BRAIN NATRIURETIC PEPTIDE AND TROPONIN I IN ACUTE MYOCARDIAL INFARCTION

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Myocardial infarction, in the diagnostic and therapeutic aspects, is of one of the great social and medical problems. Clinical diagnosis requires the presence of clinical symptoms in combination with indirect indicators of cardiac necrosis, such as biochemical markers- enzymes, electrocardiographic (ECG) and echocardiography findings. Assessment of heart failure by determining markers of myocardial damage is very significant challenge in the process of clinical assessment of patients with myocardial infarction, for further diagnosis, treatment and prognosis. Heart failure occurs in all patients with myocardial infarction, to a lesser or greater extent. Bearing in mind that, a myocardial infarction involving the anterior wall of the heart has worse prognosis, the subject of interest of this study is whether the markers of myocardial damage will be higher in patients with this localization of myocardial infarction. It was interested too, in whether it is possible to find elevated markers of myocardial damage- failure indicators, brain natriuretic peptide, in corelation with clinical signs of cardiac insuficiency.

Key words: myocardial infarction, brain natriuretic peptide, cardiac insufficiency

Introduction: Myocardial infarction, in the diagnostic and therapeutic aspects, is of one of the great social and medical problems. Assessment of heart failure by determining markers of myocardial damage is very significant challenge in the process of clinical assessment of patients with myocardial infarction, for further diagnosis, treatment and prognosis. Heart failure occurs in all patients with myocardial infarction, to a lesser or greater extent. Bearing in mind that, a myocardial infarction involving the anterior wall of the heart has worse prognosis, the subject of interest of this study is whether the markers of myocardial damage will be higher in patients with this localization of myocardial infarction. It was interested too, in whether it is possible to find elevated markers of myocardial damage- failure indicators, brain natriuretic peptide, in corelation with clinical signs of cardiac insuficiency. By analyzing the results of research showed that people with acute myocardial infarction have elevated levels of plasma brain natriuretic peptide particular the first and fifth day from the onset of acute myocardial infarction. Patients with larger myocardial infarction, involving the anterior wall of the heart, showed a secondary increase in BNP the 5th day after the occurrence of myocardial infarction, reflecting a process- postinfarction remodeling.

Objectives: The objectives of this study was to determine the amount of markers of cardiac necrosis troponin I (TNI) and brain natriuretic peptide (BNP) in patients with myocardial infarction measured in two time-point, the first and the fifth day of development of a myocardial infarction and their association with localization of myocardial infarction and the degree of heart failure.

Patients and methods: Prospective study was performed in the Department of Intensive Care and Department of Cardiology, Clinic of Internal Diseases, University Clinical Center Tuzla, in the course of three months. The group included a sample of 50 respondents, of both sexes, diagnosed a myocardial infarction. Acute myocardial infarction was confirmed on the basis of clinical presentation, electrocardiographic findings and biochemical markers of cardiac necrosis. With regard to the objectives of the research respondents in the sample were divided into two groups. Group 1 consisted of 29 patients diagnosed with acute myocardial infarction of the lower wall, and group 2 consisted of 21 patients diagnosed with acute anterior wall myocardial infarction. All patients take a blood sample to determine the level TNI and BNP the first and the fifth day after the appearance of symptoms of myocardial infarction, and the same labeled as TNI1 and TNI2 or BNP1 and BNP2 variables. Determining the level of TNI and the BNP to be the MEIA method on AxSYM SYSTEM apparatus (Abbott Laboratories Ltd. Diagnostics). TNI and the level of BNP is interpreted according to standardized values. Values were obtained based on

the AxSYM BNP essays. Subjects with myocardial infarction were also classified according to New York Heart Association- NYHA classification, the degree of I-IV, with regard to symptoms and signs of cardiac insuficiency, which is expressed as variable "NYHA" the research. Subjects with acute myocardial infarction were classified according to the development of symptoms and signs of heart failure.

Results: By analyzing the results of research showed that people with acute myocardial infarction have elevated levels of plasma brain natriuretic peptide particular the first and fifth day from the onset of acute myocardial infarction. Patients with larger myocardial infarction, involving the anterior wall of the heart, showed a secondary increase in BNP the 5th day after the occurrence of myocardial infarction, reflecting a process- postinfarction remodeling.

INTRODUCTION

Pathohistologic diagnosis of myocardial infarction indicates necrosis or death caused by prolongated ischemia of cardiac cells (1). Clinical diagnosis requires the presence of clinical symptoms in combination with indirect indicators of cardiac necrosis, such as biochemical markers- enzymes, electrocardiographic (ECG) and echocardiography findings (1). The most common cause of myocardial infarction are atherosclerotic changes in coronary arteries with additional thrombosis, resulting in a narrowing of lumen vessel until complete occlusion (2). Generally, occlusion of the left main coronary artery before branching into two main branches leading to a large infarct, which affects the anterior on the left ventricule. Therefore, the myocardial infarction of the anterior wall has worse prognosis, and myocardial infarction of inferior wall, the lower wall area, is usually smaller and better forecasting (3).

Due to necrosis of cardiac cells into the bloodstream, there appears enzymes whose activity can be measured. Significant practical value in diagnosing of myocardial infarction has troponin I (TNI) (4,5,6). In addition to determining troponin, another cardiac marker- brain natriuretic peptide (BNP) is of particular benefit. BNP is a hormone and its importance as an indicator that helps in the early methods for risk, ie the allocation of patients in the further course have raised the risk of developing heart failure after a myocardial infarction (7).

Myocardial infarction leads to disruption of regional heart function as a pump. Disorder becomes clinically manifested if in the process of contraction is absent for at least 20-25% infarcted- necrotic zone. Heart failure is one of the major cause of morbidity and mortality in western civilization, and the leading cause of hospitalization and hospital mortality. The role of natriuretic peptides the first shown in patients with cardiac insuficiency. Their release into the bloodstream is stimulated by stress weakened heart and wall stress. It is important to note that research White et al. (8) showed that BNP can also be used as an early predictor of left-ventricular remodeling. Remodeling of the left ventricule is a complex process of progressive expansion- dilatation of the heart, which leads to cardiac dysfunction and insuficiency in patients with myocardial infarction.

BNP is significantly elevated in patients with acute myocardial already the first day of admission to hospital (9,10). Morita et al. (9) indicates that patients with higher myocardial infarction may have secondary peak of BNP level, approximately five days later, reflecting the postinfarction remodeling. The size of the secondary rise in plasma BNP is related to the size of necrotic zone, the weight of the global insuficiency of the left ventricule, or both (9,11). In clinical practice, using the weight distribution of cardiac insuficiency by limiting the level of physical activity, most commonly used is the division of the New York Heart Association- NYHA to four levels (I-IV) (12).

OBJECTIVES

The objectives of this study was to determine the amount of markers of cardiac necrosis, TNI and BNP, in patients with myocardial infarction measured in two time-point, the first and fifth day of development of a myocardial infarction and their association with localization of myocardial infarction and the degree of heart failure.

PATIENTS AND METHODS

Prospective study was performed in the Department of Intensive Care and Department of Cardiology, Clinic of Internal Diseases, University Clinic Center Tuzla, in the course of three months. The group included a sample of 50 respondents, of both sexes, with diagnosed a myocardial infarction. Myocardial infarction was confirmed on the basis of clinical features, electrocardiografic findings and biochemical markers. According electrocardiografic leads estimated localization of a myocardial infarction. Respondents, in relation to the localization of a myocardial infarction, were divided into two groups, approximately equal by gender, age, absence of previous myocardial infarction, without chronic cardiac, renal or hepatic insuficiency and no malignant disese present. The study used the primary data to which there is direct application of standardized reagents for the determination of cardiac necrosis markers for each of the respondents, in accordance with the set purpose of research. All patients take a blood sample to determine the level TNI and BNP the first and fifth day after the appearance of symptoms of myocardial infarction, and the same labeled as TNI1 and TNI2 or BNP1 and BNP2 variables. Blood sample was sent for both markers in EDTA test tubes in the Central Laboratory of the Institute of Biochemistry and Diagnostics University Clinic Center Tuzla. Determining the level of TNI and the BNP to be the MEIA method on AxSYM SYSTEM apparatus (Abbott Laboratories Ltd. Diagnostics). TNI and the level of BNP is interpreted according to standardized values. Values were obtained based on the AxSYM BNP essays. Subjects with myocardial infarction were also classified according to NYHA classification, the degree of I-IV, with

regard to symptoms and signs of cardiac insuficiency, which is expressed as variable "NYHA" the research. The first group consisted of 29 subjects with myocardial infarction of inferior wall and second group of 21 subjects with myocardial infarction of anterior wall. Taking into account that the sample of respondents intentionally formed with the findings of a myocardial infarction that estimated examiner best suit the research purpose, it can be concluded that it was a quota sample. Limited amount of reagents for the determination of markers TNI and BNP (100 available reagents, for financial reasons, was a major aggravating factor in the formation of the sample). The resulting data were analyzed using statistical program SPSS 8.0 for Windows. Calculate the basic statistical parameters: Mean value (arithmetic mean), Standard deviation, Minimum and maximum results. To test the significance of the difference between the arithmetic mean of the observed variables between subjects with myocardial infarction of inferiror and anterior wall used Student T-test for independent samples, the significance

level of 5%. Pearson correlation coefficient tested the correlation between the observed variables TNI and BNP levels and NYHA cardiac insufficiency certain degree.

RESULTS

In this study covered a sample of 50 patients diagnosed with acute myocardial infarction. Age of

respondents ranged from 40 to 76 years, and the average age was 57.36 years with standard deviation of 9.55. The majority of respondents belonged to age group 51-60 years (40.0%) and the lowest number of respondents belonged to the age group above 70 years (13.3%). Next age group of 40-50 years (30.0%) and 61-70 years (16.0%). Of the total 40 patients were male (80.0%) and 10 women (20.0%).

Results of descriptive statistics for the group of patients with myocardial infarction of inferior and anterior myocardial infarction are shown in Tables 1. and 2.

Table 1. Descriptive statistic for patients with inferior myocardial infarction

Variables	N	Minimum	Maximum	Aritmetic mean	Standard deviation
BNP 1*	29	41,09	1254,89	256,5000	296,1805
BNP 2**	29	50,00	1500,00	351,4389	324,3257
TNI 1***	29	2,04	83,79	14,0579	21,1916
TNI 2****	29	0,39	91,00	11,0174	20,0831

*   BNP1 means "BNP determined 1st day"
**   BNP2 means "BNP determined 5th day "
***   TNI1 means "TNI determined 1st day"
****   TNI2 means "TNI determined 5th day"

Table 2. Descriptive statistic for patients with anterior myocardial infarction

Variables	N	Minimum	Maximum	Aritmetic mean	Standard deviation
BNP 1	21	57,40	1482,00	483,3373	435,0370
BNP 2	21	157,40	1642,14	934,0936	576,1626
TNI 1	21	2,05	91,00	34,8164	28,0390
TNI 2	21	0,10	160,20	41,8891	48,4590

Bearing in mind that the baseline for brain natriuretic peptide-BNP is <of 100.0 (pg / ml) can be concluded that people with myocardial of inferior and anterior wall had an elevated mean value of BNP. Since the reference value for troponin I is <than 0.1 (μg / l) can be concluded that

both groups of subjects had elevated mean value of TNI. Student T-test for testing significance of differences between mean values of tested variables between subjects with inferior and anterior myocardial infarction, on the significance level of 5%, are shown in 3rd table.

Table 3. T-test results for patients from all over the sample

Variables	Patients with inferiror myocardial infarction		Patients with anterior myocardial infarction		T-test	df
	$\overline{X}$	SD	$\overline{X}$	SD		
BNP1	256,50	296,18	483,34	435,04	-1,700	28
BNP2	351,44	324,33	934,09	576,16	-3,564	28
TNI1	14,06	21,19	34,82	28,04	-2,296	28
TNI2	11,02	20,08	41,89	48,46	-2,459	28

Analysis of T-test results can be seen that the respondents with myocardial infarction of inferior wall, compared to respondents with anterior myocardial infarction, significantly different for the variable BNP2 at 1% significance level, and the observed variables TNI1 and TNI2 at the level of significance of 5%, while the variable BNP1 is not shown statistical significance.

Myocardial infarction of anterior wall is bigger and worse prognosis, and myocardial infarction of inferior wall is usually smaller and more favorable prognostic (2). This, and the fact that in patients with myocardial infarction,

more value troponin is indicator of worse outcome (1), shows that the obtained results on the higher value TNI1 and TNI2 in patients 2nd groups, ie patients with myocardial infarction of anterior wall, as expected.

In addition to determining the difference between the average values of the examined groups align with the objectives we have examined what are the relations between observed variables, and that is the nature of these connections in the entire sample of subjects with myocardial. Results of correlation analysis, the significance level of 1% and 5%, are presented in Table 4.

Table 4. The results of correlation analysis between the observed variables in the full sample

Variables	BNP1	BNP2	TNI1	TNI2	NYHA
BNP1	1,000	,804**	,029	-,102	,240
BNP2	,804**	1,000	,163	,020	,393*
TNI1	,029	,163	1,000	,759**	-,057
TNI2	-,102	,020	,759**	1,000	,044
NYHA	,240	,393*	-,057	,044	1,000

** Correlation is significant at level 0.01 (2-tailed). * Correlation is significant at level 0.05 (2-tailed).

From the table 4. it is observed that the variable BNP2 achieved a statistically significant positive correlation with variable BNP1 (r = 0.804) and NYHA (r = 0.393). Statistically significant and showed a correlation between the variables TNI1 and TNI2 (r = 0.759). The obtained results of correlation analysis indicate that the observed variables BNP1 and BNP2 achieved a statistically significant correlation with each other positive signs. This means that the BNP were examined in proportion dependent on each other or as variable BNP1 higher, time is variable BNP2 higher, and vice versa. Results of correlation analysis indicate that the observed variable BNP2 and variable NYHA (which we expressed the degree of heart failure of I-IV) also achieved a statistically significant correlation of positive signs. This means that the investigated dependent variables in proportion to one another, and higher values of a certain level of BNP determined 5th correlates with higher degree of heart failure, also called, NYHA higher level.

DISCUSSION

In this study covered a sample of 50 patients diagnosed with acute myocardial infarction. According to the localization of heart attack patients in the sample, 21 (36.6%) had anterior wall myocardial infarction and 29 (63.3%) had myocardial infarction of the lower wall. Age of respondents ranged from 40 to 76 years, and the average age was 57.36 years. The majority of respondents belonged to age group 51-60 years (40.0%), followed by age group of 40-50 years (30.0%), from 61-70 years (16.0%) and over 70 years (13.3%). Of the total 40 patients were male (80.0%) and 10 were women (20.0%).

These results are expected. Ischemic heart disease and myocardial infarction in all age groups often attack men than women at a ratio of 4:1. If one looks at the younger age groups below 40 years, the ratio is even higher, up to 8:1, and to the older age groups above the 70th year, this ratio is equal (13). The largest number of men is

aged between 50 and 60 years and women between 60 and 70 years (14). Intensive increase of ischemic heart disease starts from the age group 45-49 years (for cerebrovascular disease in ten years the elderly, or aged 55-59 years). From 75th age mortality rates for women approaching death rates for men, especially for cerebrovascular disease (13).

Patients with myocardial infarction, have elevated levels of troponin and brain natriuretic peptides determined the 1st and the 5th day of the incident. There was a statistically significant difference in the amount of troponin levels in relation to the localization of a heart attack. Since in most cases, myocardial infarction involving the anterior wall, thus the degree of damage of cardiac cells larger, accordingly higher increase of cardiac enzyme troponin-markers of cardiac muscle damage.

Patients with larger myocardial infarction, involving the anterior wall of the heart, showed a secondary increase in BNP the 5th day after the occurrence of myocardial infarction, reflecting a process- postinfarction remodeling. In our study, respondents from groups with a anterior myocardial infarction had significantly higher levels of BNP particular the fifth day compared to a group of patients with patients with inferior myocardial infarction. In the case of determining markers – BNP determined the 1 st day did not show a statistically significant difference compared to the localization of a heart attack.

The obtained results of correlation analysis showed that the variables examined "brain natriuretic peptide" determined 5th day and "NYHA ", degree of heart failure, showed a significant correlation statistic positive sign and that the proportion dependent on each other. In other words, increasing the value of "BNP determined 5 th day" corresponds to a higher degree of "NYHA"; conversely, a higher degree of heart failure "NYHA" joins the higher value of "BNP determined 5 th day". The results obtained are consistent with previous research and were expected. Previous studies demonstrated a significant correlation between the size of the secondary increase in plasma BNP in the size of the necrotic zone, and with the severity of the global weakness of the left ventricle, or both, which reflects the degree of remodeling and heart failure followers (8,9).

The results obtained can not be generalized because the sample was deliberately elected because of the small number of respondents. To ensure the results were as specific as necessary to carry out research on a larger number of subjects. Similar studies are very useful considering the very great importance of early assessment of heart failure, which is a very important indicator in the diagnosis, treatment and prognosis of heart attack. Early separation of patients in the further course have increased risk of extensive remodeling of the heart and heart failure after a heart attack is achieved prevention of heart failure.

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