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Modern Aspects of the Use of Antiagregatant and Hypolipodemic Therapy After Coronary Artery Stent Surgery

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Abstract: This article will discuss current issues and modern problems of coronary heart disease, antiplatelet therapy, its effects, hypolipidemic therapy, indications, contraindications, possible side effects, as well as successful tactics of patient management after percutaneous coronary intervention with subsequent use of drug eluting stents.

Keywords: Coronary artery disease; Antiplatelet therapy; Hypolipidemic therapy; Stenting.

Introduction: Cardiovascular diseases (CVDs) are one of the most important medical and social problems of our time and occupy almost two-thirds of the causes of mortality and almost half of the causes of disability in the population [1], resulting in significant socioeconomic losses [2], reduced life expectancy and lower quality of life [3]. Experts estimate that more than 23 million people worldwide will die from them annually in the next 15 years [1]. Understanding the causes of these diseases, as well as improving the capacity to prevent, diagnose and treat them, is one of the key priorities of modern cardiology. [6,7,8]. At the same time, coronary heart disease (CHD) - atherosclerosis of the heart vessels accounts for the lion's share of cardiovascular diseases [4,5]. Coronary heart disease (CHD) and its complications are the leading causes of mortality, despite significant progress in risk factor (RF) control and treatment, including widespread use of surgical and endovascular revascularization methods [6,7,8]. All forces of modern medicine and basic science are thrown to “extinguish this fire” in the form of heart and vascular diseases [9]. Leading RF: high blood pressure, tobacco smoking, alcohol consumption, high blood cholesterol (BC), excessive body weight, low consumption of fruits and vegetables, sedentary lifestyle determine almost 60% of all causes of CVD [10]. The strategic goals of treatment of CHD patients are to prevent premature death, prevent progression and achieve partial regression of coronary artery (CA) atherosclerosis [11], reduce the number of complications and exacerbations of the disease, frequency and duration of hospitalization. [12]. Secondary prevention of CHD includes medication and non-medication components [13]. For this purpose, drugs are used, the effectiveness of which is proved by the results of large international studies [20]. Timely diagnosis and prevention can dramatically reduce the risk of CHD and increase human life expectancy by 10-15 years [14]. In recent years, the features of development and course of coronary heart disease, in particular its acute forms, in different groups of patients depending on sex, age, comorbid and other characteristics have been actively studied [15,16,17].]. The success of IHD treatment is largely determined by the maintenance of adequate coronary blood flow, including by performing percutaneous coronary interventions (PCI), coronary artery stenting (CAS) [18]. Local changes in vessel intima (rupture of atherosclerotic plaque or fracture of the capsule covering it, less often hemorrhage into the plaque), as well as an increase in coagulation activity, are the main causes of coronary blood flow system and decreased anticoagulant activity. system, contribute to coronary thrombosis [19]. When the plaque is damaged, collagen fibers are exposed, adhesion and aggregation of platelets at the site of damage, release of platelet coagulation factors and activation of plasma coagulation factors occur [20

A thrombus forms, occluding the lumen of the artery. CA thrombosis is usually combined with its spasm. The resulting acute occlusion of the coronary artery causes myocardial ischemia, a sharp painful attack and, if there is no reperfusion, necrosis of this part of the myocardium. Atherosclerotic and thrombotic processes are closely related and are therefore currently united by the term “atherothrombosis”. The process of atherothrombosis begins at the moment of rupture of the fibrous

wall of an atherosclerotic plaque or its erosion [21]. Platelets are the first to react to plaque rupture. Platelet adhesion to the damaged endothelium leads to their further aggregation, local vasospasm, development of dynamic stenosis leading to hypoxia and ischemia of the organ [22]. Platelet aggregation is the starting point of the processes culminating in thrombus formation in resistance vessels [23]. Rupture of unstable atherosclerotic plaque, adhesion and aggregation of blood cells, inclusion of plasma coagulation factors in the process and thrombus formation are a single pathway for the development of cardiovascular catastrophes [24]. The endpoints of the latter are acute myocardial infarction, ischemic stroke, critical ischemia of the lower extremities, development of chronic heart failure, i.e. the conditions that determine the main indicators of mortality and disability worldwide. In this regard, antiaggregant therapy plays an important role in both primary and, to an even greater extent, secondary prevention [25]. The maintenance of favorable outcomes after SCA depends on the prevention of subsequent thrombotic complications [26]. Stent thrombosis is a life-threatening complication that can develop acutely, subacutely, and in remote periods after stent implantation [27]. It develops more often in case of insufficient suppression of platelet aggregation [28]. Platelet activation and aggregation play a key role in the development of ischemic events in acute coronary syndrome and during PCI. Therefore, patients are prescribed antiaggregant therapy including acetylsalicylic acid (ASC) and clopidogrel [29]. ASC blocks platelet cyclooxygenase-1 by disrupting thromboxane A2 synthesis in platelets. Thus, ASC irreversibly inhibits platelet aggregation induced by collagen, ADP and thrombin. The mechanism of antiaggregant action of clopidogrel is associated with inhibition of ADP-induced platelet aggregation by irreversible binding to membrane protein-receptor P2Y12. However, in some patients such antiaggregant therapy may be ineffective [30]. The reason for this is individual sensitivity to the drug. Modern medical treatment of coronary heart disease, in addition to taking antianginal and anti-ischemic drugs, should include the use of antithrombotic (antiaggregant) [31], hypolipidemic (statins) [32], antihypertensive and metabolic agents. Successfully performed PCI does not eliminate the cause of coronary heart disease - atherosclerosis, but only levels the pathophysiological effect of hemodynamically significant atherosclerotic plaque [33]. Atherosclerotic process can progress both in the stented or ballooned and in other segments of the coronary channel. In addition, implantation of a foreign body - stent can cause iatrogenic disease - stent thrombosis, which can develop in the remote period. In this situation, it is necessary to strictly observe all measures of secondary prevention of CHD, for which it has been proved to reduce the risk of coronary and cerebral complications, cardiovascular mortality in patients after PCI [34]. The course of the disease and prognosis of patients who underwent PCI largely depend on the completeness of compliance with the standards of drug therapy, primarily antiaggregant therapy [35]. According to the guidelines, patients who had stents placed should receive dual antiplatelet therapy (DATT) for at least 12 months. However, there are results of studies indicating that longer use of ASC and clopidogrel combination improves prognosis. At the same time, early withdrawal of DATT or one of the drugs is associated with the most unfavorable course. Unfortunately, the implementation of treatment standards does not always completely exclude the possibility of complications, which is largely due to the unfavorable background of the disease: multiple risk factors, mutations of genes responsible for the regulation of lipid metabolism, thrombosis factors [36]. The consequence of this is insufficient control of platelet aggregation, which in the end contributes to stent thrombosis - one of the main causes of complications in patients who underwent PCI. The most important direction of drug treatment of patients with coronary heart disease is the use of drugs that reduce the level of lipids in the blood [37]. The main agents that reduce the level of cholesterol and low-density lipoprotein cholesterol (LDL) in blood plasma are cholesterol synthesis inhibitors - statins [37]. The most important goal of lipid profile correction is to reduce the level of LDL-C [38]. Statins not only reduce the level of atherogenic lipids, but also the risk of complications of PCI, have a favorable effect on the course of the disease. GSC Biological and Pharmaceutical Sciences, 2021, 15(03), 212-217 214 Unfortunately, in a part of patients ischemic events recur on the background of DATT. Heterogeneity of platelet suppression response to DATT administration has been demonstrated in many clinical trials. The aim of the study: to evaluate the efficacy of antiaggregant and lipid-lowering therapy in patients with coronary heart disease after coronary artery stenting based on the analysis of clinical and laboratory parameters.

2. Material and methods. The study included 30 patients with CHD after coronary artery stenting with DES stents (26 men and 4 women) receiving antiaggregants (ASC and clopidogrel), rosuvastatin 10-20 mg/day according to current recommendations. Of the 30 patients, 16 (12 men and 4 women) had metabolic syndrome (MS) and arterial hypertension (AH) receiving appropriate therapy. Initially and after 3 months total cholesterol (TC), LDL, HDL-C, triglycerides (TG), C-reactive protein (CRP), activity of alanine and aspartate aminotransferase enzymes (ALT and AST), total cholesterol content were determined. Bilirubin (OB) was determined in the blood of patients. ...Electrocardiography (ECG), if necessary ECG with exercise, echocardiography (Echocardiography) with assessment of parameters of structural and functional state of the left ventricle (LV), Dopplerography (Samsung medison "AccuvixV20").

3. Results and discussion. Before stenting the increase of platelet functional activity, total cholesterol, LDL-C, TG, decrease of HD-C was revealed. Baseline lipid parameters: total cholesterol -6.9 mmol/L; CSLNP -3.6; CSHDL -1.1; TG - 2.3 mmol/L and CRP -7.5 mg/L. In IBS patients with MS and AH, the content of SRB averaged 16.4±1.2 mg/L. The study of lipid spectrum in these patients revealed higher level of total cholesterol - 7.2±0.6; TG-2.5±0.2; LDL-C - 3.7±0.26 mmol/l and lower level of HDL-C: 1.2±0.1 in patients with MS and AH and 1.15±0.14 mmol/l in patients without MS and AH. Total cholesterol and LDL cholesterol decreased by 30 and 36% after three months of therapy. Changes in the level of antiatherogenic HDL-CS were not so pronounced (increase of about 8%), but a 38% decrease in TG content was detected. One of the inflammatory factors, SRB, was 35% higher than normal. High level of SRB indicated instability of atherosclerotic plaque. Almost all patients initially had an increased degree of platelet aggregation (on average by 20%). In the absence of a shock dose, the antiaggregant effect of the drugs on the 5th day of administration was moderately pronounced. Normalization of all aggregative indices was observed in 11 (37%) patients. In other cases, despite the decrease in some cases, it remained elevated. After 2 months of treatment it normalized in 24 (80%) patients, and 5 (17%) patients still had elevated aggregation indices. It should be noted that spontaneous aggregation disappeared in 4 out of 5 patients, whereas ADP-induced aggregation significantly decreased. After three months, favorable changes in platelet aggregation indices (degree and rate of aggregation, indicator of the presence of disaggregation) were achieved. A favorable hypolipidemic effect of statin was revealed, manifested in normalization of lipid spectrum. Before stenting, despite almost normal ejection fraction (EF) with preserved LV systolic function, the majority of transmittal blood flow indices differed from the norm, LV diastolic function impairment was determined. Three months later, there was an increase in LV EF, which averaged 61.5%. LV early filling velocity (peak E) before stenting and after 3 months was 0.67 and 0.76 m/s, diastolic filling velocity during left atrial systole (peak A) - 0.77 and 0.7 m/s. sec, velocity characteristics ratio (E/A) - 0.87 and 1.08; LV isovolumic relaxation time - 139 and 142.5 ms; early filling velocity deceleration time was 208 and 208 ms. Before stenting, the majority of transmitral blood flow indices differed from the norm, LV diastolic function impairment was determined. Myocardial painless ischemia in patients with LV hypertrophy was more frequent than in the examined patients without altered LV geometry. Pleiotropic properties of statins were noted already in the first months of treatment. Beneficial effect of statins on the studied clinical and instrumental and laboratory parameters once again testify to their influence on pathogenetic links of ischemic heart disease, which is especially important in the treatment of such patients with concomitant MS and AH. Modern ideas about pathogenesis of ischemic heart disease indicate the necessity of differentiated approach to treatment of patients with this pathology taking into account possible components of MS. No adverse effect of the tested drugs on ALT, AST activity and OB content was revealed. Antiaggregants were well tolerated and did not cause hypocoagulation. Lipid-lowering efficacy of rosuvastatin, as well as antiaggregant effect of ASC and clopidogrel were maintained at a sufficient level when used together. The combination of these drugs did not lead to the development of liver function disorders, which was confirmed by ALT, AST and OB indices. Against the background of drug therapy, changes in the indicators of platelet aggregation were achieved. The degree of platelet aggregation in patients without MS and AH was lower than in patients with these comorbid conditions [39]. The platelet aggregation rate was also higher in patients with MS and AH [40]. The aggregation time as well as the rate of presence of disaggregation was lower in

patients without MS and AH. No side effects and drug resistance were detected. The causes of resistance to ASC and clopidogrel are heterogeneous and multicomponent: Clinical (weight, age, dose reduction or premature drug withdrawal, poor absorption, drug action, diabetes mellitus) and cellular (accelerated platelet pool formation, decreased metabolic activity, dysregulation of P2Y12 or P2Y1 receptors, impaired P2Y1 activation, insufficient suppression of catechol-induced platelet activation) [41]. Ineffectiveness of antiplatelet therapy may not be the only mechanism of ischemic events associated with antiplatelet therapy [42]. This suggests the importance of laboratory confirmation of clinical resistance [43]. Clinical studies have shown that titration of clopidogrel dose based on platelet function results improves clinical outcome in patients undergoing PCI [44]. The use of two drugs with different mechanisms of antiaggregant action allows increasing the effectiveness of antiaggregant therapy and, consequently, reducing the risk of thrombosis. Important points are the achievement of target BP level, reduction of blood lipid level, and in patients with diabetes mellitus - achievement of carbohydrate metabolism compensation. The peculiarity of secondary prophylaxis after PCI is prescription of DATT in adequate doses and necessary duration. Unfortunately, according to research data, patients' adherence to drug therapy affecting prognosis after PCI remains insufficient.4. . Conclusion Thus, personalized selection of doses of lipid-lowering and especially antiaggregant drugs taking into account individual characteristics of patients and pharmacogenetics increases the effectiveness of treatment, prevents the development of restenosis and other complications. This minimizes the side effects of drugs and the development of resistance to them. Adherence to ethical standards. Acknowledgments The authors thank A. Jabbarov for the design and critical review of the manuscript. Informed consent statement. Informed consent

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Statement of informed consent

Informed consent was obtained from all individual participants included in the study

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Compliance with ethical standards

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Informed consent statement

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Recommendations

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