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Clinical Problems

Brain Natriuretic Peptide in Acute Pulmonary Embolism: Its Association with Pulmonary Artery Pressure and Oxygen Saturations

Özkan Yetkin[1], Erdal İn[1], Yüksel Aksoy[2], Süleyman Savas Hacıevliyagil[1], Hakan Günen[1]

[1]*Inonu University Faculty of Medicine, Chest Diseases, Malatya, Turkey*
[2]*Inonu University Faculty of Medicine, Cardiology, Malatya, Turkey*

Abstract

Brain natriuretic peptide (BNP) has potent diuretic, natriuretic, and vascular smooth muscle-relaxing effects. BNP is elevated in heart failure and pulmonary disease with acute hypoxemia or cor pulmonale, and increases in proportion to the degree of right ventricular dysfunction. In this study we aimed to evaluate the time course of BNP levels in pulmonary embolism and to assess its correlation with pulmonary artery pressure (PAP) and hypoxemia. Twenty-seven consecutive patients with acute pulmonary embolism (APE) and 26 healthy subjects were enrolled in this study. BNP levels were measured at admittance and at the end of the treatment. All patients' arterial blood gas analyses were performed at admittance. Pulse oximetry testing was performed at the end of the treatment. Mean levels of BNP in patients with APE were significantly higher than those of the control group (358±350 vs 16±25 pg/ml, respectively, $p<0.001$) at admittance. In all patients, admittance BNP levels were significantly higher than discharge BNP levels (358±350 vs 32±25 pg/ml and 18±6 pg/ml, respectively, $p<0.001$ and $p<0.05$). Initial BNP levels significantly correlated with PAP ($r=0.695$, $p<0.01$). There was also a significant negative correlation between the BNP and PO_2 levels at admittance. We have shown that BNP levels decrease progressively during the course of APE, showing a positive correlation with PAP and a negative correlation with PO_2 and SpO_2. This finding suggests that frequent BNP measurement can predict the course of APE and can be used to closely monitor the patients.

Keywords: brain natriuretic peptide, pulmonary embolism, pulmonary artery pressure, hypoxemia

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INTRODUCTION

Brain natriuretic peptide (BNP) is a member of the natriuretic peptides family [1]. Although originally isolated from porcine brains, BNP is a cardiac hormone which is synthesized by the heart and secreted into the circulation [2,3]. The mammalian heart synthesizes and secretes BNP, which has potent diuretic, natriuretic, and vascular smooth muscle-relaxing effects as well as complex interactions with the hormonal and nervous systems [4]. Elevated plasma BNP levels have been reported in patients with congestive heart failure and acute myocardial infarction.[5,6[BNP is also elevated in pulmonary disease with acute hypoxemia or cor pulmonale, and increases in proportion to the degree of right ventricular dysfunction [7].

Acute pulmonary thromboembolism (APE) can present as a life-threatening illness typically with signs of right ventricular dysfunction or hemodynamic instability. Elevated plasma levels of BNP released from myocytes of ventricles upon stretch have been found in patients with congestive heart failure and even in those with asymptomatic left ventricular systolic dysfunction [8,9]. Increased plasma BNP was found in patients with primary pulmonary hypertension and chronic thromboembolic pulmonary hypertension [10,11]. Previous studies have reported that BNP levels have correlated with the severity of APE [12-14]. In this study we aimed to evaluate the time course of BNP levels in pulmonary embolism and to assess its correlation with pulmonary artery pressure (PAP), arterial oxygen pressure (PO_2) and oxygen saturation (SpO_2).

MATERIALS AND METHODS

Twenty-seven consecutive patients with APE (mean age 60±18 years, M/F: 13/14) were enrolled in this study. The diagnosis of APE was confirmed by either spiral chest computed tomography (24 patients) or high probability ventilation perfusion scan (3 patients). All patients' arterial blood gas analyses and D-dimer levels were measured at admittance. Pulse oximetry testing of patients from the finger tips was performed at the end of the treatment, at rest while breathing room air.

Echocardiographic and Spirometric Examination

Echocardiographic examination was performed at admittance and at the end of treatment in all patients. Functions of right and left ventricle, PAP and ejection fraction (EF) were measured. Patients with EF lower 50% were excluded. Spirometric evaluation was carried out in all subjects at stable state, and no obstructive or restrictive pattern was determined in any patient. FEV1 (forced expi-

Corresponding Author: Özkan Yetkin, İnönü Üniversitesi Tıp Fakültesi Göğüs Hastalıkları, 44069 Malatya Türkiye, Phone: +90 422 3410660, E-Mail: ozkanyetkin@hotmail.com

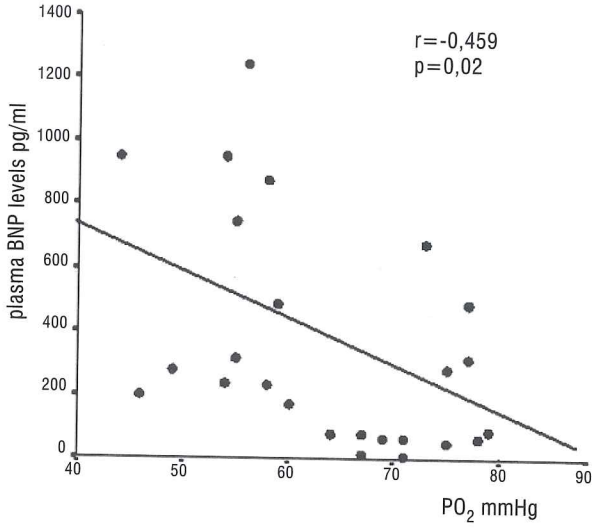

Figure 1. Negative correlation between BNP and PO_2 at admittance.

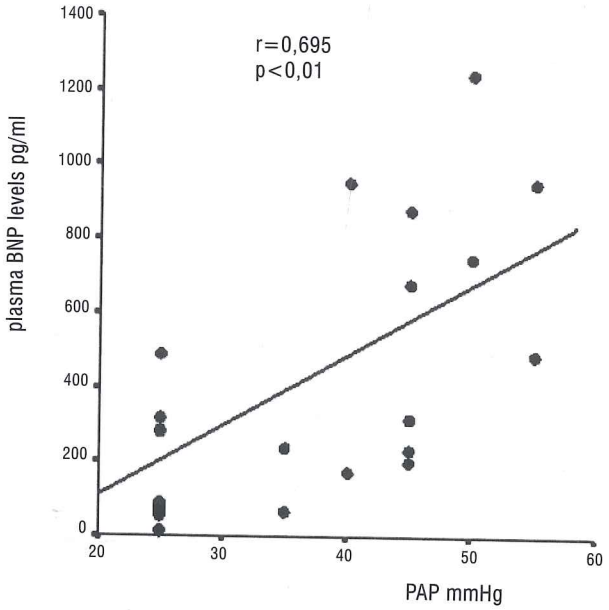

Figure 2. Positive correlation between BNP and PAP at admittance.

ratory volume in first second) and FVC (forced vital capacity) were normal. FEV1/FVC ratio was higher than 70% in all patients.

Patient Groups

According to systolic arterial blood pressure (SBP) measured on admission and the echocardiographic examination, APE patients were divided into two groups. Group I consisted of 12 patients with massive (APE with SBP<90 mmHg) or sub-massive (APE with SBP>90 mmHg, RV overload present at echocardiography) APE. Group II consisted of 15 patients with non-massive (APE with SBP>90 mmHg, no echocardiographic signs of RV overload) APE. Massive and sub-massive patients (n=12) were treated with streptokinase. Non-massive patients (n=15) were treated with intravenous heparin. All patients were given oral anticoagulant treatment. Blood samples (4 ml) for BNP were collected into a tube containing ethylene-diamine-tetra-acetate. BNP was measured immediately with a commercially available Triage BNP Test (Abbott Diagnostics, CA, USA), which uses an ELISA method. BNP levels were measured at admittance and at the end of the treatment. Control group consisted of 26 healthy subjects (mean age 61±7, 13 male and 13 female). The hospital Ethics Committee approved the study protocol, and written informed consent was obtained from all patients.

Statistical Analysis

Continuous variables were presented as mean±SD and categorical variables as percentage. Mann-Whitney U test was used to compare continuous variables between two groups, and Wilcoxon paired t test was used to compare the variables within each group. Fisher's chi-square test was used to compare categorical variables where appropriate. A p value <0.05 was considered to be statistically significant. Correlation analysis was performed by using Spearman's correlation test.

RESULTS

Mean levels of BNP in patients with APE were significantly higher than those of the control group (358±350 vs 16±25 pg/ml, respectively, p<0.001) at admittance. The massive APE group had higher BNP levels compared to the non-massive group (623±376 vs 182±190 pg/ml, p=0.001) (Table 1). There was no significant difference in mean D-dimer levels between the two groups (5900±1744 vs 4760±1656 ng/ml, p>0.05). PAP was significantly higher in the massive versus non-massive APE group (47±6 vs 28±6 mmHg, p<0.001) (Table 1). There was no statistically significant difference regarding the levels of BNP at the end of treatment between massive and non-massive APE groups (17±9 vs 18±12 pg/ml, respectively, p>0.05). In both groups, admittance BNP levels were significantly higher than discharge BNP levels (Table 2). PO_2 and SpO_2 levels were lower in Group I than Group II patients (53±5 vs 70±6 mmHg, p<0.001 and 82±5% vs 92±4%, respectively). Initial BNP levels significantly correlated with PAP (r=0.695, p<0.01; Figure 1). There was also a significant negative correlation between the BNP and PO_2 levels at admittance (Figure 2). There were no significant differences between SpO_2 and BNP levels in patients after treatment and the control group.

Table 1. Baseline characteristics of patients with pulmonary embolism

	APE	Massive-submassive APE	Non-massive APE	Control group
Number of patients	27	12	15	26
Age	60±18	59±11	62±21	61±7
Male/female	14/13	6/6	7/6	13/13
PO2 mmHg	63±8	53±5*	70±8	-
SpO2 %	88±6	82±5*	92±4	97±1
Initial mean BNP levels	358±350	623±376*	182±190	16±25
PAP mmHg	35±11	47±7*	28±6	-
D-dimer levels ng/ml	5144±2386	5900±1744	4760±1656	-

*p<0.001 vs non-massive, APE: Acute pulmonary embolism. BNP: Brain natriuretic peptide. PAP: Pulmonary artery pressure.

Table 2. Admittance and discharge values in all patients with APE

n=27	Admittance	Discharge
Plasma BNP pg/ml	358±350*	18±6
PO_2 mmHg	63±10 *	85±4
SpO_2 %	88±6 *	97±1
PAP mmHg	35±11*	26±2
BNP levels in massive-submassive group	623±326**	17±9
BNP levels non-massive group	181±169	18±12

* p<0.001 vs discharge day ** p<0.001 vs non-massive group

DISCUSSION

Secretion of BNP increases in proportion to the severity of the ventricular dysfunction, and it has been suggested that the secretion is regulated mainly by the wall tension of the left ventricle [15,16]. It has been shown that in patients with congestive heart failure, acute myocardial infarction, cor pulmonale and pulmonary embolism, the plasma level of BNP shows a marked increase [17-21]. Many studies have shown that BNP levels correlate with severity of ventricle dysfunction [16-19]. In our study, we found that BNP levels in APE were significantly higher than in the control group and BNP levels at admittance negatively correlated with PAP. Previous studies have reported that BNP levels have correlated with PAP and right ventricle dysfunction in patients with pulmonary hypertension [22,23]. We also found that BNP levels were negatively correlated with PO_2 and SpO_2. Other studies showed that BNP levels correlated with severity of systemic hypoxemia [24,25]. At the end of treatment, BNP levels demonstrated no difference compared to the control group, and mean PAP was in normal range. While BNP levels decreased with management of pulmonary embolism, PO_2 and SpO_2 values increased. These findings suggest that decreased BNP levels and increased PO_2 and SpO_2 in APE patients reflect resolution of thrombus in pulmonary circulation.

The extent of the pulmonary embolism is reflected by PAP, and this pressure load will affect the right ventricle and lead to secretion of BNP. Since the elimination half-life of BNP is relatively short [26,27], BNP levels tending to decrease suggest that the clinical severity of the pulmonary embolism also decreases.

In conclusion, we have shown that BNP levels decrease progressively during the course of APE, showing a positive correlation with PAP and a negative correlation with PO_2 and SpO_2. This finding suggests that frequent BNP measurement can predict the course of APE and can be used to closely monitor the patients.

REFERENCES

1. Saito Y, Nakao K, Itoh H, et al. Brain natriuretic peptide is a novel cardiac hormone. Biochem Biophys Res Commun 1989;158:360-8.
2. Sudoh T, Kangawa K, Minamino N, et al. A new natriuretic peptide in porcine brain. Nature 1988;332:78-81.
3. Kambayashi Y, Nakao K, Mukoyama M, et al. Isolation and sequence determination of human brain natriuretic peptide in human atrium. FEBS Lett 1990;259:341-5.
4. Clerico A, Del Ry S, Giannessi D. Measurement of cardiac natriuretic hormones (atrial natriuretic peptide, brain natriuretic peptide, and related peptides) in clinical practice: the need for a new generation of immunoassay methods. Clin Chem 2000;46:1529-34.
5. Clerico A, Iervasi G, Mariani G. Pathophysiologic relevance of measuring the plasma levels of cardiac natriuretic peptide hormones in humans. Horm Metab Res 1999;31:487-98.
6. Ndrepepa G, Braun S, Mehilli J, et al. N-terminal pro-brain natriuretic peptide on admission in patients with acute myocardial infarction and correlation with scintigraphic infarct size, efficacy of reperfusion, and prognosis. Am J Cardiol 2006;97:1151-6.
7. Cowie MR, Mendez GF. BNP and congestive heart failure. Prog Cardiovas Dis 2002;44:293-321.
8. Maisel AS, Koon J, Krishnaswamy P, et al. Utility of B-natriuretic peptide as a rapid, point-of-care test for screening patients undergoing echocardiography to determine left ventricular dysfunction. Am Heart J 2001;141:367-74.
9. McDonagh TA, Robb SD, Murdoch DR, et al. Biochemical detection of left-ventricular systolic dysfunction. Lancet 1998;351:9-13.
10. Nagaya N, Ando M, Oya H, et al. Plasma brain natriuretic peptide as a noninvasive marker for efficacy of pulmonary thromboendarterectomy. Ann Thorac Surg 2002;74:180-4.
11. Nagaya N, Nishikimi T, Uematsu M, et al. Plasma brain natriuretic peptide as a prognostic indicator in patients with primary pulmonary hypertension. Circulation 2000;102:865-70.
12. Kucher N, Printzen G, Goldhaber SZ. Prognostic role of brain natriuretic peptide in acute pulmonary embolism. Circulation. 2003;107:2545-7.
13. Tulevski II, Hirsch A, Sanson BJ, et al. Increased brain natriuretic peptide as a marker for right ventricular dysfunction in acute pulmonary embolism. Thromb Haemost 2001;86:1193-6.

14. Pruszczyk P, Kostrubiec M, Bochowicz A, et al. N-terminal probrain natriuretic peptide in patients with acute pulmonary embolism. Eur Respir J 2003;22:649-53.
15. Mukoyama M, Nakao K, Saito Y, et al. Human brain natriuretic peptide, a novel cardiac hormone. Lancet 1990;335:801-2.
16. Yasue H, Yoshimura M, Sumida H, et al. Localization and mechanism of secretion of B-type natriuretic peptide in comparison with those of A-type natriuretic peptide in normal subjects and patients with heart failure. Circulation 1994;90:195-203.
17. Richards AM, Nicholls MG, Espiner EA, et al. B-type natriuretic peptides and ejection fraction for prognosis after myocardial infarction. Circulation 2003;107:2786-92.
18. Kruger S, Graf J, Kunz D, et al. Brain natriuretic peptide levels predict functional capacity in patients with chronic heart failure. J Am Coll Cardiol 2002;40:718-22.
19. McCord J, Nowak RM, Jacobsen G, B-type natriuretic peptide levels in patients in the emergency department with possible heart failure and previous stable angina pectoris and/or healed myocardial infarction. Am J Cardiol 2005;96:1370-3.
20. Choi EY, Kwon HM, Yoon YW, et al. Assessment of extent of myocardial ischemia in patients with non-ST elevation acute coronary syndrome using serum B-type natriuretic peptide level. Yonsei Med J 2004;45:255-62.
21. Joung BY, Park BE, Kim DS, et al. B-type natriuretic peptide predicts clinical presentations and ventricular overloading in patients with heart failure. Yonsei Med J 2003;44:623-34.
22. Leuchte HH, Holzapfel M, Baumgartner RA, et al. Characterization of brain natriuretic peptide in long-term follow-up of pulmonary arterial hypertension. Chest 2005;128:2368-74.
23. Leuchte HH, Holzapfel M, Baumgartner RA, et al. Clinical significance of brain natriuretic peptide in primary pulmonary hypertension. J Am Coll Cardiol 2004;43:764-70.
24. Bando M, Ishii Y, Sugiyama Y, et al. Elevated plasma brain natriuretic peptide levels in chronic respiratory failure with cor pulmonale. Respir Med 1999;93:507-14.
25. Minder S, Gugger M. Acute dyspnea--what should I not forget? Ther Umsch 2005;62:383-91.
26. Smith MW, Espiner EA, Yandle TG, et al. Delayed metabolism of human brain natriuretic peptide reflects resistance to neutral endopeptidase. J Endocrinol 2000;167:239-46.
27. Pemberton CJ, Johnson ML, Yandle TG, et al. Deconvolution analysis of cardiac natriuretic peptides during acute volume overload. Hypertension 2000;36:355-9.