**ISCHEMIC HEART DISEASES**

The etiopathogenesis of IHD

The pathogenetic basis of ischemic heart diseases is the disturbance of the balance between oxygen demand and oxygen supply of the heart muscle. This discrepancy can be in 3 variants:

1. Although the oxygen demand of the heart muscle increases, the oxygen supply remains normal, i.e. unchanged. This is typical for coronary X-syndrome.

2. The oxygen demand of the heart muscle increases, but the oxygen supply decreases. This is typical for stenocardia (angina pectoris).

3. The oxygen demand of the heart muscle does not change, but the oxygen supply decreases. This is typical for spontaneous stenocardia (angina pectoris).

It is known that the heart itself is supplied with oxygen through the coronary vessels. It also depends on the tone of the coronary vessels and the condition of the collateral blood circulation. Violation of blood supply to the heart itself can be related to 4 groups of reasons, which are considered the main etiological factors of ischemic heart diseases:

1. Atherosclerosis of coronary arteries;

2. Spasm of coronary arteries;

3. Internal platelet aggregates in the coronary artery;

4. Microvascular dysfunction.

Atherosclerosis of coronary arteries. 90-95% of the etiological factors of İHD (coronary insufficiency) are related to atherosclerosis of coronary vessels. The formation of atherosclerotic nodes is a long-term process, sometimes it can last for several years. Although the vessel lumen is initially not significantly narrowed, endothelial integrity and dysfunction occur due to the accumulation of lipids in the vessel wall.

In recent years, the role of "endothelial factors" in the regulation of vascular tone should be specially noted. Currently, these substances are divided into 2 large groups: "vasodilators" and vasoconstrictors:

Vasodilators: Vasoconstrictors:

1. PG I2; 1. Endothelin – 1;

2. NO; 2. Thromboxane A2;

3. Endothelial hyperpolarizing factor; 3. PG H2;

4. Bradykin's. 4. Angiotensin – II.

Normally, there is a physiological balance between these substances. As a result of the impact of various damaging factors on the vascular endothelium, "endothelial dysfunction" occurs, which is accompanied by an increase in vascular tone, strengthening of platelet aggregation and acceleration of the thrombus formation process.

As the coronary artery narrows, the balance between myocardial oxygen demand and oxygen delivery is disturbed. When the coronary arteries narrow too much, the inactive capillaries also join the work of blood supply and cause the formation of new precapillary anastamoses - collaterals. However, if the vascular volume narrows by 80% or more, a critical situation occurs and blood supply to the myocardium is severely impaired.

*Spasm of coronary arteries*. Against the background of atherosclerosis of coronary vessels, arterial hypertension, diabetes, hyperlipidemia, obesity and other risk factors, primarily the decrease in NO and prostacyclin secretion from the coronary endothelium weakens the endothelium-dependent relaxation of coronary vessels. Also, endothelial vasoconstrictors - angiotensin-II, endothelin, thromboxane-A2, serotonin, etc. spasm of the coronary vessels disrupts myocardial perfusion and worsens the condition.

The decrease in endothelial production of PG I2 and NO during IHD not only has a negative effect on the relaxation of coronary vessels, but also enhances the aggregation of platelets. As a result, the thromboxane pathway of arachidonic acid metabolism is activated and an excess of thromboxane A2 is produced. Thromboxane A2 has both a vasoconstrictor effect on coronary vessels, and promotes thrombus formation by strengthening the aggregation of platelets.

One of the important causes of vasoconstriction against the background of atherosclerotic changes in patients with IHD is the activation of the sympathoadrenal system and high concentration of catecholamines during the disturbance of the nervous regulation of coronary blood circulation. The main factor here should be explained by the direct effect of catecholamines on coronary vessels through alpha-1 adrenergic receptors. Activation of the parasympathetic nervous system has a vasodilating effect due to M-cholinoreceptors.

*Intracoronary platelet aggregates.* The vascular-platelet system and coagulation hemostasis ensure the integrity of the vessel wall in healthy people. Platelet activation occurs under the influence of Willebrand factor, which is released during damage to the vascular wall, especially subendothelial tissue structures and collagen. The adhesion of platelets to the subendothelium of the damaged vessel wall is the initial stage of vascular-platelet hemostasis and related to the interaction of 3 components:

- Specific receptors of the platelet membrane (glycoprotein Ib, IIb, IIIa, etc.);

- Collagen;

- Willebrand factor.

Secreted catecholamine, serotonin and collagen released from cells damaged by ADF increase platelet aggregation ability. When platelets break down, some coagulation factors are released from them:

- Platelet factor III (thromboplastin);

- Antiheparin factor IV;

- Willebrand factor VIII;

- V Factor;

- B-thromboglobulin;

- Height factor, alpha 2-antiplasmin, fibrinogen, etc.

The interaction of fibrinogen with thrombocytes occurs due to IIb-IIIa specific receptors. Metabolites of arachidonic acid - thromboxane A2, PG I2 and other substances (thromboxane A2 is produced in platelets, and prostacyclin in vascular endothelium) also play a role in platelet aggregation. Activation of vascular-thrombocytic hemostasis in patients with coronary atherosclerosis also plays an important role.

*Microvascular dysfunction.* This mechanism is one of the important mechanisms of coronary blood circulation disorders, which is based on microvascular angina or "coronary X syndrome", which is a special form of IHD.

Although changes in large coronary arteries are not recorded during microvascular dysfunction, there are noticeable functional and morphological frustration in the distal part of coronary vessels. Changes are mainly recorded in coronary vessels-prearterioles, which are no more than 150-350 μm. At this time, due to the hypertrophy and hyperplasia of the gluteal muscles, significant narrowing of the small coronary vessels is observed.

It is considered that the significant dysfunction of the endothelium, as well as the strengthening of the production of vasoconstrictor endothelium and neuropeptide Y, are played impotant role of these changes. At the same time, the role of reduction of vasodilator nitric oxide (NO) and prostacyclin should be noted. As a result, a spasm of the prearteriole occurs and a transient ischemia area is formed in the heart muscle.

*Risk factors.* According to the recommendations of the American Cardiology Association, the following level of risk factors for the development of IHD is more dangerous:

1. Hypercholesterolemia - more than 6.7 mmol/l;

2. Triglyceridaemia - more than 2.9 mmol/l;

3. AT – 160/95 mm col. and when it exceeds;

4. More than 30% of body weight;

5. Hyperglycemia - more than 6.6 mmol/l on hungry;

6. Reduced glucose tolerance or acute glucosuria.

The classification of the IHD. Although there is no universally accepted classification of IHD, the classification put forward by G. E. Roytberg and A. V. Strutynsky in 2003 is practically more noteworthy:

1. Sudden coronary death (primary cardiac arrest);

2. Stenocardia (Angina pectoris):

2.1. Stable tension Stenocardia (angina pectoris) (mentioned with I - IV functional class);

2.2. Unstable Stenocardia (angina pectoris);

2.2.1. Primary Stenocardia /angina pectoris/ (sometimes with a stable course);

2.2.2. Progressive Stenocardia /angina pectoris/

2.2.3. Stenocardia (angina pectoris) from early post-infarction and post-surgical;

2.3. Spontaneous (vasospastic, variant, Prinsmetal) Stenocardia /angina pectoris/

3. Painless myocardial ischemia

4. Microvascular angina ("Syndrome X")

5. Myocardial infarction:

5.1. Q-shaped myocardial infarction (wide focus, transmural);

5.2. Q-toothless myocardial infarction (small focus, non-transmural);

6. Post-infarction cardiosclerosis

7. Heart failure (indicating forms and sources)

8. Violation of heart rhythm and conduction (showing its shape).

 ACUTE CORONARY SYNDROME

"Acute coronary syndrome" is a group of clinical signs and symptoms that give reason to suspect the development of acute myocardial infarction or unstable angina pectoris, and its pathophysiological basis is related to thrombosis that causes acute blockage of the coronary artery. The development of ACS can be related to exogenous and endogenous factors.

The following clinical forms of IHD can be attributed to acute coronary syndrome:

1. Unstable Stenocardia (angina pectoris);

2. Myocardial infarction with a small focus not accompanied by ST segment elevation;

3. Myocardial infarction accompanied by ST segment elevation;

4. Recurrent myocardial infarction;

5. Sudden complete blockade of the left leg of the sensory group.

**MYOCARDIAL INFARCTION**

Myocardial infarction- is ischemic necrosis of the heart muscle, which develops as a result of acute coronary insufficiency. This disease is distinguished by its high lethality among the IHD. Etiology of myocardial infarction:

- Atherosclerosis of coronary arteries;

- Embolism of coronary arteries (intraventricular thrombi, infectious endocarditis);

- Extented spasm of coronary vessels (more than 20-40 minutes).

Coronary blood flow interruption or acute deterioration is often associated with coronary thrombosis. Coronary thrombosis usually develops in the area of the atherosclerotic nodule. At this time, the background for the activation of platelet and plasma factors of the coagulation system is created. First, a " frontwall " thrombus that does not completely stop the blood flow is formed. If spontaneous lysis of the thrombus does not occur due to the activation of the fibrinolytic system, or if thrombolytic treatment is not performed, the size of the thrombus in front of the wall gradually increases, the thrombus completely closes the vessel opening (occlusion) and transmural myocardial infarction (Q-clove MI) develops.

If, for various reasons, the thrombus formed in the coronary vessels does not create a complete occlusion or spontaneous lysis of the thrombus occurs, subendocardial or intramural myocardial infarction (Q- cloveless MI) may develop. Studies show that in 70-80% of cases, the process of complete thrombus formation (occlusion) can take from 2-3 days to 2-3 weeks. During this period, the progressive deterioration of coronary blood circulation corresponds to the symptoms of unstable angina pectoris (pre-infarct condition). In about 20-30% of cases, total thrombus formation should end very quickly, suddenly. At this time, early symptoms of the disease are not manifested in the clinic.

The role of acute and extended spasm of coronary vessels in the development of myocardial infarction should be noted. These mechanisms should cause myocardial infarction without Q clove mainly in patients with acute organic narrowing of coronary vessels. As we mentioned, according to the level and depth of damage, transmural (Q-clove) and non-transmural (without Q-clove) forms of myocardial infarction are distinguished.

The following stages are distinguished in the course of myocardial infarction:

1. The most acute period (stage I) is the stage between the formation of the ischemic area in the myocardium and the formation of the necrosis center, which lasts from about 30 minutes to 2 hours;

2. Acute period (stage II) – the stage of formation of necrosis area and myomalacia, lasts for about 10 days, it should take longer if the disease has a protracted and relapsing course;

3. Semi-acute period (III stage) – the initial stage of scar tissue formation ends. This stage lasts from the 10th day of the disease to the end of the 4th-8th week;

4. The post-infarction period (stage IV) is the stage of maximum adaptation of the myocardium to the hardening of the scar tissue and the functioning of the cardiovascular system in new conditions. This stage lasts for 2-6 months from the moment of formation of scar tissue.

A complete diagnosis of myocardial infarction should be made based on ECG data and clinical and biochemical examination of blood on the basis of resorption-necrotic syndrome.

**LABORATORY DIAGNOSIS OF ISCHEMIC HEART DISEASES**

Laboratory diagnosis of ischemic heart diseases should be conventionally classified as follows:

1. Laboratory indicators of the risk of developing cardiovascular diseases;

2. Laboratory indicators of differential diagnosis of acute coronary syndrome;

3. Laboratory indicators of chronic heart failure.

**LABORATORY INDICATORS OF THE RISK OF DEVELOPING ISCHEMIC HEART DISEASES**

Classic risk factors for ischemic heart diseases belong to arterial hypertension, nicotinism, hypodynamia, alcoholism, hypercholesterolemia, and etc. diabetes. Previously, hypercholesterolemia, which developed against the background of elevated chylomicrons and low-density lipoproteins, was considered a decisive laboratory risk factor for IHD. However, it has been proven by modern studies that no risk factor was detected in approximately 20% of patients with coronary insufficiency, and only 1% of patients with 4 risk factors at the same time. In modern times, it has been proposed to determine the following as more sensitive laboratory indicators for the risk of development of IHD:

- Highly sensitive C-reactive protein (CRP);

- Lipoproteins (LP);

- Lipoprotein-associated phospholipase A2 (LP – PLA2);

- ApoB/ApoA1 ratio;

- I and T as highly sensitive cardiac troponins.

***High-sensitivity C-reactive protein*** - previously CRP in the subclinical range (less than 5 mg/l) was not considered a significant indicator. It has been proven by numerous studies that the increase in the level of high-sensitivity C-reactive protein is an indicator of the initial stage of endothelial dysfunction. So that:

- more than 3 mg/l – at high risk of acute coronary changes and stroke (at least in the next 5 years);

- 2.0 – 2.9 mg/l – moderate risk;

- 1.1 – 1.9 mg/l – low risk;

- less than 1.0 mg/l - indicates minimal risk.

It should be noted that the level of highly sensitive CRP is considered the main indicator of cardiovascular risk even in practically healthy people with low CM and LDLP.

The level of highly sensitive CRP can be considered an important prognostic indicator of developed acute coronary syndrome, especially in the first hours when the patient is admitted to the hospital. Thus, CRP less than 3 mg/l indicates a low risk of dangerous outcome.

***Lipoproteins***- are considered important risk factors not only for IHD, but also for acute coronary syndrome. It is known that its level is determined by hereditary characteristics. The level of lipoproteins in the blood of 0.3 g/l indicates a low risk of cardiovascular diseases, 0.3-0.5 g/l is a high risk, and more than 0.5 g/l is a very high risk. is evaluated as a factor. Epidemiological studies have shown that people with normal cholesterol levels, but lipoproteins above 0.3 g/l, have at least a 2-fold increased risk of IHD. If ASLP is elevated at the same time, the risk of ischemic heart diseases increases up to 8 times.

**Lipoprotein-related phospholipase A2** (platelet-activating factor - acetylhydrolase) is a specific indicator of vascular inflammation and is the main predictor of myocardial infarction and ischemic stroke. The level of lipoprotein-associated phospholipase A2 in blood plasma ranges from 0.29 to 50 ng/ml. In people whose LDLP is less than 3.36 mmol/l, the risk of acute coronary syndrome is 4.2 times higher, and the risk of strokes is 10.8 times higher in people with high sensitivity CRP and LP-PLA2 at the same time.

***ApoB/ApoA1 ratio*** – predicts MI risk even in people with normal lipid levels. Each primary lipoprotein contains a specific protein - Apo. ApoA1 is considered the main constituent protein of HDLP. They participate in the transport of triglycerides and chylomicrons, and play a role in transporting chylomicrons from the periphery (including the vessel wall) in the opposite direction to the liver. ApoB is a major component protein of LDLP, which transports TG from the intestine to adipose tissue. It is appropriate to determine both indicators for diagnostic purposes. If the ratio of ApoB to ApoA is greater than 1, the risk of ischemic heart disease is considered high.

- I and T as high-sensitivity cardiac troponins will be reported below.

**LABORATORY INDICATORS OF DIFFERENTIAL DIAGNOSIS OF ACUTE CORONARY SYNDROME**

Determination of differential diagnostic indicators of acute coronary syndrome - myocardial infarction, unstable angina, stable angina and minimal damage to the myocardium is of particular importance in practical medicine. Especially during the early periods of atypical and recurrent myocardial infarction, the study of laboratory indicators plays a major role. ECG data loses its diagnostic value in many cases. Especially in the early hours of ACS, there should be no characteristic changes.

Biochemical indicators of damage in the myocardium are called cardiomarkers. Most of these proteins contained in cardiomyocytes are practically not detected in various tissues and cells of the body.

In modern times, the main biochemical cardiomarkers of acute myocardial infarction are as follows:

- T and I troponins;

- CPK-MB isozyme;

- AsAT;

- LDH - 1 isozyme.

- Myoglobin;

Cardiac troponins T and I have unique amino acid sequences with cardiospecific properties in their structure, which are not present in skeletal muscle. Troponin T and I are of broad diagnostic importance as proteins whose concentration increases early after myocardial necrosis. Especially in the first hours of AMI, the effectiveness of thrombolytic treatment significantly increases the relevance of early diagnosis. The activity of many enzymes, except CPK-MB, increases when the chance of thrombolytic treatment is missed. Therefore, the determination of cardiospecific troponin T and I is also important for the diagnosis and prediction of CMI, which is very important. Unlike myoglobin, the detection of these isoenzymes is highly specific for myocardial damage.

Two rising waves of troponin T (norm: 0-0.2 mg/l) are observed. The first wave is recorded 3-8 hours after the injury, and the peak level is recorded 12-18 hours after the disruption of the blood supply in the heart due to the rapid transfer from the injured cardiomyocytes to the blood. The second wave of troponin T elevation is recorded on the 3-4th day after injury due to the slow release of troponin-tropomyosin complexes from the necrosis site. On the 7-10th day of myocardial necrosis, the level of Troponin T decreases to 0 and becomes completely normal. The degree of increase of this indicator in the blood serum and its duration depends on the area of the necrosis site.

Troponin I is distinguished by its high cardiospecificity compared to Troponin T, especially this indicator is of great diagnostic value if the patient suffers from IHD and renal failure at the same time. The dynamics of changes in blood serum of Troponin I during myocardial necrosis is similar to that of Troponin T, but there is no second rising phase. The normal concentration of this indicator is up to 3.1 mg/l (Figure 1.1).

**50**

**Myoglobin**

**Cardiac troponins**

**Ascent rate (how many times)**

**KFK-MB**

**fraksiyası**

**The upper limit of the norm**

**1**

**5**

**6**

**7**

**8**

**9**

**2**

**4**

**3**

**20**

**10**

**5**

**2**

**0**

**1**

**LDH**- 1

**AsAT**

**Days after the start of KMI**

Figure 1.1. The dynamics of changes in cardiomarkers during CMI

It should be noted that an increase in the level of cardiac troponins II can also be recorded during the following pathologies:

Currently, a high-sensitivity test system has been developed that allows determining troponins even in very small concentrations (1-20 ng/l). Through this system, cardiac troponins are detected in almost 100% of healthy people. This highly sensitive test system can be used to accurately distinguish between CMI and angina pectoris, as well as to predict coronary lesions, by recording the elevation of cardiac troponins in the first hours of acute myocardial infarction.

***Myoglobin*** compared with cardiac troponins, especially in the first hours of CMI

it is considered a more sensitive cardiomarker (due to its small molecular weight and presence in the cytoplasm, this protein is already detected in the blood in the first half hour of injury). The norm of myoglobin in the blood is up to 40 ng/ml. During myocardial necrosis, the concentration of myoglobin increases 10 times or more after 0.5-2 hours (the maximum increase is recorded after 4-8 hours). On the first day of CMI, normalization is already registered. The disadvantage of this indicator is related to its low cardiospecificity. Thus, myoglobin is detected in both cardiac and esophageal muscle tissue.

In clinical practice, the determination of myoglobin is important to rule out MI (myoglobin concentration does not rise after an acute pain attack in a patient, which rules out myocardial damage).

***Creatine*** ***kinase***. Although creatine kinase is present in many tissues, it is mainly detected in 3 tissues: heart muscle (myocardium), skeletal muscle and brain. This enzyme consists of M and B protein complexes. Therefore, 3 structurally different isozymes - CPK-MM, CPK -BB and CPK -MB are distinguished. Creatine kinases are organ-specific, CPK -BB is found mostly in brain tissue, CPK -MM in skeletal muscles, and CPK -MB isozyme in heart muscle. Therefore, in the diagnosis of MI, not the total activity of creatine kinase, but the determination of its CPK -MB isozyme plays an important role. 4-6 hours after the development of CMI in the patient, the level of CPK -MB rises in the blood and reaches its maximum in 24 hours. 2-3 days after the development of myocardial infarction, the level of CK-MB returns to normal. The level of elevation of this isoenzyme depends on the size of the necrosis site. To rule out a myocardial infarction, it is necessary to determine the function of CPK -MB every 8 hours (at least 3 negative results should be obtained).

A more sensitive and effective diagnostic method of KMI is not the activity of CPK -MB, but the detection of the direct quantitative level of this isoenzyme in a blood test. It has been proven that the quantitative level of CPK -MB in the blood plasma during CMI rises earlier (in the first 2-4 hours) than its total activity and returns to normal after 70 hours, that is, the "diagnostic window" of this indicator is longer. Therefore, in many countries of the world, for the diagnosis of CMI, it is preferred not to determine the activity of CPK -MB, but its quantitative level.

***Aspartate aminotransferase***. This enzyme is widely distributed in body tissues, especially in myocardium, skeletal muscles and liver. This enzyme is detected both in kidney cells and erythrocytes.

 The level of the aspartate aminotransferase enzyme begins to rise approximately 8 hours after the onset of CMI, reaches its maximum level in 24 hours, and the normalization of the enzyme activity occurs in 2-3 days.

***Lactate dehydrogenase***. This enzyme is widely distributed in body tissues. The highest activity of this enzyme is recorded in skeletal muscles, liver and myocardial muscle. But it is also found in kidneys, pancreas, erythrocytes and lungs. Functionally and structurally, several forms of LDH - isozymes are distinguished. 5 isozymes of LDH are identified. Like CPK, they are also organospecific. While LDH 5 is mainly accumulated in the liver and skeletal muscles, more LDH1 is detected in the heart muscle. In many cases, the total activity of LDH (the sum of LDH1, + LDH2 + LDH3, etc.), and in some laboratories, the activity of LDH1, which is specific for the heart muscle, is determined.

An increase in the level of the LDH1 isoenzyme during CMI is characteristic. The level of this isoenzyme begins to rise 6-12 hours after the onset of the disease. At this time, the total level of LDH is still within the norm. An increase in the activity of LDH1 is not considered an absolute criterion of CMI, so it is possible that the activity of this enzyme can increase against the background of acute coronary ischemia even without the focus of necrosis in the myocardium. However, at this time, the maximum activity of LDH1 should increase more than 2 times the normal level, and its normalization occurs in 10-12 hours. This indicator is used as an auxiliary criterion for diagnosing CMI. Table 1.1 shows the change indicators of cardiomarkers during CMI.

 Table 1.1. The duration of changes of cardiomarkers during CMI

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  **Indicators** | **Time from onset of ischemic seizures** | **Ascension period** | **Maximum rate of Ascension, with times** | **Specificity, in %** | **Sensitivity, in %** |
| **Start of Ascent (hours)** | **Maximum****(saat)** |
| **1** | **2** | **3** | **4** | **5** | **6** | **7** |
|  **Myoglobin** | **0,5 - 2** | **4 – 8** | **1 day** | **5 - 20** | **60** | **91** |
| **Troponin I** | **4 – 6** | **14 – 20** | **Up to 7 - 10 days** | **20 - 50** | **95** | **100** |
| **Troponin T** | **3 – 4** | **10 – 24** | **Up to 14 days** | **30 – 200** | **95** | **100** |
| **LDH1** | **6 – 12** | **36 – 72** | **1-2 weeks** | **20** | **90** | **95** |
| **KK - MB**  | **4 – 6** | **12 – 24** | **2-3 weeks** | **3 – 30** | **90** | **88** |

The determination of cardiomarkers is important not only in the diagnosis of CMI, but also in terms of detecting the risk of reinfarctions, minor myocardial damage, and progression of unstable Stenocardia (angina pectoris) (table 1.2).

 Table 1.2. Clinical indicators for determining the main cardiomarkers

|  |  |  |
| --- | --- | --- |
| **Cardiomarker** | **Clinical indication** | **Characterization of the marker** |
| **1** | **2** | **3** |
| **Troponin I** | **Doubt about the development of CMI****Assessment of the risk of progression of SCC****Identification of MCP****Monitoring of reperfusion** | **A specific marker during acute coronary syndrome** |
| **Troponin T** | **Doubt about the development of CMI****Unstable Stenocardia (angina pectoris) - assessment of the risk of progression of UAP****Minor injuries of the myocardium - identification of MCP****Monitoring of reperfusion** | **A specific marker during acute coronary syndrome. The specificity is less than that of Troponin I.** |
| **Myoglobin** | **Doubt about the development of CMI****Detection of reinfarction****Monitoring of reperfusion** | **A highly sensitive marker in acute coronary syndrome, but not specific enough. Elevation of the concentration factor can also be observed in skeletal muscle diseases and other pathological conditions not related to the heart.** |
|  **CPK-MB** | **Doubt about the development of CMI** | **It is a good cardiospecific marker during CMI.****A possible sporadic increase in concentration can also be observed in patients with diseases of skeletal muscles and other pathological conditions not related to the heart.** |

Heart-type protein (s-FABP, H-FABP) that binds fatty acids should be mentioned as new markers of myocardial necrosis. It is a cytoplasmic protein that binds the chain of fatty acids. This indicator increases in the blood after 1.5-3 hours during BMI, and returns to normal after 24 hours. Although s - FABP has the same growth dynamics as myoglobin, it has significantly greater specificity. The European Company of Cardiology recommends determining the amount of H-FABP in the blood to prevent early myocardial necrosis when acute coronary syndrome is suspected.

Diagnosis of CMI usually begins with an ECG based on the symptoms of the disease. The main symptoms and manifestations of myocardial infarction are as follows:

- Constant and strong pains in the chest, which can radiate to the left arm, neck and lower jaw;

- Wakefulness, cold and wet extremities;

- Shortness of breath, nausea and vomiting;

- Changes in arterial pressure;

- ECG changes - mainly ST segment elevation, T clove inversion and Q clove formation.

Against the background of these changes, the determination of the level of myocardial enzymes serves to confirm the diagnosis. The above-mentioned changes in the ECG may not be recorded in all patients with myocardial infarction. In almost 30% of cases, the typical changes on the ECG are not enough to diagnose CMI. It is in such cases, and in general, that the determination of the activity of cardiospecific enzymes is very important to make or rule out the diagnosis of acute myocardial infarction.

**EXTRACARDIAC CAUSES OF ELEVATED MYOCARDIAL ENZYMES**

The concept of "myocardial enzymes" does not mean that these enzymes are found only in the heart muscle. Creatine kinase, AST and LDH are also detected in the digestive tissues, their level increase is not only observed in heart diseases. This may complicate the interpretation of the results to diagnose MI.

The CPK enzyme is also abundant in skeletal muscles, the level of this enzyme in the blood increases in their diseases (for example, muscular dystrophy) and injuries. An increase in the level of CPK can even be caused by an intramuscular injection or physical exertion. A significant increase in the level of this enzyme is recorded against the background of muscle damage (especially frozen wounds) during trauma and surgery. Since CPK accumulates in the brain tissue, its high level can be an indicator of the destruction of nerve cells against the background of brain injuries and blood circulation disorders. A small amount of CPK -MB isozyme is detected in skeletal muscles. Therefore, its level increase (less than the total CK level) can be observed during severe injuries and diseases of skeletal muscles.

Liver cells are rich in AsAT and LDH, so an increase in the level of these enzymes can be recorded during liver diseases. Determination of the activity of these two enzymes is of diagnostic importance during liver pathologies. In particular, a high increase in their level is characteristic of acute infectious hepatitis, while a moderate increase can be recorded in cirrhosis, diseases of the biliary tract, and liver cancer.

A certain amount of LDH and AsAT enzymes are detected in erythrocytes. Therefore, the intensive breakdown and renewal of erythrocytes is accompanied by an increase in LDH activity. This includes various forms of hemolytic anemias and acute leukemias. Elevated levels of LDH are characteristic of megaloblastic anemia, which develops during vitamin B12 and folic acid deficiency. Extracardiac causes of elevated myocardial enzymes are listed in table 1.3.

Table 1.3. Extracardiac causes of elevated myocardial enzymes

Cədvəl 1.3. Miokardial fermentlərin yüksəlməsinin ürəkdən kənar səbəbləri

|  |  |  |
| --- | --- | --- |
|  | **Enzymes** | **Extracardiac pathologies** |
|  | **1** | **2** |
| **1** | **Total creatine kinase** | **Muscular diseases (muscular dystrophies)****Muscle injuries (trauma and operations)****Heavy muscle work****Intramuscular injection****Brain injuries****Cerebral circulatory disorders** |
| **2** | **Creatine kinase MB (CPK-MB isozyme)** | **It can be slightly increased during severe muscle diseases and injuries** |
| **3** | **Aspartate aminotransferase (AsAT)** | **Liver diseases****Hepatitis (very high level)****Cirrhosis****Obstructive diseases of biliary tract****(gallstones)****Liver cancer****Infectious mononucleosis****Severe hemolytic anemias** |
| **4** | **Lactate dehydrogenase (LDH)** | **Pathologies of erythrocyte damage****Hemolytic anemias****Acute leukemia****Lymphoma****Megaloblastic anemia (very high level)****Liver diseases****Hepatitis****Infectious mononucleosis****Other reasons****Pulmonary embolism****Malignant tumors of various localization** |

**LABORATORY INDICATORS OF CHRONIC HEART FAILURE**

***Natriuretic peptides*** - atrial natriuretic peptide, brain natriuretic peptide and C - natriuretic peptide are distinguished. This group of hormones is synthesized in the heart atria, ventricles and vascular wall endothelial cells, respectively. The main stimulus for the secretion of NP is the increase in myocardial tension when the pressure in the left ventricle of the heart increases.

*BNP* - when the volume of circulating blood increases, tension occurs in the atrial wall and is secreted into the blood from the atrial cardiomyocytes. This hormone is considered an antagonist of the renin-angiotensin-aldosterone system. Thus, it accelerates renal blood circulation and glomerular filtration, slows down the reabsorption of sodium and water in renal tubules, and increases their urinary excretion and diuresis. This, as a result, normalizes the volume of circulating blood. By reducing the resistance of the general vessels and the resistance of the pulmonary arteries, it increases the strength of heart contractions, produces a vasodilator effect, and reduces the concentration of renin, aldosterone, noradrenaline and endothelin-1 in the blood.

*Brain NP* – secreted mainly by ventricular cardiomyocytes during direct myocardial loading. Ventricular NP, like atrial NP, has a diuretic and vasodilator effect. This peptide was named as such because it was first detected in the brain extract of animals.

*C-natriuretic peptide* is mainly synthesized in the CNS. This peptide has a limited diuretic and vasodilator effect.

During heart failure, the concentration of NP in the blood increases. In laboratory conditions, it is preferable to determine more BNP and its precursor proBNP (especially its inactive form, NT-pro BNP). NT-pro BNP has some advantages over BNP in its biochemical marker properties. Thus, this marker circulates more in the blood at a relatively high concentration (the elimination time of BNP is 20 minutes, and for NT-pro BNP, this time is 60-100 minutes). Elevation of blood BNP and NT-pro BNP is proportional to the severity of heart failure. Even with minimal symptoms of heart failure, the level of NT-pro BNP should rise up to 25 times. An increase in the concentration of BNP in the blood over 400 pg/ml, and the level of NT-pro BNP over 2000 pg/ml is considered an indicator of chronic heart failure. The significance of this valuable test should decrease in some other pathologies (for example, renal failure) in which the level of NT-pro BNP is elevated. Determination of NT-pro BNP in patients diagnosed with chronic heart failure is also important in terms of assessing the severity of the disease and monitoring the effectiveness of the treatment. Thus, the rise of this marker 2-3 times more than the initial level after the onset of the disease can be considered an indicator of a significant worsening of the condition.