prognosis of patients who have suffered an MI is determined primarily by the negative chronotropic effect of BB. Drugs with BCA (oxprenolol, pindolol, acebutolol) do not reduce the risk of cardiovascular death, and therefore their scope of clinical use is limited.

Some BBs (carvedilol, nebivalol) have a vasodilating effect, the mechanisms of which differ. Carvedilol causes a decrease in vascular tone due to blockade of α1-adrenergic receptors, nebivolol - due to increased synthesis of nitric oxide in the endothelium. Carvedilol also has an additional direct vasodilating effect.

BBs differ in their ability to dissolve in fats. Fat-soluble drugs penetrate biological membranes well, which, in particular, determines their cardioprotective effect. Lipophilicity is a property that determines the ability of BB to penetrate the blood-brain barrier and bind to central β1-adrenergic receptors, therefore, influence the tone of the vagus nerve and form an antifibrillatory effect. Some BBs (carvedilol, pindolol, betaxolol, propranolol, acebutolol) at concentrations exceeding therapeutic ones have a quinidine-like or local anesthetic effect. Thanks to this property, they stabilize the action potential of cardiomyocytes. Membrane-stabilizing activity at therapeutic doses of drugs has no practical clinical significance.

It is customary to distinguish three generations of BBs: non-selective (I generation), β1-selective (II generation) and with vasodilating properties (III generation). Each subsequent generation differs from the previous one in the appearance of new properties useful for use in clinical practice.

An important characteristic of BB is the half-life, which is determined by the properties of the drug itself, as well as the functional state of the kidneys and liver. In most cases of BB use (especially in patients with hypertension and CHF), it is necessary to strive for a stable blockade of β-adrenergic receptors, since fluctuations in neurohumoral stimulation have a negative effect on the progression of the disease and contribute to damage to target organs even more strongly than constantly increased neurohumoral stimulation. In this regard, long-acting BBs, which are characterized by a uniform concentration of the drug in the blood plasma throughout the day, have an advantage over short-acting drugs.

The ability to block the influence of mediators on β1-adrenergic receptors of the myocardium and weakening the influence of catalytic

cholamines on membrane adenylate cyclase of cardiomyocytes with a decrease in the formation of cAMP determine the main therapeutic effects of BB, which allows them to be widely used for the treatment of both pathology of the cardiovascular system and a number of other diseases. Among cardiac diseases, indications for prescribing BB are hypertension, stable and unstable angina, “silent” myocardial ischemia, supraventricular and ventricular arrhythmias, myocardial infarction, starting from its acute phase, dissecting aortic aneurysm, hypertrophic cardiomyopathy, digitalis intoxication, mitral prolapse valve, long QT syndrome, tetralogy of Fallot, mitral stenosis, CHF, somatoform dysfunction. Good results have been obtained with the use of BB for migraine, delirium tremens, thyrotoxicosis, hyperparathyroidism, essential tremor, anxiety, glaucoma, and portal hypertension.

The most controversial issue was the use of BB for CHF. Currently, due to changes in views on the pathogenesis of CHF, the possibilities of using BB for this pathology have been reconsidered. There is evidence that the use of beta-blockers may reverse the development of left ventricular dilatation or, at least, slow down its development. The end to this issue was put in 1999, when a number of large multicenter studies were completed (CIBIS II, MERIT HF, BEST, COPERNICUS). The last of these studies was conducted to compare the effect of carvedilol and placebo on overall mortality in patients with severe CHF. The risk of death in patients even with very severe CHF decreased by 35% when treated with carvedilol, and was independent of age, gender, race, and the genesis of heart failure. It is also significant that the effect of carvedilol on mortality was noted in the category of patients with very low ejection fraction.

The metabolic effect of carvedilol is less pronounced than that of other non-selective BBs. It does not affect plasma glucose levels in patients with non-insulin-dependent diabetes mellitus. Unique to BB is the effect of carvedilol on the blood lipid spectrum. Under the influence of carvedilol, the level of total cholesterol,

low-density lipoproteins and triglycerides decreases, and the content of high-density lipoproteins in the blood plasma increases.

CONCLUSION

Thus, Carveland is a modern BB, the use of which is advisable for most cardiac diseases, including patients with comorbidity in metabolic syndrome, diabetes mellitus, and chronic kidney disease.

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