ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Effectiveness of Antiaggregants in Treatment of Acute Coronary Syndrome.

Chernykh T, Fursova E, Ovsyannikova V*, and Kochetkova I.

Voronezh State Medical University, Studencheskaya St., 10, Voronezh, 394036.

ABSTRACT

The problem of high incidence of disease and mortality from acute coronary pathology is still topical. Antiplatelet drugs are capable of increasing prognosis for life for this group of patients influencing on pathogenetic ways of development of cardiovascular accidents – coronary artery thrombosis. The most famous and researched medicine – acetylsalicylic acid – can reduce the risk of adverse cardiovascular events and could be used in various therapy protocols at high-risk patients. Moreover, there are more and more data of its efficiency for preventing oncology pathology. The representative of the group of receptor inhibitors to adenosine monophosphate – clopidogrel has proved the most efficiency to reduction of cardiovascular mortality. The researches on studying genetic determinacy of active drug form and its efficiency are conducted. The new medicine – ticagrelor – is used limitedly at lack of clopidogrel efficacy or when choosing primary coronary intervention. Furthermore, representatives of thrombocyte glycoprotein receptor antagonists – monafram, eptifibatidum, abciximabum are popular: they are used in case of development of thrombotic complications under coronarography intervention or in case of lack of efficacy of oral antiplatelet. Taking into account high probability of re-ischemic events during the first year after acute coronary pathology, as well as the tendency to invasive therapeutic approach to disease management, the long-term ingestion of two antiplatelet drugs had been proved. Heavy mortality causes integrated and personalized approaches to treating patients by anti-platelet therapy. The article contains review of modern antiplatelet drugs.

Keywords: anti-platelet therapy, acetylsalicylic acid, clopidogrel, ticagrelor, IIb/IIIa platelet receptor antagonists.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

To date, one of the leading areas of Russian health care is the reduction in mortality from cardiovascular diseases. According to the Federal State Statistics Service in the Russian Federation in 2015, the death rate from acute myocardial infarction was 43.5 cases per 100 thousand population, the average mortality rate in the country was 14.5% [1]. The effectiveness of therapy for patients with acute coronary syndrome largely depends on the organization of medical care, beginning with the prehospital stage, and ending with the application of modern methods of treatment.

A key role in the initiation and growth of coronary thrombosis is played by platelets. Antiaggregants, or antiplatelet drugs, suppressing their function, are the basis of pathogenetic therapy of acute coronary syndrome. In modern cardiological practice, several groups of drugs with proven effectiveness are used.

Acetylsalicylic acid is the most well-known antiaggregant, has been used in medical practice for more than a hundred years and is the basis of most modern antiplatelet therapy strategies. Irreversibly inhibiting cyclooxygenase of the first type, acetylsalicylic acid blocks the synthesis of thromboxane A2 in platelets, which reduces their activation. The antiplatelet effect persists throughout the life span of the platelets (5 to 10 days) until the pool is renewed [2]. The use of acetylsalicylic acid as a secondary prevention of coronary heart disease is routine and has a convincing evidence base. In a randomized placebo-controlled study, ISIS-2 reported a relative reduction in the lethal outcome of cardiovascular causes over the next 5 weeks by 21% in patients receiving acetylsalicylic acid and by 40% in patients who received both acetylsalicylic acid and thrombolytic; reduction in the risk of developing non-fatal myocardial infarction by 49%, reducing the risk of death from cardiovascular causes in the long-term (15 months) [3, 14]. A meta-analysis, including 287 studies and 77,000 patients, revealed a significant reduction in the risk of adverse cardiovascular events in patients with acute myocardial infarction and in patients with stable angina, atrial fibrillation, and peripheral arterial disease [3]. The results of a meta-analysis of 31 randomized trials suggest that the use of high doses of ASA does not additionally reduce the risk of cardiovascular complications, but significantly increases the likelihood of hemorrhagic complications; In addition, almost complete inhibition of cyclooxygenase-1 occurs at concentrations of the drug less than 162 mg [3, 4]. There is a new concept of chronotherapy, according to which the administration of the drug should correspond to the circadian rhythm of the disease in order to achieve an optimal antiaggregant effect and minimize adverse reactions [4]. Based on the current recommendations for achieving a rapid blockade of cyclooxygenase-1, a single application of a loading dose of 150-300 mg is indicated, possibly intravenous administration of the drug at a dose of 150 mg equivalent to 300 mg for oral administration. In the absence of contraindications, acetylsalicylic acid is recommended for all patients with acute coronary syndrome indefinitely in a maintenance dose of 75-150 mg per day without special control [5, 6].

Thus, given the proven need for continued use of acetylsalicylic acid, the approach to prescribing the drug should be personalized.

The second drug for the prescription in the world is clopidogrel [7] - a derivative of thienopyridine, an oral inhibitor of P2Y12 receptor platelets. The drug is a prodrug that is rapidly metabolized in the liver with the participation of cytochrome P450 enzymes to form active metabolites that irreversibly inhibit the platelet receptor to adenosine monophosphate (ADP), which provides an antiaggregant effect throughout the lifetime of the platelet. The results of the CARPIE study, the main purpose of which was a direct comparison of the efficacy of clopidogrel and acetylsalicylic acid, indicate the high efficacy of clopidogrel in secondary prevention in patients with high cardiovascular risk: its appointment at a dose of 75 mg per day compared with acetylsalicylic acid therapy at a dose of 325 mg per day resulted in a statistically significant relative reduction in the risk of death from cardiovascular causes by 8.7% [3], and hemorrhagic risks with both drugs were comparable [2]. Since 2001, the standard for the treatment of patients with acute coronary syndrome is double antiplatelet therapy, which includes the simultaneous administration of an inhibitor of P2Y12 receptors and acetylsalicylic acid within 1 year after acute coronary syndrome (it may shorten the term to 3-6 months with a high risk of bleeding and prolongation of more than 12 months in patients with a high risk of thrombotic and low hemorrhagic complications) [5, 6]. Its validity is proved by the results of the CURE study, which included 12562 patients with unstable angina, myocardial infarction without ST segment elevation. Antiplatelet therapy was associated with a decrease in the relative risk of adverse events (death from cardiovascular causes, nonfatal myocardial infarction, stroke) by 20% [2, 3]. The most pronounced effect was registered in patients

who underwent percutaneous coronary intervention and aortocoronary bypass surgery, a 31% reduction in risk [2, 3]. The results of the double-blind study CLARITY-TIMI-28, which included 3,491 patients, indicate an improvement in the angiographic pattern and a reduction in the number of urgent revascularizations in patients with acute ST-segment elevation on ECG treated with fibrinolytics; when clopidogrel is added to acetylsalicylic acid, the relative incidence of myocardial infarction, death from any cause is reduced by 36%, the number of cases of achieving successful myocardial reperfusion by 21% is increased [3, 7, 8].

A new drug from the group of thienopyridines is ticagrelor, an active inhibitor of P2Y12-receptors of reversible platelets. The degree and duration of blockade of receptors depends on the concentration of the drug in the blood plasma, when it is canceled, the function of platelets is restored more quickly than after the withdrawal of clopidogrel [9, 15]. The main study in which data on the efficacy and safety of ticagrelor was obtained was a large, multicenter, randomized, placebo-controlled study of PLATO that included 18,624 patients with acute ST-segment elevation coronary syndrome if they were scheduled for primary transcutaneous intervention, as well as patients with acute coronary syndrome without ST segment elevation, hospitalized within 24 hours of onset of symptoms, showing signs of high risk of developing complications. When comparing the efficacy of clopidogrel and ticagrelor it was noted that at 12 months from the start of treatment in the ticagrelor + acetylsalicylic acid group, the relative reduction in the risk of death from vascular causes, myocardial infarction, stroke was 16% compared to the clopidogrel + acetylsalicylic acid group [10]. In the PEGASUS-TIMI 54 study, which evaluated the combination of ticagrelor and acetylsalicylic acid for secondary prevention of atherothrombotic complications in patients who underwent myocardial infarction for 1-3 years prior to enrollment, a significant decrease in thrombotic complications was demonstrated [11, 16]. Despite the proven clinical and economic validity of the application, ticagrelor should be preferred in patients with acute coronary syndrome without sustained elevation of the ST segment on the ECG [12]. The advisability of switching to ticagrelor in patients with acute coronary syndrome with the development of thrombotic complications with the use of clopidogrel is not confirmed by special clinical studies. An additional group of antiaggregant drugs, routinely not used in patients with acute coronary syndrome, are inhibitors of glycoprotein IIb / IIIa receptors - abciximab, eptifibatide, monaphram. They prevent the binding of fibrinogen and von Willebrand factor to the glycoprotein IIb / IIIa receptors of platelets, which leads to reversible suppression of their aggregation. On the example of the clinical case, the successful use of eptifibatide in a patient with myocardial infarction of the left ventricular lower wall with ST segment elevation during the development of stent thrombosis is shown in the case of a clinical case [13] and the appointment of an additional antiplatelet drug (IIb / IIIa antagonist of glycoprotein receptors) in all patients with ACS with an extended zone implantation of stents.

Thus, antiplatelet therapy in patients with acute coronary syndrome is the basic component of complex treatment aimed at saving the patient's life. The use of antiplatelet agents has a broad evidence base based on the results of many international, randomized clinical trials, but the high efficacy and mortality reduction from ischemic events balances with an increased incidence of hemorrhagic complications. Correction of risk factors can reduce their negative impact on the course of the disease and achieve one of the main goals of treatment - improving the quality and extending the life of the patient [17]. Competent antiplatelet therapy with current clinical recommendations forms the basis of effective and safe medical care for patients with acute coronary syndrome.

REFERENCES

[1] Federal State Budgetary Institution "Russian Cardiology Research and Production Complex of the Ministry of Health of the Russian Federation", Register of ACS / http://cardioweb.ru.
[2] Napalkov DA. Modern antiplatelet therapy in patients with high cardiovascular risk. Consilium Medicum. 2015; 17 (12): 36-39.
[3] Yakovlev AN. Antiagregants in cardiology: the choice of best individual treatment. Medical Council. 2015; 12: 34-43.
[4] Dzhioeva ON, Oganezova LG. Acetylsalicylic acid in the treatment of cardiovascular diseases: blast from the past. Chronotherapy concept. RMJ. 2016; 19: 1295 - 1300.
[5] Diagnosis and treatment of patients with acute coronary syndrome without ST-segment elevation of the electrocardiogram. Of the Society of Experts in Emergency Cardiology. Emergency Cardiology. 2016; 2: 26-62.

[6] Diagnosis and treatment of patients with acute coronary syndrome with ST-segment elevation of the electrocardiogram. Of the Society of Experts in Emergency Cardiology. Emergency Cardiology. 2014; 1: 42-62.
[7] Tarasov AV, Vishnevskiy VI. Efficiency of the antiplatelet therapy of aspirin and clopidogrel in clinical practice. Scientific notes of Orel State University. 2015. 4 (67): 407 - 409.
[8] Trifonov IR. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation improved all angiographic measurements and reduced rate of urgent revascularization. CLARITY-TIMI28 results. Cardiology. 2005; 5: 73-74.
[9] Karpov YA, Sorokin YV. Acute coronary syndrome without ST-segment elevation on the electrocardiogram: the features of the modern approach to tactics: focus on ticagrelor. Atmosphere. News of cardiology. 2016; 1: 1 - 6.
[10] Erlih AD. Results of clinical studies PLATO and place of ticagrelor in the treatment of acute coronary syndrome. Cardiosomatika. 2015; 1: 53-59.
[11] Averkov OV. Prevention of recurrent ischemic events in patients after myocardial infarction. New options for long-term dual antiplatelet therapy. Results of the PEGASUS-TIMI54 study. Aterotromboz. 2015; 1: 65-72.
[12] Kozik VA, Lozhkina NG, Khasanova MK, Glebchenko EA., Kuimov AD. Acute coronary syndrome: modern strategy reperfusion and medication. Modern problems of science and education. 2017; 1.
[13] Dolotovskaya PV, Reshetko OV, Malinova LI, Furman NV. Ratio "cost-effectiveness" for Clopidogrel and Tikagrelor in acute coronary syndrome with ST elevation in real clinical practice. Pharmacoeconomics: theory and practice. 2016; 1: 206.
[14] Kochetkova IV, Chernykh TM. Experience with ivabradine in patients with comorbid pathology. Consilium Medicum. 2016. Vol. 18. No. 1. 80-82.
[15] Chernykh TM, Sobolev YA, Ahmatova EV. Prevention of thrombosis in the patients with chronic heart failure against rheumatic heart diseases. Rheumatology Science & Practice. 2004. № 4 . (Suppl.) 28.
[16] Fursova EA. The state of the hemostasis system for rheumatic heart disease. Applied information aspects of medicine. 2008. № 2 (11). 269-272.
[17] Ovsyannikova VV, Istomina MS. Influence of risk factors of cardiovascular diseases on the prognosis of life of patients with type 2 diabetes. Doctor-graduate student. 2017. No. 6.1 (85). 150-155.