Original paper

Dynamics of changes of the BNP concentration in patients with stable angina pectoris qualified for PTCA. Dependence on the selected morphological and haemodynamic parameters

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Abstract

Introduction: Cardiomyocytes of human heart ventricles synthesize and generate BNP. The effect of BNP on the volume of the vascular bed contributes significantly to successful arterial pressure control. The usefulness of its determination has been proved in acute coronary syndromes, and chronic heart failure. The aim of the study was to estimate the BNP concentration in patients with stable angina pectoris during temporary myocardial ischaemia in the course of PTCA and the assessment of the effect of selected morphological and haemodynamic parameters on the BNP concentration.
Material and methods: The study comprised 27 patients, mean age 57.4 years with a clinically confirmed diagnosis of ischemic disease. All of them were qualified for coronary angiography to evaluate the condition of coronary vessels and to undertake emergency treatment if necessary. During PTCA blood was collected three times from the coronary sinus of the qualified patients: before the procedure, at rest and after the first and second inflations of a balloon in the coronary artery. Echocardiography was performed prior to PTCA in all the patients. LVMI, EF and LA-d were estimated.
Results: A nearly double increase of the BNP concentration was observed after the first and second balloon inflations. A correlation was discovered between the determined concentrations of BNP and LVMI and EF. No correlation was found between BNP concentration and LA-d.
Conclusions: The obtained results confirm significant importance of BNP concentration determination in clinical practice in order to evaluate left ventricular function. The ventricular muscle seems to play a key role in the BNP generation.

Key words: stable angina pectoris, BNP, PTCA.

Introduction

In the first half of 1980s, a peptide inducing diuresis and natriuresis, at present known as atrial natriuretic peptide (ANP), was detected in atrial cardiocytes [1]. In the following years, a factor was isolated from

experimental animals brain, which was called brain netriuretic peptide (BNP) [2]. Soon, ventricular cardiocytes appeared to be capable of synthesizing BNP. 32 aminoacidic peptide is released in response to ventricular pressure or volume overload [3]. The biological activity of natriuretic peptides is realised through peripheral receptors (type A, B and C) localized in various tissues of the organism, e.g. in epithelial cells or renal tubules [4]. Natriuretic peptides neutralise the effect of renin-angiotensin--aldosterone system (RAA) activation.

BNP having a natriuretic activity, similarly as ANP, takes part in the regulation of water balance in an organism [5]. The effect of BNP on vascular bed volume contributes significantly to successful arterial pressure control. Inhibition by BNP of endothelin (Et-1) secretion in endothelial cells also plays an important role in this mechanism [6].

In recent years numerous researchers have pointed to the advantages resulting from the determination of natriuretic peptides in everyday clinical practice. BNP appeared to be a sensitive marker of left ventricular systolic dysfunction [7]. The usefulness of its determination has been proved in acute coronary syndromes, particularly in those with ST segment elevation [8]. Many authors emphasize the high prognostic value of BNP determination in chronic heart failure [9].

The aim of the study was to estimate the BNP concentration in patients with stable angina pectoris during temporary myocardial ischaemia in the course of PTCA and the assessment of the effect of selected morphological and haemodynamic parameters on the BNP concentration.

Material and methods

The study comprised 27 patients (10 women, 17 men), mean age 57.4 years with a clinically confirmed diagnosis of ischaemic disease, angina 2 criterion according to the Canadian Cardiovascular Society and symptoms of angina for at least 2 years. All the investigated were qualified for coronarography to evaluate the condition of coronary vessels and to undertake emergency treatment if necessary.

Echocardiography was performed prior to PTCA in all the patients. In each case the same person estimated the results. The dimension of left atrium (LA-d) and ejection fraction by the Simpson's method (EF) were investigated. For final assessment mean values were considered in three heart cycles.

To calculate left ventricular mass the thickness of the posterior wall, interventricular septum and end-diastolic volume were examined. Left ventricular mass was calculated according to Penn convention [10]. In further studies, a more objective, according to numerous authors, index was used, that is left ventricular mass index (LVMI g/m^2) [11].

In the investigated group, in the course of coronarography in 24 subjects an attempt was undertaken to dilatate a critically constricted coronary artery with PTCA. The intervention was stopped in 3 patients due to the nature of atheromatous changes not prognosticating a good effect after coronary angioplasty. During PTCA blood was collected three times from the coronary sinus of the qualified patients: before the procedure, at rest (1a) and after the first (1b) and second (1c) inflations of a balloon in the coronary artery. The time of the ischaemic episode from the moment of the balloon filling to emptying was about 1 minute. The time between inflations, in which the initial estimation was performed of the results of angioplasty was from 5 to 10 minutes.

The BNP concentration was determined in each collected blood sample with the ready Peninsula radioimmunological kits.

The statistical analysis was performed with Statistica 5.1.PL and Office 97 programs on the basis of the determination of means of the variables and their standard deviations. To find normal distribution, variation of the distribution of the investigated variables was checked with W. Shapiro-Wilk test, while variances homogeneity with F test. Further analysis was performed with t-Student test for related pairs. Correlations between the tested parameters were analysed by calculating r Pearson's correlation coefficient. The results were statistically significant at the level of significance $p<0.05$.

Results

The mean BNP concentration determined at rest was 83 pg/ml in the investigated group. After the first inflation of the balloon in the coronary artery the mean BNP concentration increased to 142 pg/ml and was significantly higher as compared to the concentration determined before PTCA ($p<0.05$).

After the second inflation of the balloon, the BNP concentration was 120 pg/ml and was statistically significantly higher as compared to the initial concentration, however it was significantly lower in comparison to the BNP concentration determined in the same group after the first inflation ($p<0.05$).

The calculated LVMI was 159 g/m^2 in the studied group. The determined BNP concentrations had a positive correlation with LVMI (Figures 1-3).

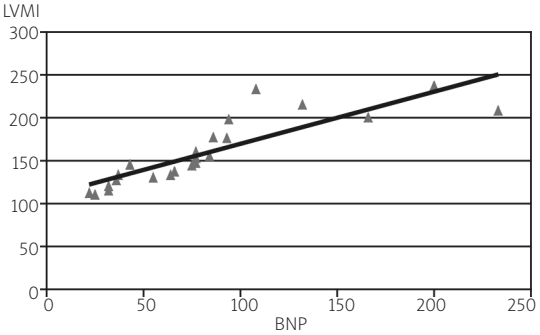
The mean dimension of the left atrium was 42.58 mm. The determined BNP concentration did not correlate significantly with LA-d ($p>0.05$).

Mean ejection fraction was 50%. The determined BNP concentrations had a negative correlation with EF (Figures 4-6).

Discussion

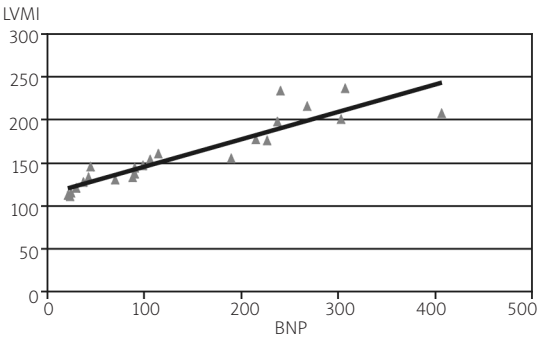
In the group of patients with stable angina pectoris, the BNP concentration at rest is significantly elevated as compared to healthy subjects [12].

The results of our studies seem to confirm the above observation. However, the coronary artery



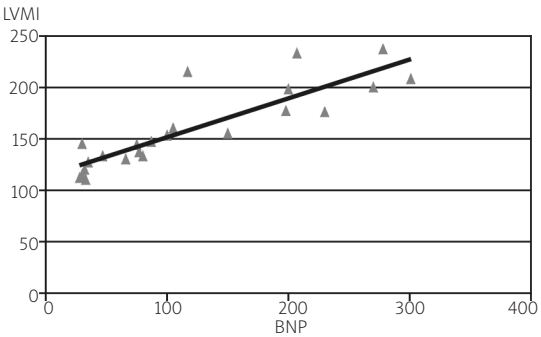
y=0.6081x+108.75
r=0.7571
p<0.05

Figure 1. The correlation between LVMI and BNP at rest (1a)



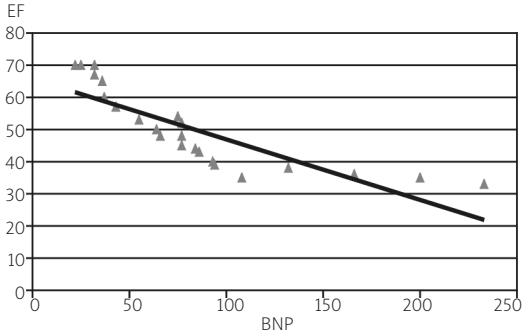
y=0.3171x+114.25
r=0.7133
p<0.05

Figure 2. The correlation between LVMI and BNP after the first inflation of the balloon in the coronary artery (1b)



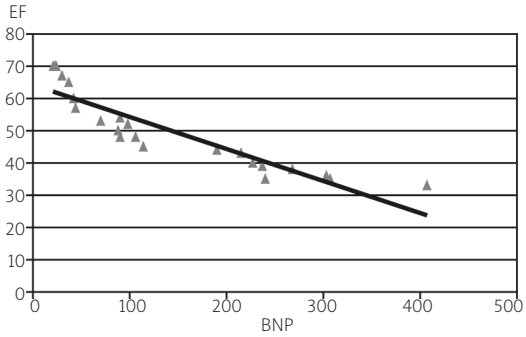
y=0.3778x+113.74
r=0.6685
p<0.05

Figure 3. The correlation between LVMI and BNP after the second inflation of the balloon in the coronary artery (1c)



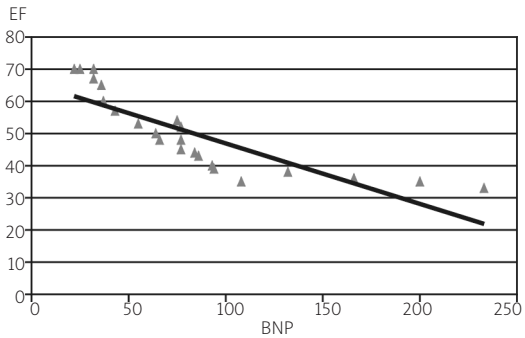
y=-0.1881x+65.739
r=-0.8409
p<0.05

Figure 4. The correlation between EF and BNP at rest (1a)



y=-0.0993x+64.214
r=-0.8073
p<0.05

Figure 5. The correlation between EF and BNP after the first inflation of the balloon in the coronary artery (1b)



y=-0.1881x+65.739
r=-0.7803
p<0.05

Figure 6. The correlation between EF and BNP after the second inflation of the balloon in the coronary artery (1c)

angioplasty affects the BNP concentration in a diverse way. After the first inflation of the balloon, plasma BNP concentration doubled its value, whereas after the second inflation its value was equally high but significantly lower as compared to the values determined after the first inflation.

BNP is released from storage granules localized in myocardial cells. Dilatation of ventricular walls and left ventricular systolic dysfunction induced by ischaemia are equal stimuli of its increased secretion [13]. The sensitivity of BNP concentration determination, even in mild forms of cardiac failure,

is very high and reaches 100% [14]. Thus, regression of the BNP concentration after the second inflation of the balloon, with high probability, can be interpreted as the after-effect of the improvement of perfusion followed by limitation of myocardial dysfunction after the first effective dilatation of the artery. However, it cannot be excluded with total certainty that the BNP pool stored in cardiocytes is limited, which considering the time interval between the inflations could also be the reason of a decreased elevation of the peptide concentration after the second inflation.

The increase of LVMI exceeding the values accepted as normal was observed in the investigated group in the stable phase of angina pectoris [10]. A strong positive correlation was determined between the BNP concentration and LVMI. A positive correlation between the tested parameters was also observed after the first and the second inflations, but a weaker one. The mean value of LA-d exceed slightly the value accepted as normal, which should be interpreted as the sign of insignificant right atrial overload. However, a significant correlation between the BNP concentration and LA-d was not noted in the studied group. Such a result suggests that ventricular but not atrial cardiocytes play the basic role in the BNP secretion.

An interpretation of the observed dependences is not simple. Left ventricular hypertrophy is proportional to the increase of the cardiac load [15]. The increase of preload or afterload is a known factor leading to structurally differentiated: concentric or eccentric left ventricular hypertrophy. Such a mechanism is observed in arterial hypertrophy or in some organic heart diseases [17]. In angina pectoris, particularly of many years', a gradual increase of cardiac muscle tone caused by excessive load of sufficiently perfused myocardial segments compensating the work of ischaemic areas seems to play an important role. The increased tone stimulates directly the protooncogene expression, e.g. c-Fos or c-Jun and proteins transcription. These changes progress simultaneously in the ventricular muscle and coronary vessels wall [18]. Activation of the local RAA system results in the increase of angiotensin II concentration in the myocardium, which besides pressor activity promotes cell proliferation and increases NADPH oxidase activity, intensifying superoxide anion radicals production [19]. Furthermore, the overgrowth of cardiocytes can be a source of vascular epithelium growth factor, transforming growth factor, A and B chains of platelet-derived growth factor or BNP [20]. An increase of left ventricular tone, paracrinic system stimulation and intensified in time tissue hypoxia stimulate increased angiogenesis. However, increased proliferative activity was observed to be attenuated by myogenic tone in response to increased pressure in the small arteries [21]. If such a phenomenon is also observed in the coronary bed then thickening of the middle layer and narrowing of coronary arteries lumen are indispensable to maintain normal perfusion pressure in microcirculation. It is not always like that. Intensification of atherogenic changes in a big vessel and its critical narrowing may totally disturb the state of the obtained balance. In such a situation there occurs a disproportion between the functional state of big arterial vessels and coronary microcirculation. Mechanical restoration of vascular stenosis restores normal perfusion in the small vessels and thus it restores the disturbed homeostasis.

Remodelling of chronically ischaemic myocardium leads to the deterioration of diastolic function. Diastolic dysfunction is observed in the majority of patients with angina pectoris [22]. Slight diastolic impairment does not usually cause any significant clinical consequences. A decrease of left ventricular muscle relaxation is however associated with impossibility of obtaining proper left ventricular filling pressure and then with the decrease of end-diastolic volume. Intensification of this unbeneficial haemodynamic burden leads to a radical decrease of blood flow through the heart and to pulmonary haemostasis [23]. In this period compensatory hyperkinesis of segments sufficiently supplied with blood cannot ensure normal cardiac output. In consequence, ejection fraction is limited.

Conclusions

The demonstrated in our studies negative correlation between the BNP concentration and ejection fraction, both in the initial period and after each inflation of the balloon is a confirmation of this hypothesis and points to the significant role of BNP as a sensitive indicator and regulator of heart failure.

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