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A Look at Thrombolytic Therapy in Prehospital Acute Coronary Syndrome (ACS) With ST Elevation in Menopausal Women (Literature Review)

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Abstract: Cardiovascular diseases and acute coronary syndrome (ACS), in particular, are an urgent public health problem in most countries of the world, including Uzbekistan, despite significant progress in recent decades in the diagnosis and treatment of this pathology. WHO experts predict a further increase in cardiovascular morbidity and mortality, both in developed and developing countries, due to the aging of the population and lifestyle habits.

Keywords: Women, ACS, Therapy.

Mortality from myocardial infarction in Russia is 45 cases per 100 thousand of the population, the average mortality rate ranges from 16 to 28%. According to the Scientific and Practical Society for Emergency Medical Care (NNPOSMP), about 25,000 patients with coronary artery disease [D.S. Yunevich, S.B. Aksentiev, JI.B. Deniskina, O.V. Fokina, Yu.M. Kopylova Academician I.P. Pavlov].

Acute coronary syndrome (ACS) is any group of clinical signs or symptoms suggestive of myocardial infarction or unstable angina.

ST segment elevation is usually a consequence of transmural myocardial ischemia and occurs with the development of complete occlusion of the main coronary artery. Persistent ST-segment elevation lasting more than 20 minutes is associated with acute total thrombotic occlusion of a coronary artery.

ST-elevation OKC is diagnosed in patients with anginal attack or chest discomfort and ECG changes in the form of persistent ST-segment elevation or "new", i.e. for the first time (or presumably for the first time) a complete blockade of the left leg of the His bundle (LBB) on the ECG. ACS is a working diagnosis used in the first hours and days of the disease, while the terms myocardial infarction (MI) and unstable angina (UA) are used to formulate the final diagnosis, depending on whether signs of myocardial necrosis are detected.

The problem of choosing the most effective and safe method of treating acute coronary syndrome (ACS) in certain groups of patients (taking into account gender, age, etc.), as a frequent form of IHD exacerbation, has not been fully resolved. At this point in time, in clinical and theoretical cardiology, it seems relevant to search for new and improve existing methods of treating ACS, the main of which continues to be myocardial reperfusion. There is a need for a competent distribution of expensive methods of pharmacological revascularization, a scientifically based organization of the treatment and diagnostic process when a patient is admitted to a hospital, a clear choice of a treatment strategy and a drug arsenal for various categories of patients. Today, there are many thrombolytic drugs on the market that are recommended for use in reperfusion therapy in patients with ACS, however, the question of the appropriateness, efficacy and safety of their use in certain categories of patients, in particular, in elderly and senile patients, who make up the majority of patients with ACS, remains open. specified pathology [D.S. Yunevich, Russian Biomedical Bulletin named after Academician I.P. Pavlova , 2017]

Currently, the most effective, pathogenetically substantiated methods of treating acute myocardial infarction are thrombolytic therapy (TLT) and coronary angioplasty. Emergency angioplasty in Uzbekistan is performed only in a few medical centers of large cities (Tashkent, Samarkand, Bukhara), so this treatment method practically affects the statistics of disease outcomes in the whole country.It would seem that thrombolytic therapy, which requires significantly less financial and organizational costs, should be carried out everywhere, but even it is far from being performed in all medical institutions for a number of reasons. The main ones include insufficient supply of medicines with this direction of action, the presence of a number of sometimes fatal complications that occur against the background of its implementation. That is why solutions to the problems of further improvement of methods and the introduction of thrombolysis into practice are still topical healthcare.

More than 20 years of experience in the use of thrombolytic therapy has made it possible to focus the attention of non-cardiological doctors on its key positions and to designate a clear algorithm for treatment tactics in this nosology.

We consider it appropriate to reflect the treatment algorithm in the sequence that occurs most often at the prehospital stage.

Anesthesia - anesthesia is an integral part of the complex therapy of ACS, not only for ethical reasons, but also due to excessive sympathetic activation during nociceptive stimulation. This leads to increased vasoconstriction, increased myocardial oxygen demand, and increased stress on the heart. If the use of aerosol forms of nitrates is ineffective, immediate intravenous administration of morphine hydrochloride 2-4 mg + 2-8 mg every 5-15 minutes or 4-8 mg + 2 mg every 5 minutes or 3-5 mg is recommended until pain relief. With systolic blood pressure (BP) above 90 mm Hg. an intravenous infusion of nitroglycerin at a dose of 20–200 mcg /minute should be initiated. In case of severe anxiety, European authors consider intravenous administration of small doses of benzodiazepines to be indicated, however, in most cases, the use of opioid analgesics achieves satisfactory results (Van de Werf F., Bax J., Betriu A. et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the Task Force on the Management of ST-Segment Elevation Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J 2008;29(23):2909-45).

Acetylsalicylic acid - non-steroidal anti-inflammatory drugs, COX-2 inhibitors Absolutely all patients with ACS should take a loading dose of acetylsalicylic acid (ASA) 160-325 mg of non-enteric forms under the tongue as soon as possible. A valid alternative is the use of intravenous ASA (250-500 mg) and ASA in the form of rectal suppositories. Contraindications to the use of a loading dose are active gastrointestinal bleeding, known hypersensitivity to ASA, thrombocytopenia, severe liver failure. Non-steroidal anti-inflammatory drugs (NSAIDs) and selective COX-2 inhibitors are associated with an increased risk of death, recurrent ACS, myocardial rupture, and other complications (Collaborative meta - analysis of randomized trials of antiplatelet therapy for prevention of death , myocardial infarction , and stroke in high risk patient . Br . Med . J. _ 2002. V. 324. P 71).

If ACS occurs, all drugs from the groups of NSAIDs and COX-2 inhibitors should be discontinued. In the future, all patients should receive low doses of ASA (75-160 mg) every day indefinitely (Scottish Intercollegiate Guidelines Network. Acute coronary syndromes. A national clinical guideline. Available on http://www.sign.ac.uk/pdf /sign93).

Clopidogrel - the addition of clopidogrel to ASA at the prehospital stage significantly improves clinical outcomes, reduces morbidity and mortality in patients with ACS. The dosage of clopidogrel varies depending on the type of ACS and the type of treatment being given. In the future, the dosage of clopidogrel is 75 mg. The duration of dual antiplatelet therapy (ASA plus clopidogrel) also varies by type of ACS and treatment approach (invasive/non-invasive) and ranges from 4 to 52 weeks (at least 4 weeks, ideally 1 year) (Dudek D. , Rakowski T. , Dziewierz A. _ et al . PCI after lytic therapy: when and how? Eur Heart J Suppl 2008; 10(suppl J): J15-J20).

Antithrombotic therapy (Heparins) are a standard part of anticoagulant therapy in patients with ACS. The introduction of unfractionated heparin is recommended to start with an intravenous bolus injection (no more than 5000 U for ACS without ST segment elevation and 4000 U for ACS with ST segment elevation) with a further transition to intravenous infusion at a rate of 1000 U/hour and control of the activated partial thromboplastin time every 3-4 hours. The use of low molecular weight heparins avoids laboratory control, facilitates the heparin therapy regimen. Among the representatives of the group, the most studied is enoxaparin [Sulimov V.A. Thrombolysis or primary percutaneous intervention in ST-segment elevation myocardial infarction? STREAM Study Rational Pharmacotherapy in Cardiology.2013;9(6)].

It has been shown that the combined use of enoxaparin and thrombolytic therapy is associated with additional clinical benefits for the patient. In addition, if anticoagulant therapy is planned for more than 48 hours, then the use of unfractionated heparin is associated with a high risk of thrombocytopenia. Enoxaparin in a non-invasive strategy for the treatment of ACS is used according to the following scheme: an intravenous bolus of 30 mg, then subcutaneously at a dose of 1 mg/kg 2 times a day until the 8th day of illness [Kashtalap V.V., Kochergina A.M., Kochergin N.A. . Bleeding in invasive management of patients with acute coronary syndrome: prevalence, current approaches to risk assessment and prevention (literature review). Russian Medical Journal. 2016;12:739-43].

The first 2 subcutaneous doses should not exceed 100 mg. In persons over 75 years of age, the initial intravenous dose is not administered, and the maintenance dose is reduced to 0.75 mg / kg (the first 2 doses should not exceed 75 mg). With creatinine clearance less than 30 ml / min, the drug is administered s / c at a dose of 1 mg / kg once a day. In an invasive approach to the treatment of ACS for the administration of enoxaparin, it is necessary to remember the following: if no more than 8 hours have elapsed after a subcutaneous injection of 1 mg / kg, additional administration is not required. If this period is 8-12 hours, then immediately before the procedure, enoxaparin should be administered intravenously at a dose of 0.3 mg/kg [Oganov R.G., Mamedov M.N. Diagnosis and treatment of patients with acute myocardial infarction with ST elevation ECG. National clinical guidelines. MEDI Expo; 2009].

Other drugs (beta-blockers) - in order to reduce myocardial oxygen demand in ACS, it is necessary to prescribe beta-blockers. At the prehospital stage, it is advisable to use intravenous forms of beta-blockers both for the speed of onset of the clinical effect and for the possibility of a rapid decrease in the effect if side effects may occur. ACE inhibitors - during the first 24 hours from the development of ACS, it is advisable to use drugs from the group of blockers of the activity of the renin-angiotensin system, ACE inhibitors or angiotensin receptor antagonists. However, the start of such therapy is recommended after the patient is hospitalized [Chazov E.I., Boytsov S.A., Ipatov P.V. Big task. Improving the technology of ACS treatment as the most important mechanism for reducing cardiovascular mortality in the Russian Federation. Modern medical technologies 2008;(1):35-8].

For acute myocardial infarction myo carda With rise segment ST on the ECG (STEMI) administration of thrombolytic agents is recommended in all cases where it is not possible to perform percutaneous endovascular treatment within 2 hours of start symptoms (Class recommendations 1A), a with a low risk of bleeding - within 90 minutes (class 2B), then there is on the prehospital stage [ESC Guidelines for the management of acute myocardial infarction in patients presenting with st - segment elevation . European Heart journal, 2012]

However, against the background of new ideas about In the treatment of STEMI, the direct efficacy of thrombolytic agents must not be forgotten. Thrombus formation in atherosclerotic plaque going on in due to its erosion or ulceration. High- risk plaques with a large active lipid-necrotic core have a high chance of depleting antithrombotic mechanisms on their surface. Normally, endothelial glycocalyx, which contains oxide nitrogen, prostacyclin, heparin, thrombomodulin, a also system natural anticoagulants (heparin, clotting factor inhibitors, antithrombin, proteins C, S, Z and other substances). With the predominance of risk factors (stress, smoking, dyslipidemia, high levels of lipoprotein a, sugar diabetes and others) going on activation of hemostasis in the plaque area with concomitant weakness natural anticoagulant and fibrinolytic system. Embedded in the formed

thrombus antiplasmin, modifies fibrin, and the latter becomes resistant to the action of plasmin. The mechanism of action of fibrinolytic agents is similar: they all activate natural plasminogen with the formation of plasmin, which dissolves thrombus [9, ten]. But on the this resemblance ends.

First-generation drugs, streptokinase and urokinase, as Frendl et al. (2011) are of historical significance. They are not fibrin-specific. By inducing fibrinolysis, they reduce the level fibrinogen, factors clotting blood and von Willebrand factor. Streptokinase also has restrictions, related With immunization [Murray] V , Norrving b , sandercock PAG , et al . The molecular basis of thrombolysis and its clinical application in stroke. J Intern honey, 2010;].

The second generation drugs, alteplase and prourokinase , are non-immunogenic, but their important disadvantage is the short half-life of 4–5 minutes for alteplase and 7 minutes for — for prourokinase [Murray V , Norrving b , sandercock PAG , et al . The molecular basis of thrombolysis and its clinical application in stroke. J Intern Med, 2010].

Alteplaza, in addition, has the property to modify the hematoencephalic barrier, what maybe raise risk hemorrhagic strokes. The third generation of fibrinolytic agents (plasminogen activators) include reteplase and tenecteplase. Their most notable difference is the extended period semi -elimination, allowing them to be administered as a bolus rather than an infusion. There are also more significant differences. A drug fourth generations — desmo teplase - not used in the treatment of myocardial infarction [Friendl A , Csiba L. _ pharmaceutical and non - pharmacological recanalisation strategies in acute ischaemic stroke . Front neurol , 2011].

Despite the shift in the focus of therapy acute infarction myocardium With rise ST on the ECG in direction of endovascular treatment, the relevance of fibrinolytic drugs continues to be high. The period of the largely emotionally driven priority of percutaneous interventions over thrombolysis seems to be over. Current data, including data from cohort studies in the real population, strongly suggest that systemic thrombolysis is equivalent to other treatments. Moreover, the FAST-PCI strategy (administration of “preparatory” low doses of fibrinolytic drugs before performing, for example, an invasive procedure) provides even more options for managing patients, but requires further study. Among thrombolytic drugs, the advantage belongs to new drugs and resistance to the action of antiplasmin - streptokinase and tenectoplasma.

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