

Features of Use of Combined Glow-Lowing Therapy in Patients with Type 2 Diabetes and IHD

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Abstract: Relevance. Diabetes mellitus (DM) is a serious medical and social problem in all countries and at all ages. The combination of type 2 diabetes (T2DM) and coronary heart disease (CHD), according to some data, is 70–80% in patients with diabetes mellitus. Poor glycemic control is the most significant risk factor for the development of cardiovascular complications, which has been confirmed in various basic studies. One of the socially significant diseases is type 2 diabetes mellitus (T2DM). Large clinical studies have shown that diabetes mellitus increases the risk of developing CVD: coronary heart disease (including myocardial infarction), cerebral ischemic stroke, atherosclerosis of the great vessels, thrombosis of arteries and veins, chronic heart failure and worsens the prognosis for these pathologies. Myocardial contractility is a basic characteristic of the pumping function of the heart, and its determination in pathology is of considerable interest. The literature has repeatedly described a decrease in myocardial contractile activity against the background of T2DM, however, recent in vivo studies on ischemic myocardium of an experimental model cast doubt on the irrefutability of this statement. Recent years have been characterized by a steady increase in the number of patients with type 2 diabetes mellitus (DM). According to experts from the International Diabetes Association (IDF), by 2035 the number of people with diabetes in the world will reach 592 million people, which is almost every tenth inhabitant of the planet [29]. In the Russian Federation, according to the State Register as of January 1, 2015, the number of patients with diabetes amounted to 4.094 million people [4]. Type 2 diabetes is characterized by a high risk of developing coronary heart disease (CHD), myocardial infarction, stroke, heart failure, and it is also known that diabetes and cardiovascular diseases (CVD) mutually aggravate each other. In type 2 diabetes, the risk of developing coronary artery disease increases 2–5 times [45]. Numerous studies show that more than half of patients are unaware of the presence of type 2 diabetes, and diagnosis often occurs against the background of existing cardiovascular complications [9, 49]. Almost 50% of patients with an established diagnosis of coronary artery disease are diagnosed with newly diagnosed type 2 diabetes, impaired glucose tolerance, or fasting hyperglycemia [9]. In this regard, the American Heart Association (AHA) has defined the presence of type 2 diabetes patients as equivalent to a high risk of vascular complications, comparable to that of overt CVD [22]. Against the background of the prevalence of type 2 diabetes, there is a high mortality rate and early disability in patients of working age. Thus, more than 50% of diabetes-related mortality is mediated by cardiovascular pathology [4]. Mortality among patients with type 2 diabetes from CVD is 3–4 times higher than similar rates in the general population. In developed countries, where significant progress has been made in the fight against coronary heart disease, it was noted that patients with diabetes are the only group in which mortality from this disease decreased slightly in men and increased in women [17]. Patients with type 2 diabetes are characterized by a high incidence of “painless” myocardial infarction and sudden cardiovascular death. The presence of a blurred clinical picture leads to late diagnosis of the disease, often already at the stage of severe complications in the form of sudden death or blood supply failure [11]. The

high mortality rate of patients with diabetes is associated with systemic atherosclerotic lesions of the vascular bed. Mixed or isolated dyslipidemia (increased levels of triglycerides and/or serum cholesterol) is usually determined in every second elderly patient with type 2 diabetes [13]. In diabetes in the pathogenesis of atherosclerosis, well-studied risk factors are distinguished, including non-correctable (age, gender, heredity) and correctable (arterial hypertension, smoking, unbalanced diet, obesity and physical inactivity), as well as partially correctable (dyslipidemia, insulin resistance, psycho-emotional stress). Atherosclerotic damage to vessel walls in type 2 diabetes is characterized by earlier development and rapid progression of the process [11, 33]. In its turn, hyperglycemia in diabetes promotes the development of atherogenesis in the vascular wall with a high prevalence of atherosclerotic lesions with endothelial damage, growth of smooth muscle cells, fibrinolysis, thrombus formation, proliferation and increased oxidative stress with the triggering role of cytokines [3].

Key points: type 2 diabetes mellitus, stable coronary heart disease, continuous glycemic monitoring, heart rate variability.

Introduction. In modern diabetology, increasing attention is paid not only to point measurements of glycemia and fixation of points of hyper- and hypoglycemia, but also to daily excursions in blood glucose levels, which can become predictors of cardiovascular events. One of the promising areas in the pharmacotherapy of T2DM is the incretin mechanisms for regulating glucose homeostasis, which have a physiological, glucose-dependent hypoglycemic effect. In order to effectively and safely improve the level of glycemic control in patients with T2DM and coronary artery disease, it is necessary to carefully study the effects of various options for combined glucose-lowering therapy on carbohydrate metabolism.

Target– to evaluate the effectiveness and safety of glycemic control in patients with type 2 diabetes and coronary artery disease when using DPP-4 inhibitors in combination with metformin.

Material and methods. Patients with T2DM and stable coronary artery disease in a state of decompensation ($HbA1c > 7\%$) on monotherapy with metformin in a daily dose of no more than 2000 mg; at the first stage of the study, a clinical examination, laboratory and instrumental studies are carried out, including a clinical blood test, biochemical blood test, determination of oxidative markers stress, 24-hour blood glucose monitoring (CGMS), 24-hour ECG monitoring with calculation of heart rate variability. At the second stage of the study, correction of glucose-lowering therapy will be carried out in order to improve carbohydrate metabolism. To do this, after randomization into 2 groups, patients of the 1st group will receive sitagliptin in addition to metformin, and patients of the 2nd group will receive metformin in combination with glibenclamide. The duration of treatment will be 3 months, after which a control examination of patients will be carried out according to the previous plan.

Expected results. During the study, it is planned to assess changes in the level of glycemic variability in the study groups and obtain the maximum physiological fluctuations in glycemic variability. The data obtained will make it possible to determine the range of preferred oral hypoglycemic drugs (OHLDS) in patients with T2DM and IHD, as well as to clarify the criteria for assessing the prognosis of IHD in patients in this category.

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