Biochemical indicators of acute myocardium infarction

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Content

Acute coronary syndromes (ACS; acute myocardial infarction , AMI, and unstable angina pectoris) arise due to coronary artery occlusion, mostly due to thrombotic complications. When blood flow is reduced, *myocardial ischemia* occurs , which is initially *reversible* . If blood flow is not restored in time, *irreversible* changes accompanied by cell death and necrosis (definitive myocardial infarction) occur after about an hour.

Laboratory examination methods play an important role in the diagnosis of acute coronary syndrome. Biochemically important components of the cardiomyocyte are found *in the cytoplasm or mitochondria* and others are part of the *contractile apparatus* . In myocardial infarction, they are released into the circulation. The course of their serum levels depends on several factors:

- for localization in the cell;

  In *short-term ischemia ,* cytoplasmic proteins are flushed into the bloodstream due to functional and later structural changes in cell membranes .
  With *longer-term ischemia , tissue necrosis develops and* structural proteins are released into the bloodstream . Thus, cytosolic proteins are released faster than structural proteins.

- at relative molecular weight - smaller proteins are released into the circulation faster;
- on the rate of excretion - smaller molecules are eliminated more quickly by the kidneys;
- on blood flow in the affected area.

Basic characteristics of biochemical parameters of myocardial infarction

Component	Mr [Da]	Biological half-life	Cell localization
Creatine kinase (CK)	86 000	17 h	cytoplasm
• isoenzyme MB (CK-MB)	86 000	13 h	
Lactate dehydrogenase (LD) (mainly isoenzyme LD 1)	135 000	110 h	
Myoglobin	17 800	15 min	
Cardiac troponin T (cTnT) (cytoplasmic fraction)	37 000	2-4 h	
Cardiac troponin I (cTnI) (cytoplasmic fraction)	22 500	2-4 h	
Cardiac troponin T (cTnT)	37 000	2-4 h	fibrillar contractile complex
Cardiac troponin I (cTnI)	22 500	2-4 h	
Aspartate aminotransferase (AST) (mitochondrial isoenzyme)	93 000	34 h	mitochondria

The course of biochemical levels in acute myocardial infarction

Parameter	Start of rising levels [h]	Peak levels [h]	Normalization [days]	Maximum level increase [multiple of upper limit of normal]	Normal values
Myoglobin	0.5-2	4–10	0.5-1	20 ×	M 19–92 µg / l F 12–76 µg / l
CK mass	2-6	12-24	2-3		0.0–5.0 µg / l
CK-MB	3-6	16–36	3-5	25 ×	M 0.2–3.6 µkat / l Ž 0.2–3.1 µkat / l
cTnT	3-8	12-18 (1st peak) 72-96 (2nd peak)	7–14	300 ×	0.00-0.05 µg / l
cTnI	3–12	12-24	5–10		0.0–0.1 µg / l
AST	4-8	16–48	3-6	25 ×	0.05–0.72 µkat / l
LD	6–12	24–60	7-15	8 ×	3.5–7.7 µkat / l

1. ↑ The upper limit depends on age - the values given are for the age of 40-50 years.

Cytoplasmic proteins

Myoglobin

Conformation of the myoglobin molecule Myoglobin is a globular protein consisting of a single chain of amino acids that contains heme as a prosthetic component . It reversibly binds and transports oxygen in muscle cells. Myoglobin from skeletal muscle and myocardium is identical . In the kidneys , it is filtered through the glomerular membrane and excreted in the urine. It has a very short biological half-life - 10-20 minutes.

Unlike hemoglobin , myoglobin contains only one heme group and one globin chain, and therefore can transport only one O 2 molecule . The affinity of myoglobin for oxygen is higher compared to hemoglobin .

As *a low molecular weight cytoplasmic protein,* it is rapidly released from the affected tissue. Elevated serum myoglobin levels in acute myocardial infarction (AMI) begin rapidly (0.5–2 hours) from the onset of chest pain. Myoglobin levels, which can reach 20 times physiological levels, peak in about 6-12 hours and return to baseline

within 12-24 hours. Myoglobin is considered to be the most sensitive biochemical marker of acute myocardial infarction suitable for early detection . The disadvantage of myoglobin determination in AIM is the lack of cardiospecificity . Its increase can be observed:

- any skeletal muscle damage (including eg intramuscular injections or minor bruising after a fall),
- after a large muscular load (including, for example, the connection of the abdominal press during prolonged vomiting),
- in renal insufficiency.

Myoglobin determination may rule out an acute myocardial infarction: if it is certain that the blood was taken outside the diagnostic window, ie more than 2 hours after the onset of chest pain or other symptoms, and if serum myoglobin is within the reference range, the diagnosis of acute infarction is myocardial infestation. If myoglobin is positive, it is necessary to differentially consider the reason for its increase (myocardium, skeletal muscle, renal insufficiency) and it is usually necessary to evaluate more specific cardiomarkers - troponin or CK-MB mass .

Various immunochemical methods are used for the determination (immunoturbidimetry, immunonephelometry, enzyme immunoassays, rapid immunochemical tests).

Creatine kinase

Creatine kinase (CK , EC 2.7.3.2) is a predominantly cytoplasmic enzyme that catalyzes the phosphorylation of creatine to creatine phosphate by ATP. In the absence of ATP, the reaction proceeds in the opposite direction. CK is found mainly in skeletal muscle, myocardium and brain tissue. It consists of *two subunits* , which are of two types - M (*muscle*) and B (*brain*), each with a relative molecular weight of about 40,000. The different subunits represent *three creatine kinase isoenzymes* :

- CK-BB (CK-1, brain isoenzyme);
- CK-MB (CK-2, myocardial isoenzyme);
- CK-MM (CK-3, muscle isoenzyme).

CK-MM predominates in skeletal muscle, but CK-MB isoenzyme is also present. In the brain, we find the isoenzyme CK-BB, which we do not detect when the blood-brain barrier is intact. CK-MB is typical for the myocardium, but the heart muscle also contains CK-MM.

The catalytic concentration of total CK increases within 3-6 hours from the onset of myocardial ischemia. Due to insufficient cardiospecificity, its determination is of limited importance in acute myocardial infarction. The value of total CK is influenced by various factors (age, gender, muscle mass and physical activity).

Examination of the CK-MB isoenzyme has greater diagnostic value. Even CK-MB is not fully cardiospecific. The increase may also be due to skeletal muscle damage (trauma, muscular dystrophies, intramuscular injections, resuscitation, defibrillation), extreme exercise and chronic renal failure. Spatial structure of creatine kinase CK-MB can be determined as an *enzyme activity* that captures only the active molecules of the enzyme, or immunochemically as a protein *in terms of mass concentration* . In this case, we are talking about CK-MB mass , which is clearly preferred today. The determination of CK-MB mass is *more specific and sensitive* , because it also demonstrates partially degraded molecules that have already lost enzyme function.

According to current recommendations, the determination of CK-MB mass is acceptable only in the case of unavailability of the determination of cardiospecific troponins. Furthermore, CK-MB mass is used to detect reinfarction at a time when high concentrations of cTn still persist.

Lactate dehydrogenase

Pyruvate is reduced to lactate with NADH consumption Lactate dehydrogenase (LD or LDH , EC 1.1.1.27) is an redox enzyme that catalyzes the reversible conversion of lactate to pyruvate . The structure of the molecule consists of 4 subunits with a relative molecular weight of 34,000. Each of these subunits can be either M (*muscle*) or H (*heart*), so there are a total of 5 isoenzymes called LD 1 (with subunit composition H 4) to LD 5 (M 4). LD is present in the cytoplasm of many tissue cells. It is released into the circulation even with mild tissue damage.

Lactate dehydrogenase isoenzymes

isoenzyme	subunits	occurrence
LD 1	H 4	myocardium + erythrocytes
LD 2	H 3 M	myocardium + erythrocytes
LD 3	H 2 M 2	skeletal muscles
LD 4	HM 3	liver + skeletal muscles
LD 5	M 4	liver + skeletal muscles

Examination

An increase in the catalytic concentration of total LD in the serum accompanies a number of diseases. Currently, the determination of total LD activity is used as a non-specific marker of cell lysis, eg in cancer (leukemia , testicular tumors). A late increase in total LD after myocardial infarction , which can last for up to 15 days, is also

characteristic. Due to the high erythrocyte content, haemolysis may falsely increase serum concentrations . The use of LD and its isoenzymes for the diagnosis of acute coronary syndrome is now considered obsolete.

The physiological upper limit of LD for adult men and women is 4.10 μkat / l.

An optical test is used for the determination . The presence of isoenzymes can be determined electrophoretically .

Mitochondrial proteins

Aspartate aminotransferase

Aspartate aminotransferase (AST) is present in the myocardium in relatively high concentrations. Historically, it is one of the first used biochemical indicators of acute myocardial infarction, but today it is no longer recommended in this indication.

See the Aspartate aminotransferase page for more information .

Structural proteins

Troponins

Troponin T (TnT) and troponin I (TnI) are used as cardiomarkers . TnT and TnI occur in skeletal muscle and myocardium . Cardiac isoforms (cTnT and cTnI) have a unique amino acid composition and are therefore specific for the myocardium . In most cases, the cardiac isoforms TnT and TnI are contained in the contractile apparatus and are released due to proteolytic degradation. Only 6-8% cTnT and 2.8-8.3% cTnI form the unbound cytosolic component. Troponin structure Troponin cTnT is not normally present in the blood . The course of cTnT release is *biphasic* . The increase in troponin after the onset of an acute myocardial infarction occurs within 3–8 hours and the first peak is reached 12–18 hours after myocardial injury. It is induced by the rapid release of the free *cytoplasmic fraction of cTnT* . The initial peak is followed by another peak in 3-4 days, which corresponds to a slower leaching of cTnT *bound in the troponin-tropomyosin complex* in the necrotic deposit. It drops to undetectable levels within 7-10 days .

With early resumption of coronary artery blood flow, the maximum rise is about 14 hours, followed by a later second, significantly lower peak. The length of the increase depends on the size of the heart attack. For larger heart attacks , cTnT can be detected for up to 21 days . A disadvantage of cTnT is its non-specific increase in patients with renal insufficiency .

The onset of elevated cTnI levels , which is characterized by high specificity, occurs similarly to cTnT about 3 hours after the onset of ischemia . Elevated levels persist for 5-10 days. Compared to cTnT, no second maximum (smaller cytosolic fraction) is usually observed for cTnI.

Troponin C (TnC) is not suitable for the diagnosis of acute coronary lesions because it is identical in heart and skeletal muscle.

Troponins are determined by sensitive immunochemical methods.

Rapid test for cTnT

AIM requires rapid diagnosis, which may include the use of biochemical tests to determine myoglobin and troponins, which can be performed at the patient's bedside.

We will describe a rapid test for the determination of cardiac troponin T, based on GLORIA technology (G old L abelled O ptically R ead I mmuno A ssay) by Roche. It uses two different *monoclonal antibodies* against cTnT - one is *labeled with biotin* , the other *with colloidal gold* .

Performing the test

The patient's blood is applied to *an application zone* containing labeled antibodies, which form a sandwich complex with the troponin molecules in the sample (if present) in *the reaction zone .* Before entering the detection zone, erythrocytes are separated using glass fibers and only the plasma containing the immunocomplexes proceeds. In *the detection zone* there is a *signal strip* with anchored streptavidin (protein with high affinity for biotin) and another *control strip*with immobilized troponin. An excess of gold-labeled antibodies bind to the control strip. The color of the control strip confirms that the test is functional and the test is valid. The troponin sandwich immunocomplex is captured by streptavidin, which is indicated by the second colored band. In a positive test, therefore, 2 stripes develop - in the area of the control and signal lines, in the case of a negative result, we observe only the colored control line.

Links

https://www.wikiskripta.eu/index.php?curid=7546

related articles

- Biochemical examinations in acute myocardial infarction

- Heart-attack
- Ischemic heart disease

Reference

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