

THE ACTIVITY OF CYTOLYSIS ENZYMES IN ACUTE CORONARY SYNDROMES

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Abstract: The determination of enzyme activity in the organism's humours or in different tissues is an important means of detecting and following the evolution of numerous pathological states. In our study we have determined the activity of some cytolysis enzymes (lactate dehydrogenase, LDH; alanine-aminotransferase or glutamic-pyruvic transaminase, GPT; aspartate aminotransferase or glutamic-oxaloacetic transaminase, GOT ; creatine kinase, CK and gamma-glutamyltranspeptidase, GGT) on patients with acute coronary syndromes : angina pectoris (AP), chronic painful ischemic heart disease (CPIHD), arterial hypertension (HTN), arterial hypertension with chronic painful ischemic heart disease (HTN+CPIHD) and acute myocardial infarction (AMI). The results show that the levels of activity of cytolysis enzymes are different in patients with acute coronary syndromes (ACS). The activity of LDH, GPT, GOT, CK and GGT do not have the same values for one and the same coronary disease measured in patients from different groups of age and sexes (male and female).

INTRODUCTION

The data gathered from medical literature show that acute coronary syndromes [angina pectoris(AP), chronic painful ischemic heart disease (CPIHD), arterial hypertension (HTN), arterial hypertension with chronic painful ischemic heart disease (HTN+CPIHD) and acute myocardial infarction (AMI)] are currently in third place for cause of death.

The metabolic changes that are specific for acute coronary syndromes (ACS) are reflected in the activity of different enzymes, such as lactate dehydrogenase (E 1.1.1.27, LDH), alanin-aminotransferase or glutamic-pyruvic transaminase (EC 2.6.1.2 , GPT), aspartate aminotransferase or glutamic oxaloacetic transaminase (EC 2.6.1.1, GOT), creatine kinase or creatine phosphokinase (EC 2.7.3.2, CK) and gamma-glutamyltranspeptidase or gamma-glutamyltransferase (EC 2.3.2.2, GGT).

Lactate Dehydrogenase (LDH) is a cytoplasmatic enzyme which participates in the anaerobe glycolysis and catalyzes the interconversion of lactic acid in pyruvic acid [Selwood et al., 2011]. LDH is a marker of tissue damage. LDH's activity is higher in striated muscles, the liver, the myocardium, kidneys and lymph nodes and lower in the pancreas, erythrocytes and lungs. LDH can be separated through electrophoresis in 5 fractions which contain a different proportion from the two types of monomers, H (heart) and M (muscle) :LDH₁ (H₄) - LDH₅ (M₄).

L-Alanine 2-oxoglutarate aminotransferase (alanine transaminase or glutamic-pyruvic transaminase, GPT) is found in larger quantities in the cytoplasm of hepatic cells and in smaller quantities in the myocardium, the kidneys and pancreas. The variations of the enzyme's activity are important for the hepatic pathology [Popescu și colab., 1991].

L-Aspartate-2-oxoglutarate aminotransferase (aspartate aminotransferase or glutamic-oxaloacetic transaminase, GOT) is found in the liver, myocardium and striated muscles. In kidneys, the pancreas, lungs and erythrocytes it is found in smaller quantities.

Creatine kinase (CK) catalyses the transfer of phosphate from phospho-creatine to adenosine diphosphate. CK is found as three different isoenzymes: MM, BB and MB. In cases of myocardial necrosis, the levels of CK-MB go up in 4-6 hours, reaching its peak at 24 hrs. The elevation recurs earlier with the reperfusion of the myocardium with thrombolytics, angioplasty or spontaneous lysis. CK levels stay elevated for 2-3 days. CK can be elevated in other pathological states, heart interventions, myocarditis, muscular trauma and others. There is a link between the levels of CK-MB in the plasma and myocardial necrosis. It is effective in the diagnostics of non Q-AMI and in AMI with Q waves, for prognosis and duration. Dosing CK can differentiate unstable angina, whether it is normal or elevated by non Q-AMI [Carp,2003]. Because the most elevated CK level is after 24 hours and it persists two days, the dosage of myoglobin which rises early on in blood and urine can be useful. After this period, it is necessary to determinate the activity of lactate dehydrogenase(LDH). LDH can be found as the isoenzymesLDH₁ și LDH₂(H₃M₁). The first of these isoenzymes, reaches the highest level in AMI after 72 hours and it stays elevated for 7-10 days. The elevated input in favour of LDH₁ is an indicator of AMI [Carp, 2003].

Although elevated levels of LDH₁ and CK-MB are more common in AMI, lately cardiac troponins (cTn), T (cTnT) and I (cTnI) are being given much more attention. Cardiac troponins have a regulator role in the muscle contraction of the cardiac muscle. The rise of these troponins has a specific value as a prognosis and diagnostic in AMI. The rise of cTnT and cTnI is considered as a new 'golden' standard in the diagnostic of myocardial necrosis [Hamm et

al., 1997]. The rise of cTnT and cTnI in AMI appears in 3-4 hours and it lasts up to 3-4 weeks [Antman et al., 1996]. There is a moderated rise of cTnT or cTnI in unstable angina, in about 20-40% of the patients. For those who did not have elevated levels of CK-MB, it shows a great sensibility [Lindahl, 1996].

In our studies, modifications of the cardiac troponin I (cTnI) concentration appeared based on the sex and age of the patients with myocardial infarction [Vasile et al., 2012].

Gamma-glutamyltransferase (GGT) can be found in the liver, kidneys, pancreas and the prostate. GGT is the most sensitive marker for alcoholism, being the enzyme which elevated levels exceed the others hepatic enzymes [Leschke, 2008]. GGT is a biomarker for diseases of the liver, biliary system, and pancreas and also alcohol ingestion. The rising mechanisms of this serum enzyme vary [Deac și colab., 2010]. More data show that the enzyme participates in the pathophysiologic mechanisms of some affections: acute cardiovascular syndromes, hyperglycemia, metabolic syndrome, inflammatory diseases, malignant tumour. In these cases, risen GGT is due to oxidative stress [Emdin et al., 2002].

The aim of our study is to highlight the variations in the activity of some cytolysis enzymes (LDH, GPT, GOT, CK and GGT) sampled from the blood of patients with different ages and sexes, suffering from acute coronary syndromes : angina pectoris (AP), acute myocardial infarction (AMI), chronic painful ischemic heart disease (CPIHD), arterial hypertension (HTN) and arterial hypertension with chronic painful ischemic heart disease (HTN+CPIHD).

MATERIALS AND METHODS

The biochemical investigations were performed in the Medical Analysis Laboratory from the Bacau County Hospital on a number of 925 subject, from 2008 to 2012 years. The subjects were grouped by sexes and in the following age groups:

Group I : 21-35 years ;

Group II : 36-50 years ;

Group III: 51-65 years and

Group IV: >65 years.

In the blood sampled from this study's subjects, we determined the activities of the 5 mentioned cytolysis enzymes (LDH, GPT, GOT, CK and GGT), using a automatic biochemical analyser Cobas Integra 400 Plus-Germany. The determination of enzymes activities were achieved with chemical agents kits, acquired through Roche Romania company for Cobas Integra 400 Plus.

The trial data acquired were statistically processed with the help of Student test [Văleanu și colab., 1990].

RESULTS AND DISCUSSION

From the total of 925 patients (male and female), 122 (13%) were patients diagnosed with angina pectoris, 155 (17%) had AMI, 102 (11%) patients with chronic painful ischemic heart disease; 376 (41%) had arterial hypertension (HTN) and 170(18%) suffered from arterial hypertension with chronic painful ischemic heart disease. For every syndrome, the patients were distributed on sexes (female-F and male-M) and age group as show in Table 1.

Table 1 The distribution of patients on sexes (female-F and male-M) and age group for the 5 coronary syndromes.

Acute coronary syndromes 925 patients		AGE GROUPS							
		21-35 years		36-50 years		51-65 years		>65 years	
		F	M	F	M	F	M	F	M
Angina pectoris(AP) 122 de patients	n	0	4	7	8	49	50	2	2
AMI 155 de patients	n	0	5	2	19	25	78	8	18
CPIHD	n	0	0	6	12	33	35	9	7

102 de patients									
HTN	n	4	0	46	30	107	125	38	26
376 de patients									
HTN associated with CPIHD	n	0	0	16	13	44	80	7	10
170 patients									

The trial data acquired by us show that the activities of the 5 cytolysis enzymes (LDH, GPT, GOT, CK and GGT), have varied levels in female and male subjects from the same age group, as well as from a syndrome to another.

From fig. 1 it can be determined that the **activity of LDH** is between 229,5 U/L on female patients from the age group 21-35 years with HTN and 387,5 U/L on female patients from the age group 36-50 years, diagnosed with AMI. For men, LDH activity varies from 229,5 U/L for 21-35 years age group suffering from angina pectoris (AP) and 359,1 U/L on patients <65 years age group suffering from HTN associated with CPIHD. **We mention that the referential value for LDH activity is 130-225 U/L.**

Comparing the numbers of the LDH activity in female patients with male patients, it is determined that LDH activity passes the superior referential limit (225 U/L) on females diagnosed with CPIHD (age group >65 years), HTN+CPIHD (age group >65 years), angina pectoris (age group 36-50 years) and CPIHD (age group 36-50 years). For males the levels pass on patients with HTN+CPIHD (age group 36-50 years), CPIHD (age group >65 years), AMI(age group 21-35 years) and CPIHD (age group 51-65 years).

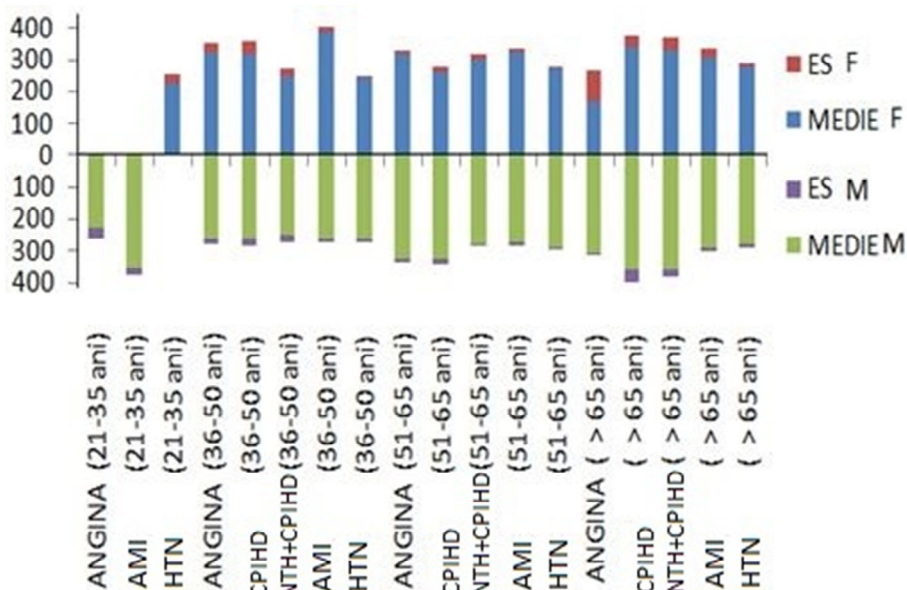


Fig. 1. LDH activity (U/L) (the average and standard error - ES) on female and male patients diagnosed with coronary syndromes.

Entire unspecific LDH elevated levels can be found in myocardial infarction, acute viral hepatitis, pernicious anaemia, neoplastic states, acute leukosis [Mihele, 1997].

From the data in fig. 2 it is obvious that **aspartate aminotransferase (GOT) activity** passes the superior referential value (**0-38 U/L**) in cases of female patients with AMI (age group >65 years and 51-65 years) and with CPIHD (age group >65 years). In males, elevated levels can be found in patients suffering from AMI (age groups >65 years, 36-50 years, 21-35 years and 51-65 years) and HTN (age group 51-65 years).

As pathological variations, elevated levels can be found in myocardial infarction in the first 24-48 hours, with annealing in the first 4 up to 6 days, as well as in hepatopathy and hemolytic states [Mihele, 1997].

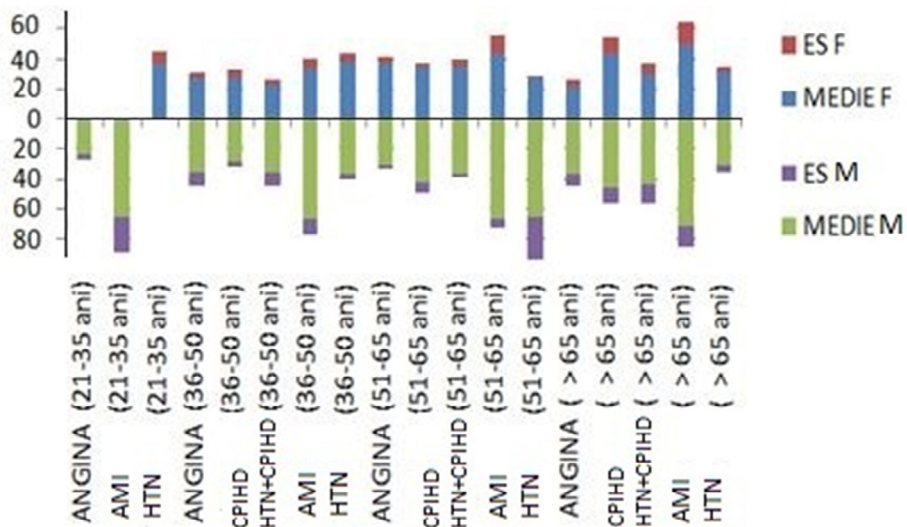


Fig. 2. GOT activity(U/L) on male and female patients diagnosed with coronary syndromes.

Alanine transaminase activity (GTP), shown in fig. 3, has slightly elevated values above the superior referential one (**0-41 U/L**) in females with AMI (age group 51-65 years), angina pectoris (age group 51-65 years) and HTN (age group 36-50 years). Found also for males with angina pectoris (age group 36-50 years), with AMI (age group 21-35 years) and HTN+CPIHD (age group >65 years)

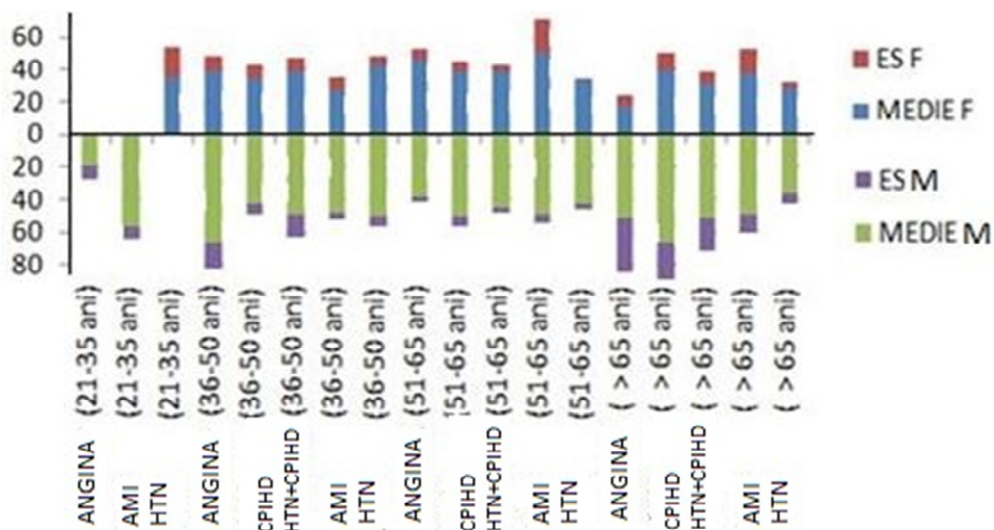


Fig. 3. GPT activity(U/L) on male and female patients diagnosed with coronary syndromes.

Creatine kinase levels raise in myocardial infraction [Lindahl, 1996 ; Carp, 2003]. But, our data show that CK activity does not pass the superior referential value (0-190 U/L) for both female and male patients (fig 4).

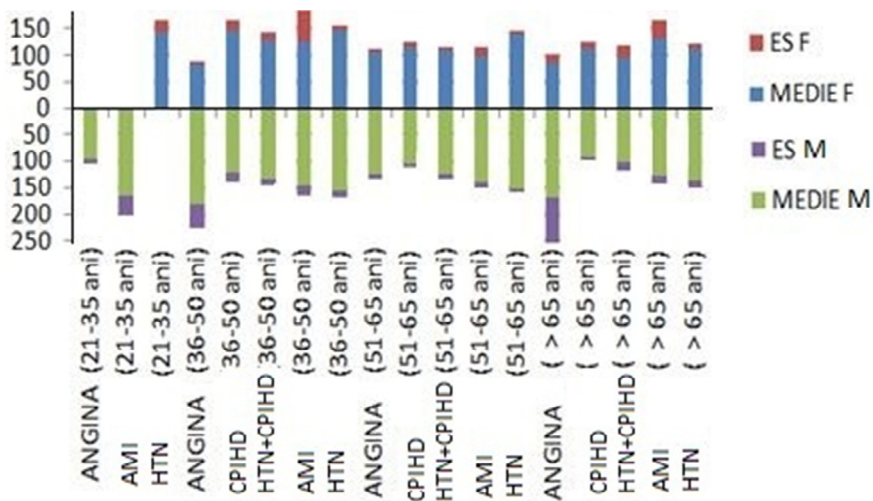


Fig. 4. CK activity (U/L) on male and female patients diagnosed with coronary syndrome.

More epidemiological observations come to support the bond between the **activity of gamma-glutamyltransferase(GGT)** and general death, death caused by cardiovascular events and death caused by hyperglycemia, mentioning the implication of oxidative stress in the pathological mechanisms [Emdin et al., 2005 ; Paolicchi et al., 2004].

For healthy people the GGT activity varies from **3-61 U/L**. According to our results, shown in fig.5, it can be seen that the GGT activity does not pass the superior referential values for females. On the other hand, on males the GGT activity passes the superior referential values for patients with CPIHD (age group >65 years and 51-65 years), with HTN+CPIHD (age group 51-65 years and 36-50 years), with angina pectoris (36-50 years), with AMI (21-35 years) and with CPIHD (age group 36-50 years)

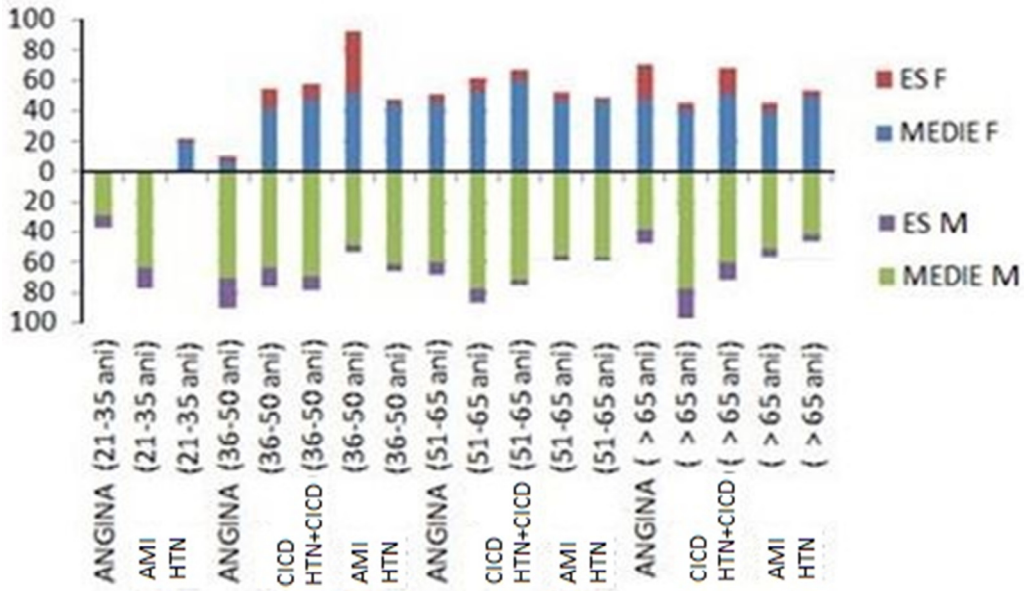


Fig. 5. GGT activity (U/L) on male and female patients diagnosed with coronary syndrome

Based on the results shown in fig.5, we can say that the GGT activity is higher for males diagnosed with acute coronary syndromes than females who suffer from the same coronary affections.

CONCLUSIONS

Our research highlighted different levels of cytolysis enzymes on patients with acute coronary syndromes (angina pectoris, AMI, HTN, HTN associated with CPIHD and CPIHD) hospitalized in Bacau County Hospital, in the time period 2008-2012

The activities of LDH, GPT, GOT, CK and GGT have different values in females diagnosed with acute coronary syndromes, compared to the enzymes values in males suffering from the same coronary syndromes.

On patients from the same sex, the LDH, GPT, GOT, CK and GGT activities have different values from a age group to another, in the case of every coronary syndrome studied.

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