MJMR, Vol. 35, No. 1, 2024, pages (70-74)

Open Access
ISSN:2682-4558

Research Article

Value of N-terminal proBNP in patients with mitral stenosis

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DOI: 10.21608/MJMR.2024.257417.1573

Abstract

Background: Mitral valve stenosis (MS) is an important valvular disorder in developing countries. N-terminal part of pro B type natriuretic peptide (NT-proBNP) has been used as a diagnostic and/or prognostic biomarker for clinical outcomes in some cardiac disorders. **Aim:** To show the association between NT-proBNP levels and hemodynamic variables in mitral stenosis patients. **Patients and methods:** Forty six patients with severe MS and sinus heart rhythm and twenty five healthy individuals as a control group were enrolled and NT-proBNP levels were assessed in them. **Results:** Mitral stenosis patients have higher levels of NT-proBNP in comparison of the control subjects. The severity of dyspnea was correlated with NT-proBNP levels. Also, left atrial size and pulmonary arterial pressure were significantly related to NT-proBNP levels. **Conclusion:** NT-proBNP is increased in MS patients and is associated with clinical and haemodynamic variables. Therefore, NT-proBNP may be used as a complementary variable with the clinical and echocardiographic evaluations in MS patients.

Keywords: Mitral stenosis, NT- proBNP.

Introduction

Mitral stenosis (MS) is an important valvular disorder which can cause significant morbidity and worse clinical outcomes[(1)]. Rheumatic heart disease (RHD) and degenerative mitral annular calcification can be considered as main causes of mitral stenosis[(2)].

Mitral stenosis severity can be evaluated by different methods. The mitral stenosis severity was based on hemodynamic parameters using the mean gradient (MG), pulmonary arterial systolic pressure (PASP), and mitral valve area (MVA). Echocardiography evaluation is the best imaging modality for the diagnosis and estimation of the mitral stenosis severity. Cardiac biomarkers as BNP and ANP also could play an essential role in determining the severity of valvular heart disorders; particularly when BNP levels are markedly increased, the prognosis becomes poor[(3,4)].

BNP, a cardiac hormone, has an essential role in the heart by its natriuretic and vasodilator effects. NT-proBNP has more stability than that of BNP. Several studies have demonstrated the value of NT-proBNP in LV failure of different causes[(5-7)]. Also, some studies have revealed that NT-proBNP levels raise in diseases such as pulmonary embolism, cor-pulmonale, and disorders of right side of the heart and the pulmonary bed [(8,9)]. The value of different NPs in valvular diseases has been previously studied [(10-12)]. MS affects the left atrium as well as the right sided heart, and rise of BNP levels in patients with MS have been shown on some situations[(13)].

We aimed to show the relation between NT-proBNP levels and the clinical and hemo-dynamic variables in mitral stenosis patients.

Subjects and methods

The study was performed in the cardiovascular departments at Assuit and El-Minia University Hospitals between January 2022 and November 2022. Forty six patients with severe MS and sinus rhythm and twenty five healthy individuals as a control group were enrolled. Patients with LV systolic dysfunction, systemic arterial hypertension, cardiomyopathies, chronic respiratory diseases, those with concomitant moderate to severe mitral incompetence or significant stenotic and incompetent other valvular lesions, left ventricular hypertrophy, renal impairment and liver cell failure were excluded.

Clinical examination was performed and the patient dyspnea was assessed by using NYHA classification. Resting surface 12 leads electrocardiogram to detect the heart rhythm was done. Transthoracic echocardiography, involving M-mode, 2D and Doppler, was performed and mitral valve area (2D-MVA), mitral valve gradient, LA diameter and pulmonary artery systolic pressure were measured using Philips IE-33 machine. Blood samples were taken by venipuncture from a peripheral vein for NT-pro BNP measurement within 30 minutes.

All population have a given informed & written consent before enrollment after informing them about the nature of the study.

All data were tabulated, digitized, and fed into a personal computer program of high statistical capabilities (SPSS version 18) for statistical analysis. Parametric data were expressed as means± standard deviations, while non-parametric data were expressed as percentages. Parametric quantative data were analyzed using independent sample test. Non parametric quantative data were analyzed by Mann Whitney test. Qualtative data were analyzed by Chi square test. Parametric correlation was done by Pearson and non-parametric correlation was done by Searman test. A p-value of < 0.05 was chosen as the level of statistical significance.

Results

The patient and control subjects did not differ in terms of age, gender and height. The mean age of MS patients was 30.4 ± 7.7 years and out of 46 patients, 18 cases (39.2%) were males and 28 cases (61.8%) were females. While in the control group, The mean age of the subjects was 29.4 ± 6.6 years and male/female ratio was 2/3. The range of height of the patients was from 158 to 176 cm, with a mean 167.2 ± 4.2 cm, while the height of control subjects ranged from 156 to 176 cm, with a mean 166.4 ± 3.8 cm. As regard NT-proBNP, its levels in MS patients were higher than those in control subjects ($P < 0.001$) (Table 1).

The severity of dyspnea assessed by NYHA classification was correlated with NT-proBNP levels ($r=0.474$ and P value <0.001) (Table 2).

Table (1): Comparison of demographic data and NT-pro BNP levels between the two study groups.

	Patients (n=46)	Control (n=25)	P value
Age (years)			
Range	(21-49)	(21-50)	0.544
Mean ± SD	30.4 ± 7.7	29.4 ± 6.6	
Sex			
Male	18 (39.2 %)	10 (40%)	0.732
Female	28 (60.8 %)	15 (60%)	
Height (cm)			
Range	(158-176)	(156-176)	0.631
Mean ± SD	167.2 ± 4.2	166.4 ± 3.8	
NT pro-BNP (pg/mL)			
Median	561	58	< 0.001
IQR	(326.3-841.5)	(30.2-92.6)	

NT- proBNP: N-terminal part of pro B type natriuretic peptide

Table (2): Correlation between levels of NT-pro BNP and NYHA class.

	NYHA class	
	r	**P value**
NT-pro BNP	0.474	<0.001

NT- proBNP: N-terminal part of pro B type natriuretic peptide, NYHA: New York Heart Association.

Table (3): Correlation between levels of NT-pro BNP and echocardiographic variables.

	NT pro-BNP	
	r	**P value**
LV EF	0.011	0.936
LA diameter	0.889	<0.001
MVA	0.148	0.296
Trans mitral MG	0.257	0.066
PASP	0.925	<0.001

LV EF: left ventricular ejection fraction, LA: left atrium, MVA: mitral valve area, MG: mean gradient, PASP: pulmonary artery systolic pressure

There was significant positive correlation between NT pro-BNP levels and left atrial diameter (r=0.889 and P value <0.001) and PASP (r=0.925 and P value <0.001) **(Table 3).**

Discussion

NT- proBNP levels are increased response to chronic increase pressure of the ventricles such as in heart failure or ventricular dysfunction. Its value in heart failure is well established[14], but its direct relation in MS patients is not well known. The rise of BNP levels in MS patients may be due to the result of pressure and volume overload in cases of moderate to severe lesions that is why its importance is not well established yet.

Our study revealed that 1) NT-proBNP levels were raised in MS patients in comparison of control subjects and 2) severity of dyspnea assessed by NYHA classification and some echocardiographic variables like left atrial size and pulmonary systolic arterial pressure were correlated with the NT-proBNP levels.

Our results that NT-proBNP levels were elevated in MS patients agreed with the findings of

previous studies that studied the association between mitral stenosis and levels of BNP [15-20]. The main presenting symptom in patients of MS was dyspnea. Similar to Arat Ozkan et al.,[4] and Seluck et al.,[16], we demon-strated that NT-proBNP levels were correlated with the dyspnea severity. Dyspnea mainly related to the pulmonary arterial and pulmonary capillary wedge pressures demonstrating that a rise in NT-proBNP levels with progressive dyspnea. Thus, NT-proBNP measurement can be used as a tool for assessment of disease progression in MS.

As regard its correlation with echocardiographic variables, our study conducted a significant positive correlation between NT- pro-BNP and left atrial size and systolic pulmonary pressure. In agreement with us, Shang et al.,[15], Seluck et al., [16], Chadha et al.,[17], Esteves et al.,[20] and Ranganayakulu et al.,[21] conducted a significant correlation between NT-proBNP and pulmo-nary artery pressure (PAP). The significant association between NT-proBNP levels and PAP may reflect the response of cardio-myocytes to increase of pressure in right ventricle in MS patients. Also, previous studies demonstrated that in patients with rheumatic MS, a larger left atrial size correlated with a greater NT-proBNP levels[21, 22] indicating BNP synthesis in atrial myocytes in response to rise of LA pressure.

In conclusion, NT-proBNP levels were increased in severe mitral stenosis patients and related to their clinical and hemodynamic variables. Therefore, we recommend that BNP may be used to complement the clinical and echocardiographic assessments in patients with MS and could tailor the timing for intervention.

Limitation of our study that must be taken into account when interpreting the results is the relatively limited study population included, so it is recommended that multi-center studies with larger and different populations should be carried out.

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