ORIGINAL ARTICLE

Changes of natriuretic peptides concentration in early phase of acute myocardial infarction

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ABSTRACT

Aim To analyze a change of level of natriuretic peptide (NT pro-BNP) caused by stress distension of myocardial wall in cases of acute myocardial infarction (AIM), as a possible predictor of early heart failure.

Methods Patients with myocardial infarction were followed up. Standard clinical and laboratory examination, including NT pro-BNP, and other laboratory analyses, were performed on the day of admission, the next day and on the eighth day of hospitalization. Statistical analyses included variance for repeated measurement (ANOVA), factorial multivariate analysis and test of multiple correlations.

Results The most important predictors of early heart failure in acute myocardial infarction were age, diastolic blood pressure, creatin kinase (CK) on admission, larger field of infarction zone and so on. Multiple correlations showed statistically significant correlation of age, diastolic pressure and larger zone of myocardial infarction with an increase of NT pro-BNP concentration. The activity of CK on the day after admission was higher than on admission (p=0.02) and myocard-binding CK (CK-MB) the next day after admission was higher than on admission (p=0.016). A statistically significant increase was found on the next day for NT pro-BNP in comparison with the value on admission (p=0.0049), but the level of activity of CK was markedly decreased on the eighth hospital day.

Conclusion The significant increase of the concentration of NT pro-BNP during myocardial infarction is an important predictor of early heart failure, therefore, in case of a significant increase of NT pro-BNP in the early phase of the infraction a therapy that could prevent clinically relevant heart failure should be administered.

Key words: ischemic heart disease, infarction, NT pro-BNP, heart failure

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INTRODUCTION

Many changes of diagnostic tools and the treatment of myocardial infarction have been seen in last two decades. Invasive procedures, like stent implementation, were developed as a very successful early treatment of myocardial infarction (1). Mortality of myocardial infarction was decreased substantially after the establishment of these procedures (2,3). Many very useful diagnostic procedures were developed at same time. Among others, the most important are biomarkers of tissue damages, like any type of troponins, myoglobin (4). All natriuretic peptides (there is a very large family of peptides with same function), are natural products of myocardial wall during distension. Any situation with stress distension of myocardial wall causes a release of these peptides fibers. Natriuretic peptides have been released as a result of distension of myocardial wall. Any stress of myocardial wall should be followed by an increase of natriuretic peptides secretion regardless of ongoing pathophysiological events (5). Distension of whole myocardium or any of his part should be a provocation for release of natriuretic peptides (6). Any situation with tendency for distension of atrial or ventricular inner spaces should be followed by an increase in the concentration of natriuretic peptides, as the answer and as the signal for the increase of strength of contraction of myocardium (7). There are only two situations when natriuretic peptides were released more than usually – tendency of water overload, as it could be seen in kidney diseases with kidney failure, or if very serious arterial hypertension was present (8). The same situation could be present if very high resistance was present in peripheral arterial bloodstream (9,10).

In recent literature natriuretic peptides and their precursors have been described (11). It was noted that natriuretic activity was present in natriuretic peptides and in their precursors too (12). Thereafter, any of natriuretic peptides and their precursors were directed to the same receptors of target cells (13). So, any of these members of the family of natriuretic peptides are overlapped in their actions and metabolism (14).

The aim of this study was to analyze the use of results of laboratory analyses of natriuretic peptides in the prediction of early heart failure in myocardial infarction, as the most important clinical entity of ischemic heart diseases.

PATIENTS AND METHODS

Patients with acute myocardial infarction treated at the Intensive Care Unit (ICU) of the General Hospital Tešanj, Bosnia and Herzegovina, were analyzed for clinical, laboratory and markers of myocardial tissue damage. Diagnostic procedures for these patients were performed according to the Guidelines of European Society of Cardiology (ESC) (15,16). Data related to risky behavior (cigarettes smoking, food intake, alcohol intake, physical activity) were noted as well as other risks for myocardial infarction. Analyses of lipid status were performed, including total cholesterol, low (LDL) and high density cholesterol (HDL), triglycerides, fibrinogen, C-reactive protein (CRP), blood cell count, e. g. red blood cells (RBC), medium cell volume (MCV), hematocrite, white blood cells (WBC), thrombocytes (Tr), as well as troponin, myoglobin, lactate dehydrogenase activity (LDH), creatinine phosphate kinase activity (CPK), myocardial binding creatinine phosphate kinaze (CK-MB). Natriuretic peptides were analyzed by performing examination of concentration of N-terminal precursor of brain natriuretic peptide (NT pro-BNP). Important clinical parameters were noted on admission (systolic blood pressure, diastolic blood pressure, heart rate). All parameters were followed up according to the protocol of ICU. Measurement of enzymes activities (LDH, CK, CK-MB) and NT pro-BNP were followed up on the day of admission, the first day after admission and on the eight day after admission. Inclusion criteria involved patients with acute myocardial infarction, or the first reinfarction. Exclusion criteria involved patients with acute myocardial infarction, or the first reinfarction. Exclusion criteria involved heart failure on III or IV class according to NYHA (New York Heart Association) (17), or other causes of NT pro-BNP elevation, if the level was up to three times above normal (more than 360 pg/ml) before myocardial infarction. Statistical analyses included variance for repeated measurement (ANOVA), factorial multivariate analysis and test of multiple correlations.

RESULTS

Patients treated for myocardial infarction in ICU during the period of one year, admitted to hospital in the period between 01. 01. 2008 and 31.12.
2008 were analyzed. All 67 patients were treated. The average age was 61.2 (SD 14.53) years. Forty patients (61%) were males, and 27 (39%) were females. Males were younger (average age of 60.02 years) than women (average age 64.14) at the time of admission. The commonest age on admission was 51-70 years. Most patients were smokers (38 smokers versus 29 non smokers/ never smokers). Most of the smokers used cigarettes during a long period of time, and many of them were heavy smokers having more than 30 cigarettes a day.

The localization of myocardial infarction was as follows: anterior wall 7 (10.45 %), anteroseptal 10 (14.92 %), widespread size-anterior 10 (14.92 %), diaphragm wall 33 (49%), anterolateral 3 (4.8 %) and posterolateral 4 (5.97 %) cases.

The statistical method of multiple correlations showed a statistically significant correlation of age, diastolic blood pressure and larger zone of myocardial infarction with the increase of NT pro-BNP concentration at the level of p<0.05 for any. Blood pressure was measured on admission and at least 6 times a day, sometimes event more often, depending on the general patient’s status (Table 1).

Table 1. Blood pressure according to gender

<table>
<thead>
<tr>
<th>Blood pressure (mmHg)</th>
<th>All cases</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAS 1</td>
<td>140.44 (14.53)</td>
<td>130.98 (22.61)</td>
<td>155.38 (35.11)</td>
</tr>
<tr>
<td>TAS MAX</td>
<td>153.51 (30.77)</td>
<td>145.24 (20.95)</td>
<td>166.54 (29.08)</td>
</tr>
<tr>
<td>TAS MIN</td>
<td>105.97 (26.74)</td>
<td>107.80 (13.88)</td>
<td>103.08 (31.96)</td>
</tr>
<tr>
<td>TAD 1</td>
<td>85.82 (22.97)</td>
<td>83.41 (15.59)</td>
<td>89.61 (18.50)</td>
</tr>
<tr>
<td>TAD MAX</td>
<td>93.13 (17.18)</td>
<td>90.24 (11.10)</td>
<td>97.69 (12.50)</td>
</tr>
<tr>
<td>TAD MIN</td>
<td>65.00 (12.30)</td>
<td>65.24 (9.47)</td>
<td>64.61 (19.85)</td>
</tr>
</tbody>
</table>

Parameters of myocardial damage were followed up by analyses of CK, CK-MB, and LDH activities, and by measurement of NT pro-BNP. On first day after admission mean activity of CK was 776.61 IU/mL (SD 1118.20). Mean level of CK-MB on admission was 28.58 IU/mL. SD 30.50 (normal level less than 16 IU/mL). One day after admission the average level of activity of CK-MB was 77 IU/mL (SD 99.04). The average activity of LDH on admission was 620.44 IU/mL (SD 569.57). One day after admission the average level of activity of LDH was 1005.05 IU/mL (SD 883.23) (Table 2).

Table 2. Hematologic and biochemical analyzes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All cases (SD)</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (g/L)</td>
<td>137.7 (15.47)</td>
<td>142.56 (16.09)</td>
<td>127.75 (16.28)</td>
</tr>
<tr>
<td>Htc (%)</td>
<td>38.90 (4.56)</td>
<td>39.95 (4.26)</td>
<td>37.17 (4.41)</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>86.44 (5.55)</td>
<td>87.36 (4.14)</td>
<td>84.96 (6.84)</td>
</tr>
<tr>
<td>Tr (x106/L)</td>
<td>237.87 (61.32)</td>
<td>226.49 (64.61)</td>
<td>257.17 (47.96)</td>
</tr>
<tr>
<td>Glucose on admission (mmol/L)</td>
<td>10.27 (5.63)</td>
<td>8.93 (4.50)</td>
<td>12.33 (6.40)</td>
</tr>
<tr>
<td>Glucose max. (mmol/L)</td>
<td>14.45 (6.61)</td>
<td>12.31 (6.00)</td>
<td>16.73 (6.23)</td>
</tr>
<tr>
<td>Glucose MIN (mmol/L)</td>
<td>6.92 (2.67)</td>
<td>6.99 (2.10)</td>
<td>6.86 (3.08)</td>
</tr>
<tr>
<td>Cholesterol total (mmol/L)</td>
<td>5.68 (1.27)</td>
<td>5.50 (0.90)</td>
<td>6.00 (1.67)</td>
</tr>
<tr>
<td>Cholesterol HDL (mmol/L)</td>
<td>0.99 (0.27)</td>
<td>0.95 (0.24)</td>
<td>1.07 (0.29)</td>
</tr>
<tr>
<td>Cholesterol LDL (mmol/L)</td>
<td>3.66 (1.21)</td>
<td>3.60 (1.22)</td>
<td>3.78 (1.12)</td>
</tr>
<tr>
<td>Triglycerids (mmol/L)</td>
<td>1.94 (1.48)</td>
<td>1.85 (1.28)</td>
<td>2.08 (1.72)</td>
</tr>
<tr>
<td>Acidum uricum (mmol/L)</td>
<td>356.65 (102.67)</td>
<td>376.44 (100.14)</td>
<td>312.12 (86.68)</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.79 (2.47)</td>
<td>7.17 (1.76)</td>
<td>8.82 (2.96)</td>
</tr>
</tbody>
</table>

Hb, hemoglobin concentration; Htc, hematocrit; MCV, medium cell volume; MAX, maximal, MIN, minimal; SD, standard deviation; HbA1c, glycosylated hemoglobin;

Mean level of NT pro-BNP on admission was 389.5 pg/mL (SD 620.79) (normal value 70-125 pg/mL for person not older than 70 years). One day after admission the average level of NT pro-BNP was 1371.12 pg/mL (SD 1158.9), on the eighth day after admission the mean value of NT pro-BNP was 786 pg/mL (SD 868.08) (Table 3).

Table 3. Changes of N-terminal precursor of brain natriuretic peptide (NT pro-BNP) during hospitalization

<table>
<thead>
<tr>
<th>Hospitalization time</th>
<th>All cases</th>
<th>Males SD</th>
<th>Females SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>On day of admission</td>
<td>389.50 (1260.79)</td>
<td>471.41 (750.46)</td>
<td>273.10 (298.93)</td>
</tr>
<tr>
<td>One day after admission</td>
<td>1371.12 (1373.23)</td>
<td>1391.27 (1391.27)</td>
<td>1337.23 (914.03)</td>
</tr>
<tr>
<td>Eight days after admission</td>
<td>786.38 (860.08)</td>
<td>892.22 (960.16)</td>
<td>612.50 (582.20)</td>
</tr>
</tbody>
</table>

SD, standard deviation

Multivariate analysis performed the stratification of importance for an increase of NT pro-BNP of these parameters. All the parameters were analyzed by multivariate analysis. This stratification was as follows: age, maximal measured diastolic pressure, and diastolic pressure on admission, CK on admission, hemoglobin level, gender, triglycerides, maximal measured glucose level, and localization of myocardial infarction (including size of damaged area, high-spread infarction of anterior wall was the most important), cholesterol level and thrombocytes.
The activity of CK one day after admission was higher than that of the day of admission at the statistical significance level of $p=0.02$. The difference of the level of activity of CK-MB on the day after admission in comparison with the admission day was statistically significant, at the level $p=0.016$. NT pro-BNP level was higher on the first day after admission, in comparison with that on admission at the significance level ($p=0.0049$).

**DISCUSSION**

Results of analyses of parameters of patients with myocardial infarction showed that the average age and gender structure were similar with those reported in recent literature (18). It is necessary to note that males were more vulnerable for myocardial infarction than females. But in analyses of the followed parameters known as risk factors for myocardial infarction, there was no complete correlation according to the gender. Regulation of glycemia was better in males (percentage of HbA1c, maximal glucose level). Average cholesterol level was higher in female than in male patients. Only risky behavior of cigarette smoking was predominant in males, so it could be concluded that the risk of smoking, which was noted in males, was much more important than any others.

During the follow up of NT pro-BNP concentration changes in this study a substantial increase was found the next day after admission comparing to the day of admission, and a decrease on 8th day after admission in almost all patients except those with any degree of heart failure. It was noted that the increase of NT pro-BNP concentration was higher in patients with larger size of myocardium wall damaged by myocardial infarction. The increase of NT pro-BNP concentration was correlated with age, what was described in recent literature (19).

The most important predictor for the increase of NT pro-BNP in this study was diastolic blood pressure on admission, and maximal measured diastolic blood pressure during the entire period of hospitalization. A possible explanation is a higher stress of end-diastolic pressure on myocardial wall in high diastolic pressure (20). It is known that natural stimulation of release of any cardiac natriuretic peptides, like NT pro-BNP, is distension of myocardial wall (21-23).

Myocardial infarction described as “anterior high-spread” had a larger size of damaged myocardium than any other localization. The increase of concentration of NT pro-BNP was in a very close correlation with that localization of infarction, as may be concluded in this analysis. Repercussion on heart strength to eject blood in bloodstream during systolic period occurred only in situations when a larger part of myocardium was damaged. Therefore, patients with a higher degree of increase of NT pro-BNP were at higher risk to develop heart failure than others (24,25).

The change of NT pro-BNP concentration was shown in the early phase of myocardial infarction. It was pointed out that the substantial increase of NT pro-BNP was one day after admission, in comparison with those on admission, and slowed down on eight day after admission. A higher increase of NT pro-BNP was shown in patients with larger size of damaged myocardium, and in patients with higher diastolic blood pressure. Patients prone to developing higher level of NT pro-BNP were more likely to develop heart failure, what we took in consideration when making decisions on early diuretic treatment of these patients.

In conclusion, recognition of early increase of NT pro-BNP in acute myocardial infarction could be used for decision making on modalities of early treatment of myocardial infarction, the treatment of heart failure, clinical course of myocardial infarction.

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**TRANSPARENCY DECLARATION**

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REFERENCES


Promjene koncentracije natriuretskih peptida u ranoj fazi akutnog infarkta miokarda

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SAŽETAK

Cilj rada
Analizirati značaj promjene koncentracije natriuretskih peptida (u radu NT pro-BNP), uzrokovane distenzijom miokarda, kao ranih prediktora kardijalne dekompenzacije kod akutnog infarkta miokarda.

Metode
U radu su analizirani klinički i laboratorijski parametri kod bolesnika s infarktom miokarda. Uz standardne laboratorijske analize, određivana je koncentracija NT pro-BNP i to na dan prijema, te drugi i osmi dan hospitalizacije. Statistička obrada rađena testom analize varijance za ponavljana mjerenja (ANOVA), faktorijalnom multivarijantnom analizom i testom multiple korelacije.

Rezultati
Stratifikacija značaja prediktora za rano srčano popuštanje pokazala je sljedeći redoslijed: godine starosti, dijastolni krvni tlak, CK kod prijema, širina zone infarkta itd. Metoda multiple korelacije pokazala je statistički značajnu povezanost ovih parametara s porastom NT pro-BNP. Aktivnost CK bila je veća dan poslije nego na dan prijema, uz statističku značajnost (p=0,02), dok je CK-MB također imao veću aktivnost drugi dan nego na dan prijema (p=0,016). Nađen je statistički značajan porast koncentracije NT pro-BNT na dan nakon prijema u odnosu na vrijednost kod prijema (p=0,00049), s tim da je nivo NT pro-BNP značajno padao nakon osmog dana liječenja.

Zaključak
Značajno povišenje razine NT pro-BNP, u toku infarkta miokarda, predstavlja značajan prediktor ranog srčanog popuštanja, pa bi se, u slučaju vrlo značajnog porasta NT pro-BNP u ranoj fazi infarkta, trebala uključiti terapija koja će preduzijediti klinički relevantno srčano popuštanje.

Ključne riječi
ishemijska bolest srca, infarkt, NT pro-BNP, srčano popuštanje