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UNSTABLE PROGRESSIVE ANGINA

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✓ ***Resume***

The review presents data on progressive angina pectoris – exacerbation of chronic ischemic heart disease. The risk of sudden death and myocardial infarction in such patients is higher than in those with stable angina. Despite the widespread introduction of modern diagnostic equipment, the emergence of a large number of drugs, the problem of verification and treatment of coronary heart disease (CHD) remains very relevant. In particular, issues related to the diagnosis and treatment of the disease during its exacerbation, the development of myocardial infarction (MI) and sudden death (VS) are of particular importance.IHD is a common disease caused by atherosclerosis of the coronary arteries, as a result of which the balance between oxygen delivery and myocardial demand is disturbed.

Key words: unstable angina, progressive angina pectoris, silent myocardial ischemia, Holter monitoring.

НЕСТАБИЛЬНАЯ ПРОГРЕССИВНАЯ СТЕНОКАРДИЯ

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✓ ***Резюме***

Несмотря на широкое внедрение современной диагностической техники, появление большого количества лекарственных препаратов, остаётся весьма актуальной проблема верификации и лечения ишемической болезни сердца (ИБС). В частности, особое значение имеют вопросы, связанные с диагностикой и лечением заболевания в период его обострения, развитием инфаркта миокарда (ИМ) и внезапной смерти (ВС). ИБС - распространённое заболевание, обусловленное атеросклерозом коронарных артерий, в результате чего нарушается равновесие между доставкой кислорода и потребностями в нём миокарда.

Ключевие слова: нестабильная стенокардия, прогрессирующая стенокардия, немая ишемия миокарда, холтеровское мониторирование.

ЗЎРАЙИБ БОРУВЧИ СТЕНОКАРДИЯ

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Ностабил стенокардия, зўрайиб борувчи стенокардия, миокард ишемияси, холтер мониторинги.

Замонавий диагностик усулларнинг кенг жорий этилишига, кўплаб дори-воситаларнинг пайдо бўлишига қарамай, юрак-қон-томир касалликларини текшириш ва даволаш муаммоси жуда долзарб бўлиб қолмоқда. Хусусан, касалликнинг кучайиши даврида диагностика ва даволаш, ўткир миокард инфаркти ва тўсатдан ўлимнинг ривожланиши билан боғлиқ. Стенокардия юрак коронар артерияларнинг атеросклерозидан кейин келиб чиқадиган касаллик бўлиб, бунинг натижасида кислород етказиб бериш ва миокард талаби ўртасида мувоазанат бузилади.

Калит сўзлар: нестабил стенокардия, зўрайиб борувчи стенокардия, жим миокард ишемияси, холтер текшириш

Relevance

Despite the widespread introduction of modern diagnostic technology, the emergence of a large number of medicines remains highly relevant the problem of verification and treatment of coronary heart disease (CHD). In particular, of particular importance are issues related to the diagnosis and treatment of the disease during its exacerbation, the development of a heart attack myocardial infarction (MI) and sudden death (VS). IHD is a common disease caused by atherosclerosis of the coronary arteries, as a result of which disrupts the balance between oxygen delivery and myocardial demand. Recently in the definition of various forms of its course, the terms "unstable angina" (UA) and "acute coronary syndrome with and without ST segment elevation" are widely used (OKSpST and OKSbpST). ACS includes NS and MI and has been introduced for convenience as a preliminary diagnosis, allowing the doctor at the first contact with the patient to determine urgent organizational and therapeutic measures. In the future, when monitoring the patient, with taking into account the results of clinical studies, a final, more specific diagnosis is made. NS -this is a severe period of exacerbation of coronary artery disease, threatening the development of MI or VS. In terms of clinical manifestations and prognostic value, it occupies an intermediate position between stable exertional angina and acute myocardial infarction. Previously used its definitions such as: “pre-infarction state”,"threatening myocardial infarction", "pre-infarction angina", "prodromal syndrome" [5].

Theroux (1995) recommends that the following clinical forms of the disease be classified as NS: progressive angina pectoris (PSK); first-time angina pectoris of exertion and rest; early postinfarction angina pectoris; angina pectoris after angioplasty; angina, developing after coronary artery bypass grafting; Prinzmetal's angina. Thus, we can say that we have, as cardiologists say, a “matryoshka doll”: ACS is divided into MI and NS, which in its the queue consists of several of the above and others known (Chernov S.A., Chernov A.P.) clinical forms, one of which is the most common PSC. PSC is characterized by an increase in frequency, the intensity and duration of attacks of retrosternal or other equivalent pain for angina pectoris, decreased tolerance for habitual physical or emotional stress, an increase in the number of nitroglycerin tablets consumed to relieve pain.

To date, it has become obvious that the causes of the progressive course of coronary artery disease in most cases are due to changes in the atherosclerotic plaque (AP) (inflammation, erosion and rupture plaques followed by thrombosis and microembolism coronary arteries). At the same time, the size of the plaques has relative importance for the development of critical conditions. It is necessary to have the so-called “vulnerable” plaque, the features of which are a large lipid core and a thin cap [1,2,5]. Factors contributing to atherosclerotic plaque damage can be divided into external and internal.

The former may include arterial hypertension, increased activity of the sympathoadrenal system, vasoconstriction (spasm of the coronary arteries), high levels of LDL, triglycerides, molecules such as fibrinogen, fibronectin, von Willebrand factor, the presence of a pressure gradient before and after stenosis, which along with periods of "extension-compression" in the places of branching and bending of the vessels leads to a weakening of the plaque structure [6,7]. Internal factors contributing to the weakening of the plaque structure are the predominance of the lipid core, a decrease in the number of smooth muscle cells and collagen synthesis, an increase in the activity macrophages inside the plaque and their apoptosis, inflammation inside the plaque, accompanied by its infiltration teg by macrophages [4].

Angiographic data [5,7], the results of intravital angioscopy [3] showed that with PSC in in most cases, there are tears, defects surfaces, ruptures of atherosclerotic plaques with release of highly thrombogenic contents, platelet activation, release of vasoactive substances and thrombus formation [5]. In some cases, a thrombus forms on the surface, i.e. located above the rupture (crack, defect) of an atherosclerotic plaque, penetrates into the plaque, leading to a rapid increase in its size [3]. In other cases, intermittent arterial occlusion occurs. The thrombus, protruding into the lumen of the vessel, does not cause its complete occlusion, but reduces blood flow, which is manifested by the PSC clinic.

Thrombi, both parietal and occlusive, are dynamic, so the blood flow in the corresponding vessel can repeatedly resume, then stop in for a short time. Thrombosis may develop suddenly or gradually (over several days) and is a dynamic process. But blood clots can completely close the lumen of the artery for a long time, leading to the development of myocardial infarction.

A thrombus that has not dissolved is replaced by a cicatricial tissue produced by smooth muscle cells. The results of this process can be a wide range of changes, from complete chronic vessel occlusion until full or partial restoration of its patency. The latter, apparently, determines the transition of the MCS to a stable state, but often with an increase in the functional class of the disease.

Spasm of the coronary vessels [3, 4], neurohumoral, and metabolic factors also play an important role in the pathogenesis of PSC. Spasm of the arteries, like a problem instability of AB, is inextricably linked with dysfunction endothelium (DE), which is understood as an imbalance between mediators that normally ensure the optimal course of all endothelium-dependent processes. risk factors for coronary artery disease, such as hypertension, diabetes mellitus, an increase in the amount of LDL, smoking contribute to an increase in the activity of peroxide lipid oxidation, which leads to the accumulation of anions oxygen superoxide. As a result of this process, a whole cascade of reactions is triggered: oxide inactivation nitrogen (NO), formation of peroxynitrite radical, oxidation of LDL, increased formation of adhesive molecules in vascular cells. Each of these reactions affects processes of atherogenesis, up to the rupture of the AB (Steinberg D.A., 1989). Along with this, endothelial NO deficiency leads to the predominance of vasoconstrictor reactions. In addition, the function of the endothelium (NO-synthase) is closely related to the oxygen transport function of the blood. (KTFK). For example, the inhibition of NO synthesis causes a decrease in tissue pO2, from which, in turn, turn dependent NO metabolism (formation of nitrate from nitrosohemoglobin). And the oxygen-binding properties of blood affect the activity of the L-arginine-NO system, which, in turn, affects the functional properties of hemoglobin, its affinity for oxygen (Zinchuk V.V., Borisyuk M.V., 2000). However, to date, with progressive angina pectoris, this interaction and the mutual influence of the function of the endothelium and CTFC not studied.

Glucose and free fatty acids (FFA) are the "fuel" for the heart. When a sufficient amount of oxygen is supplied, FFAs are the supplier of 60-80% of ATP. But to form the same amount of ATP, FFAs require 10% more oxygen than glucose. Therefore, under conditions of ischemia, aerobic oxidation of FFA and glucose decreases and the main source of ATP becomes anaerobic glycolysis. When the blood flow is restored, about 95% of ATP is again formed in due to FFA oxidation [16]. As a result of oxidation, hydroperoxides (diene conjugates) are formed, which then metabolized into secondary – malonic dialdehyde (MDA) and tertiary peroxide products lipid oxidation (LPO) - Schiff bases. LPO processes occur in all cells, but most leukocytes and platelets, as well as hepatocytes, serve as powerful generators of free radicals [24]. So Thus, hypoxia enhances lipolysis with excessive mobilization of fatty acids, which, in turn, activates the free radical oxidation of the latter. A pronounced predominance of FFA oxidation over glucose, and also their increased content in the ischemia zone is one of the main factors of reperfusion damage and development of myocardial dysfunction, dangerous cardiovascular complications, including cardiac arrhythmias [7].

Diagnosis of PSK is primarily based on the data of the anamnesis. Patients most often indicate the day (date) increasing the frequency, intensity and duration of pain. The nature of pain sensations, their irradiation may change. Pain appears in response to less stress or first appears at rest. Reduced effect nitroglycerin, the need for it increases. New symptoms for the patient join, such as shortness of breath, palpitations, nausea. Among laboratory data, a special place in the diagnosis of PSC is occupied by the determination of troponins T and I in peripheral blood, which are markers of damage to the heart muscle in patients with unstable angina [1,2]. Most often they are determined in the blood in those patients in whom the last seizure at rest developed within the next 48 hours or in patients in the presence of changes in the final part of the ventricular complex, transient changes in the ST segment on the ECG [7]. For the most accurate diagnosis of damage myocardium, it is recommended to determine the level of troponins T and I upon admission to the hospital, after 6-12 hours and after each intense attack of retrosternal pain (A.L. Syrkin, A.V. Dobrovolsky, 2001).

An increase in the level of troponin T in the peripheral blood is sometimes recorded in patients with PSK, but its numbers never reach the level of those in MI. True, a clear border, below which we have a "troponin-positive" PSC, and above - MI is still not installed. However, any increase in troponin T levels is a predictor of poor outcome diseases [1]. The level of activity of the cardiospecific CPK isoenzyme - MB in PSK remains normal or not exceeds 50% of the upper limit of normal. There is an increase in non-specific markers of inflammation, such as C-reactive protein (CRP), fibrinogen, etc. At the same time, there is evidence that an increase in the level of CRP is also a prognostically unfavorable factor, especially in "troponin-positive" patients.

Signs of myocardial ischemia in PSK are recorded on the ECG, especially during an attack, and consist of depression of the ST segment or, less commonly, in its rise above the isoelectric line, the appearance of tall T waves or their inversion. It is possible to observe various rhythm disturbances, conduction disturbances (atrial or ventricular extrasystoles, atrial fibrillation, transient blockade of the legs of the His bundle and etc.). These changes sometimes persist for up to 2-3 days. At Prinzmetal's angina often occurring changes on the ECG of the ST segment, T wave, and sometimes the complex

QRS, various cardiac arrhythmias and conduction disorders disappear after the attack stops. However, a number In patients with PSK, the above ECG data are not detected. In these cases, it is diagnostically important to use 24-hour ECG monitoring, which makes it possible to register episodes of transient ischemia both in the acute period of the disease and during the period of stabilization. With using this method, one can not only register ischemia, but also establish the number of painful, painless episodes, their distribution during the day, the direction of ST segment displacement, the magnitude of this displacement, the duration of each ischemic episode and total for the day, to identify violations of the heart rhythm. According to available data [8], painless myocardial ischemia (MIM) in 1/3 patients with PSK is accompanied by arrhythmias. It is believed that rhythm disturbances occur as manifestations of electrical instability. myocardium during its ischemia and are prognostic an unfavorable factor, since myocardial ischemia is fertile ground for the occurrence and fatal arrhythmias (A.N. Martynov et al., 1990). Another area of application of Holter ECG monitoring in patients with MI should be mentioned.

Its results can also be used to evaluate the effectiveness of antianginal therapy, since it is known that in some patients who have undergone treatment, there is a decrease or even disappearance angina attacks, but signs of painless ischemia of the heart muscle persist. Repeated studies using Holter monitoring ECG is also useful in the appointment and selection doses of drugs, including B-blockers that affect both heart rate and conduction, since with the help of only traditional clinical and electrocardiographic research methods individual response to medications difficult to predict and not always easy to detect.

Echocardiography in PSK can reveal a violation of the mobility of ischemic areas of the myocardium with a decrease in segmental contractility. The degree of these changes directly depends on the severity of the clinical manifestations of the disease, and as stabilization currents they disappear.

Therapeutic tactics in PSK. All patients with PSK are subject to urgent hospitalization in wards (blocks) of intensive observation and treatment. Patients are assigned bed rest. The full range of necessary clinical trials is being carried out. In parallel with the treatment, an ECG recording is performed in dynamics, and, if possible, round-the-clock ECG monitoring, which allows you to monitor the dynamics of the disease and the effectiveness of the therapy. With adequate treatment, a favorable course of the disease, stabilization of the process in a hospital is most often observed at 5-10 days [2], at this time, tests are carried out to determine the functional class of CH.

The treatment program consists of stopping pain, preventing the development of acute MI and related complications (anticoagulants and antiplatelet agents), eliminating myocardial ischemia with the use of nitrates, B-adrenoblockers, calcium antagonists, prescribing metabolic therapy, conducting balloon coronary angioplasty and coronary artery bypass grafting.

In the presence of coronary pain at the time of admission, the patient is given nitroglycerin 0.5 mg sublingually (up to three tablets with an interval of 5 minutes). Intravenous infusions of nitroglycerin are prescribed (avoiding a decrease in systolic blood pressure less than 100-90 mm Hg). With initial arterial hypertension, systolic blood pressure decreases by 15-20% of the original. Infusions of nitroglycerin are carried out within 1-2 days. If necessary, administration of narcotic analgesics should not be avoided. The introduction of morphine is especially indicated in those cases where attacks against the background of the maximum adequate treatments are repeated. Its administration is contraindicated in hypotension, respiratory disorders, confusion.

In the absence of contraindications, all patients with PSK should receive aspirin, the antithrombotic effect of which is based on the irreversible inhibition of platelet cyclooxygenase. As a result, platelets lose their ability to synthesize thromboxane A2 (TXA2), which induces platelet aggregation and has vasoconstrictive properties. AT As a result, the possibility of platelet aggregation and thrombus formation is reduced. With early use of aspirin, the number of developed MI is reduced by more than 50% compared with placebo [3]. In recent years, other antiplatelet drugs, such as clopidogrel, have increasingly been added to aspirin therapy. More favorable results are obtained by the combination of aspirin with heparin. Heparin infusion is carried out continuously for 48-72 hours with gradual cancellation under control of the activated partial thromboplastin time (APTT), increasing it in 1.5-2.5 times from the original. If it is impossible to control the APTT, the introduction of unfractionated heparin (UFH) under the skin of the abdomen is acceptable. Particularly promising in the treatment of NSCs are low molecular weight heparins (fraxiparin, dalteparin, etc.), which inhibit the blood coagulation cascade at the level Ha factor. They have a longer and more predictable effect compared

to conventional heparin, because they are better absorbed when administered subcutaneously, bind to blood plasma proteins less, are inactivated to a lesser extent by platelet factor 4.

Beta-blockers are important in the treatment of NSCs. They contribute to the elimination of myocardial ischemia, prevent sudden hemodynamic changes, reduce damage to blood vessels, inhibit the formation of lipid plaques and prevent their rupture, have an antiarrhythmic effect. When saving pain during therapy with beta-blockers, oral nitrates are also prescribed at the same time. The use of calcium antagonists is limited following clinical situations: arterial hypertension, variant angina, intolerance or lack of effect of adequately prescribed ?-blockers and nitrates. The appointment of calcium antagonists is contraindicated in unstable angina occurring in combination with heart failure.

It is known that only the above pathogenetic therapy is often not effective enough. It is necessary to prescribe metabolically active drugs with the purpose of regulating the existing violations.

So, formed in recent decades of the last century, the concept of the important role of free radical lipid peroxidation (LPO) makes justified and promising inclusion in the complex therapy of antioxidants - cytoprotectors (AO) [3, 4]. Numerous randomized doubles blind placebo-controlled clinical studies performed in the 90s of the XX century on large contingents [18, 20], using in some cases angiographic control to document the reduction of coronary stenosis [6], demonstrated a positive effect of tocopherol and other AOs on the course and outcome of cardiovascular diseases. However, the results of the multicenter Heart Protection Study (HPS), which ended in 2002, showed that the use of vitamins and other antioxidants requires further substantiation of their effectiveness [1, 5]. Recently studies are actively conducted with the use of cytoprotective antioxidants, in particular, emoxipin and trimetazidine. It is known that trimetazidine normalizes the level of ATP; reduces LPO and unfavorable influence of free radicals, has a positive influence on the clinical course of stable exertional angina (reduces the number of painful and painless episodes of ischemia).

Conclusion

Questions related to the effect of these drugs on CTFC and endothelial function have not been sufficiently studied. Accounting for these indicators and clinical manifestations (in particular, episodes of ischemia), in our opinion, will allow us to develop more effective modern tactics for the treatment of patients with progressive angina pectoris.

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