BNP concentration in patients with mitral stenosis. Dependence on selected morphological parameters

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Abstract

Introduction: The study was carried out to estimate BNP concentration in patients with mitral stenosis and to check dependence of this concentration on the selected morphological parameters.
Material and methods: Investigations were performed in two groups. Group I comprised 24 patients (mean age 55 years) with mitral stenosis without other coexistent heart diseases. Group II included 18 subjects (mean age 53 years) with excluded circulatory system diseases. The following parameters were examined: mean mitral valve area (MVA), mean mitral valve gradient (MVG) and maximal pulmonary arterial pressure (MPAP). Dimensions of cardiac cavities were also compared: left ventricular end-diastolic diameter (LVEDd), left atrial diameter (LAd), right ventricular diameter (RVd), and thickness of posterior wall diameter (PWd) and interventricular septum diameter (IVSd) were estimated. BNP was determined in blood samples by the radioimmunological method.
Results: Mean BNP concentration in group I was elevated as compared to group II. In subgroups: Ia (with atrial fibrillation) and Id (with right ventricular hypertrophy), BNP concentration was also significantly elevated as compared to group II. Mean BNP concentration in group I correlated with MVA (r=-0.500) MVG (r=0.701), MPAP=(r=0.898) and with Lad (r=0.630) and RVd (r=0.870).
Conclusions: The results of the study allow to state that BNP can be a useful, biochemical indicator of progression of morphological lesions accompanying mitral stenosis.

Key words: atrial fibrillation, BNP, mitral stenosis, haemodynamic parameters.

Introduction

Mitral stenosis is a relatively frequently observed heart disease. It mainly develops on the background of rheumatic fever suffered in childhood. Then, the inflammatory process leads to epithelial damage within the valvular area and within other elements of the mitral valvular system [1]. Spread in time degeneration of a valve results in its stenosis and activates mechanisms of compensation. Echocardiography and Doppler evaluation are of great value in establishing the level of

progression of organic changes in the valve itself as well as in determining the direction of further management, whereas echocardiographic follow-up examinations allow to monitor the progression of valvular degeneration and finally decide on the patients' qualification for surgical correction of this disease [2]. Brain natriuretic peptide (BNP) is released from the ventricular myocardium in response to pressure and/or volume overload [3]. There are numerous reports on the significant role of both natriuretic peptides in the estimation and prognostication of patients with acute coronary syndromes or in heart failure [4, 5]. However, not many studies raise the issue of heart diseases monitoring by determining plasma concentration of natriuretic peptides. As a matter of fact, in mitral regurgitation significant correlations were observed between plasma BNP concentration and ejection fraction or left ventricular end-diastolic dimension [6]. Yet, the estimation of the effect of increased left atrial pressure in patients with mitral stenosis and the lack of data indicating left ventricular dysfunction, on the level of plasma BNP concentration is still the subject of investigations.

The aim of the study was to investigate plasma BNP concentration in patients with mitral stenosis and to find out whether there is a dependence between this concentration and selected echocardiographic parameters.

Material and methods

Two groups were investigated. Group I comprised 24 patients with diagnosed mitral stenosis (mean age 55 years) and group II – 18 subjects without circulatory system diseases (mean age 53 years). Patients with excluded arterial hypertension, cardiomyopathy and chronic diseases of the respiratory tract were included in group I. Patients with mirtal requrgitation, aortic stenosis and/or regurgitation and left ventricular hypertrophy confirmed on echocardiography were excluded from the study. In all patients the same person performed echocardiography with Acuson 128. All measurements were repeated in accordance with the recommendations of the American Society of Echocardiography, three times in patients with sinus rhythm and five times in those with atrial fibrillation (AF). Estimation of the pressure gradient across the mitral valve was calculated with Bernouilli's equation, while the area of the mitral valve on the basis of pressure gradient half-time (PHT). To investigate maximal pulmonary arterial pressure, a method was used based on calculations with the use of the highest pressure gradient across the tricuspid valve (MPAP). All valves were studied in the apical four-chamber projection [7].

In both groups, blood was collected from a basilic vein of all the patients after every echocardiographic examination. The blood sample was transferred to ice-cold tubes containing aprotimin (1000 kIU/ml) and Na_2 EDTA (1 mg/ml) and was centrifuged at 4°C. Plasma samples were stored at 20°C until assay. The plasma BNP concentration was measured with 250 µl of plasma using RIA according to the manufacturer's protocol (Peninsula Laboratories Inc., San Carlos, USA).

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 investigated variables distribution 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

Mean BNP concentration in group I was elevated as compared to group II and was: 211 pg/ml and 25 pg/ml, respectively. Group I was divided into two subgroups: Ia – patients with AF (15 subjects) and Ib – patients without AF (9 subjects). In both subgroups BNP concentration was: 242 pg/ml and 161 pg/ml, respectively. Two additional subgroups were selected according to the criterion of the right ventricular diameter (RVd). In group Ic – with normal right ventricle, plasma BNP concentration was 208 pg/ml, while in group Id – with right ventricular hypertrophy – 213 pg/ml. In all subgroups BNP concentration was statistically significantly higher as compared to group I (Tables I and II, Figure 1).

Mean mitral valve area (MVA) in group I was 1.49 cm^2, mean gradient (MVG) across the examined valve was 5.05 mmHg, while mean MPAP in group I was 41 mmHg. Mean left atrial diameter (LAd) in group I was significantly larger as compared to group II and was: 43 mm and 33 mm, respectively.

Mean right ventricular diameter (RVd) in group I was significantly larger as compared to group II and was respectively: 25 mm and 22 mm. Mean left ventricular end-diastolic diameter (LVEDd) in group I was: 47 mm and did not differ significantly as compared to group II. Similarly, posterior wall thickness (PWd) and interventricular septum diameter (IVSd) in group I were respectively: 11 mm and 10 mm and were comparable to group II. Ejection fraction (EF) was comparable in both groups and was in group I: 57% and in group II – 62% (Table III).

BNP concentration correlated significantly with MVA ($r=-0.500$, $p<0.05$) (Figure 2) and MVG ($r=0.701$, $p<0.05$) (Figure 3) and MPAP ($r=0.898$, $p<0.05$) (Figure 4). A significant correlation was also found between plasma BNP concentration and LA ($r=0.630$, $p<0.05$) (Figure 5) and RV ($r=0.870$, $p<0.05$) (Figure 6).

Table I. Concentrations of BNP in the examined groups

	Min	Max	Me	Mean	*SD*
BNP I	117	317	217	**211.88**	±64.47
BNP II	7	55	24,5	**25.44**	±12.09
BNP Ia	132	317	245	**242.33**	±55.85
BNP Ib	117	257	155	**161.89**	±44.52
BNP Ic	133	317	190	**208.00**	±73.09
BNP Id	117	314	233	**213.56**	±62.22

Table II. The comparison of BNP concentrations in the examined groups

	BNP I	BNP Ia	BNP Ib	BNP Ic	*BNP Id*
BNP II	p<0.05	p<0.05	p<0.05	p<0.05	p<0.05

Table III. Morphological parameters – cumulative composition

	Min	Max	Me	Mean	SD
MVA	1.1	1.9	1.5	**1.49**	±0.19
MVG	2.2	9.2	4.95	**5.05**	±1.84
MPAP	25	65	41	**41.33**	±11.26
LAD	34	63	42.5	**43.67**	±7.87
RVD	20	34	24.5	**25.08**	±4.09

Discussion

The investigation of natriuretic peptides concentrations, particularly BNP in heart failure plays an important role in monitoring the effectiveness of treatment and in estimation of the patients' clinical condition [8]. Furthermore, the importance of BNP is emphasized in prognosticating mortality in this group of patients [9]. In many clinical situations the determination of BNP concentration allows to qualify patients to groups of increased cardiovascular risk [10]. Elevated BNP concentrations were observed in mitral regurgitation [11] as well as in aortic valve regurgitation and stenosis [12, 13]. However, changes in BNP concentration in mitral stenosis are still subject of investigations. According to Tharaux et al., BNP concentration does not change significantly after mitral valvulotomy and does not correlate with mean left atrial pressure [14]. According to other authors, percutaneous commissurotomy does not affect plasma BNP concentration but basic BNP concentration correlates with left ventricular end-diastolic pressure. However, it does not correlate with other haemodynamic parameters [15]. Patients with mitral stenosis without left ventricular systolic dysfunction were qualified to our study, as ventricular cardiocytes increase BNP production proportionally to the increase of volume overload like in heart failure or pressure overload in aortic stenosis [16]. The increase of BNP concentration was observed in the investigated group in comparison to group II. Inclusion of patients with normal left ventricular function into the study seems to exclude left ventricular dysfunction as a potential source of BNP secretion. This assumption is confirmed in both investigated groups by: LVEDd, IVSd, PWd and EF. Thus, it may be assumed that the increase of BNP concentration in group I is related to the effect of mitral stenosis on the left

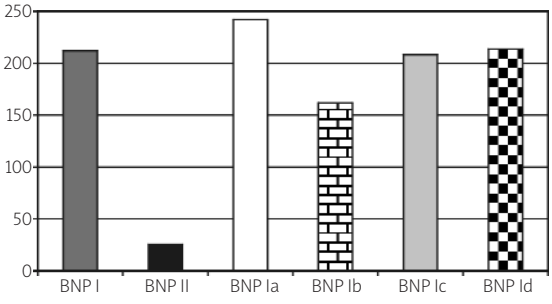

Figure 1. Graphical presentation of mean BNP values in the examined groups

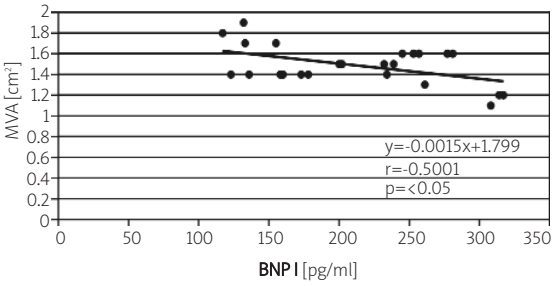

Figure 2. The correlation between BNP and MVA in group I

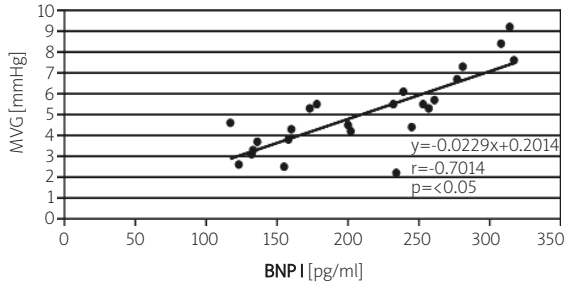

Figure 3. The correlation between BNP and MVG in group I

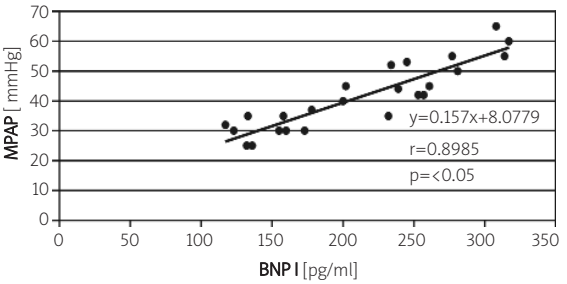

Figure 4. The correlation between BNP and MPAP in group I

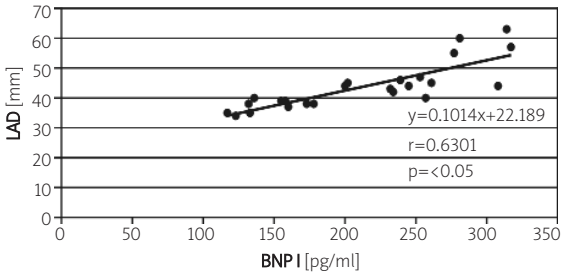

Figure 5. The correlation between BNP and LAD in group I

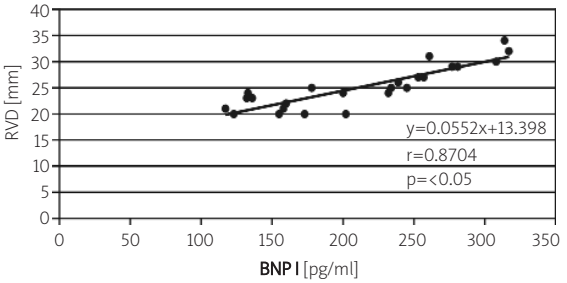

Figure 6. The correlation between BNP and RVD in group I

atrium which dilates significantly as compared to group II. The observed functional tricuspid valve regurgitation confirms the level of left atrium haemodynamic overload. Finally, a significant elevation of BNP concentration was found in patients with right ventricular hypertrophy from subgroup Id. However, among 30% of patients from subgroup Ic, in whom the dimension of the right ventricle was comparable to group II, significantly higher BNP concentrations were also observed as compared to group II. The existence of a correlation between BNP and LA seems to point to the possibility of BNP excretion by the left atrium. Inone et al. indicate the atrium as a potential source of BNP in patients with atrial fibrillation [17]. In our study in subgroup Ia of patients with AF, a significantly elevated plasma BNP concentration was observed. Thus, it may be presumed that elevated BNP concentration in this group is an effect of abnormal cardiac rhythm accompanying mitral stenosis. Yet, in subgroup Ib of patients without AF, a significant elevation of plasma BNP concentration as compared to group II was also observed in the course of the examinations.

All morphological parameters which were observed in our study are a starting point for the evaluation of mitral stenosis and allow to decide on further management. The choice of the treatment is a clinical problem which not always can be solved precisely for the patient's benefit. On the one hand, we do not want to decide on surgical treatment too early. On the other hand, it cannot be prolonged endlessly. Too preserved attitude may result in myocardial lesion and in thwarting, in a longer perspective, efforts for the patient's health. Inclusion of the determination of plasma BNP concentration into the clinical evaluation of patients with mitral stenosis seems to increase the probability of selecting a proper moment for surgical treatment of this disease. The elevated level of BNP concentration should be interpreted as a sign of cardiac chambers overload. So far, the increase of BNP concentration has been thought to result from excessive secretion by left ventricular cardiocytes in response to left ventricular dysfunction. However, in the light of our studies, it seems that the source of BNP secretion is more differentiated than it has been thought so far. The observed correlation between BNP concentration and LAd and RVd confirms the presumption that the left atrium and right ventricle take an active part in the secretion of this peptide. It is of particular importance, from the clinical point of view, in patients with mitral stenosis.

Conclusions

In the group of patients with mitral stenosis, BNP can be a new biochemical index enabling to evaluate the level of advancement of pathological changes and it can make easier to decide on surgical treatment of this disease. The continuation of studies after surgical correction of mitral stenosis seems to provide valuable information on the potential prognostic importance of the determination of BNP concentration in this group of patients.

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