

The Relationship between Serum N-terminal Pro B-type Natriuretic Peptide Level and the Severity of Chronic Obstructive Pulmonary Disease Exacerbation

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ABSTRACT

Introduction: COPD is a common preventable disease characterized by airflow limitation that is not completely reversible. Acute exacerbation is prominent and serious features of COPD. Acute Exacerbation of COPD leads to hospitalization and concomitant with morbidity and mortality. The ventricular dysfunction increases serum Brain Natriuretic Peptide (BNP). This study was conducted to evaluate the relationship between serum N-terminal pro b-type natriuretic peptide (NT-pro BNP) level and the severity of chronic obstructive pulmonary disease (COPD) exacerbation.

Material and Methods: This cross-sectional study was performed among 140 patients with COPD exacerbation referred to Imam Reza Hospital affiliated to Mashhad University of Medical Sciences, Mashhad, Iran from March 2016 to December 2017. The patients were asked about the number of exacerbations over the past year including the recent attack. The severity of COPD was determined by the measurement of forced expiratory volume in 1 second by spirometry and level of hypoxemia by pulse oximetry. Data analysis was performed using SPSS software, version 20.

Results: Regarding the results, COPD was more prevalent in males. The mean age of the patients was 57.60 ± 9.76 years old. There was a significant direct correlation between mean serum level of NT-pro BNP and age ($P=0.01$). Although mean serum NT-pro BNP level was higher in females patients (5.70 ± 0.96) than males (5.66 ± 1.24), no significant correlation was observed between mean serum NT-pro BNP level and gender ($P=0.8$). The most common chief complaints of the patients were dyspnea (97.9%), cough (88.9%), and phlegm (81.9%). There was no significant relationship between serum NT-pro BNP levels and the length of stay in hospital ($P=0.1$). However, there was a significant relationship between mean serum level of NT-pro BNP and COPD exacerbation ($P=0.004$). The mean serum level of NT-pro BNP was higher in the patients with more than two exacerbations over the last year in comparison to the other patients. Additionally, there was a significant direct relationship between mean serum level of NT-pro BNP and the severity of COPD ($P=0.009$). Moreover, a significant direct relationship was found between serum NT-pro BNP level and hypoxemia ($SpO_2 < 90\%$; $P=0.01$). Furthermore, there was a significant relationship between mean serum level of NT-pro BNP and blood pH, which means that the mean serum level of NT-pro BNP was higher in the patients with blood pH levels of 7.25 and 7.25-7.30 ($P=0.001$).

Conclusion: The serum NT-pro BNP level was a prognostic factor in the patients with COPD exacerbation.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common preventable disease characterized by irreversible airflow limitation (1). Acute exacerbation is a prominent and serious manifestation of COPD. Nowadays, the incidence of COPD is increasing world wide. Acute exacerbation of COPD leads to hospital admission and is a major cause of morbidity and mortality.

It is estimated that COPD will be the third leading cause of mortality in 2020 (1-3). Increase in brain natriuretic peptide (BNP), which is produced in the heart ventricles, indicates the ventricular dysfunction. NT-pro BNP is a subtype of protein that can release from strained ventricle among COPD exacerbations without right heart failure (4, 5). This study aimed to assess the correlation between serum BNP level and the severity of acute exacerbation of COPD.

Materials and Methods

This cross-sectional study was conducted among 140 patients referred to Imam Reza Hospital, Mashhad, Iran from March 2016 to December 2017 who were diagnosed with acute exacerbation of COPD based on American Thoracic Society (ATS) guideline. The patients with left-sided heart failure based on echocardiography, pulmonary thromboembolism, hypertension, and increased level of N-terminal pro b-type natriuretic peptide (NT-pro BNP) due to heart diseases were excluded.

In the first 24 h after hospital admission, blood samples (3 ml) were drawn from each patient. The samples were sent to the laboratory of Imam Reza Hospital affiliated to Mashhad University of Medical Sciences, Mashhad, Iran, and serum level of NT-pro BNP was checked by enzyme-linked immunosorbent assay test. The number of attacks over the past year considering recent attack was calculated.

The severity of COPD was evaluated using spirometry with the determination of forced expiratory volume in 1 second (FEV1). Forced vital capacity (FVC) and FEV1/FVC were measured three times by an experienced single

operator with one spirometer (Multifunctional Spirometer HI-801; Chest MI Inc, Tokyo, Japan) and the maximum measurements were selected.

The severity of COPD was evaluated based on Global Initiative for Chronic Obstructive Lung Disease as following:

Stage 1 (mild): FEV1/FVC < 70% and FEV1 ≥ 80%

Stage 2 (moderate): FEV1/FVC < 70% and 50% ≤ FEV1 < 80%

Stage 3 (severe): FEV1/FVC ≤ 70% and 30% < FEV1 < 50%

Stage 4 (very severe): FEV1/FVC < 70% and FEV1 < 30% or < 50% with right heart failure

Firstly, an informed written consent was obtained from all the participants and the study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences, Mashhad, Iran. Data analysis was performed using descriptive statistics, independent samples t-test, and one way analysis of variance in the SPSS software, version 20. In all the measurements, P-value less than 0.05 was considered statistically significant.

Results

According to the results, COPD was more prevalent among males (96 male and 44 female). The mean age of the subjects was 57.60 ± 9.76 years old. There was a significant relationship between serum level of NT-pro BNP and the age of the patients (P = 0.01).

Although the level of NT-pro BNP was higher in the females than the males, there was no significant relationship between serum level of NT-pro BNP and gender (P = 0.08). The most common chief complaints of the patients during their hospitalization were shortness of breath, cough, and sputum. There was no significant relationship between the mean serum level of NT-pro BNP and the length of stay in hospital (P = 0.1).

However, there was a significant relationship between the mean serum level of NT-pro BNP and the severity of acute exacerbation (P = 0.009) (Figure 1). Regarding the results, there was a

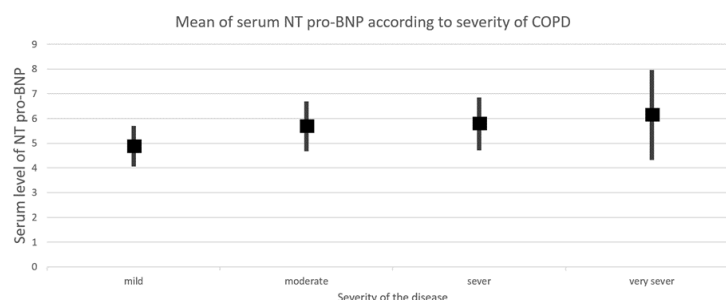


Figure 1. Mean of serum NT pro-BNP according to severity of COPD (P = 0.009)

Table 1. The level of serum NT-pro BNP according to severity of Hypoxemia

Hypoxemia	NT-pro BNP			P-Value
	number	mean	Hypoxemia	
90<	23	236.13	189.15	0.01
80-90	71	354.74	341.11	
70-80	37	1149.70	1939.90	
60-70	5	865.20	279.41	
<60	1	4762.00	-	
Total	137	600.32	1153.29	

significant relationship between the mean serum level of NT-pro BNP and hypoxemia, and the mean serum level of NT-pro BNP was higher in patients with hypoxemia (SpO₂<90%; Table 1).

Additionally, there was a significant relationship between the mean serum level of NT-pro BNP and blood pH(P=0.001).. Given the results, the serum NT-pro BNP was an important prognostic factor in patients with COPD exacerbation.

Discussion

COPD is one of the most serious health problems and it is the fourth leading cause of death (6). The ATS defines COPD as the process of disease in the form of progressive and chronic airway obstruction due to chronic bronchitis or emphysema (7). These diseases have a progressive nature and restrict the respiratory capacity, and their prevalence is increasing.

In average, 15% of adults over 55 years old have COPD that a large percentage of them are females (8). COPD is detected in 15% of smokers and almost 45% of patients have some degree of limitations in their activities (9, 10). This disease has a deep impact on patients' life because of its chronic nature.

Therefore, it affects health, family life, group support, and social and individual economic progress (11). Serum NT-pro BNP is a pre-prohormone, which is produced by cardiomyocytes and will be break into N-terminal inactive part and BNP active part and finally both of these substances are released into the blood by cardiocyte (12). The serum level of natriuretic peptides indicates the severity of heart failure, and it is a prognostic factor (13, 14). In another study conducted by O'Donoghue et al., it was showed that the serum NT-pro BNP level presents diagnostic information and prognosis in the assessment of patients with diabetes mellitus in emergency (15).

Therefore, it seems that the examination of NT-pro BNP to reveals the severity of the disease and the outcome of treatment in patients.

According to the our results, there was a significant direct relationship between the mean serum level of NT-pro BNP and age of patients (P=0.001). Furthermore, Hakala examined 88 patients who underwent coronary artery bypass

graft surgery and discovered that serum NT-pro BNP has a direct relationship with age.

In this study, 96 subjects were male. Regarding the results of the present study, there was no significant relationship between the mean serum level of NT-pro BNP and gender. Nevertheless, the level of serum NT-pro BNP was higher in female than male. In congruence with our results, in another study, it was demonstrated that a high serum level was a stronger predictor of mortality among women in comparison to men (16).

In this study, 22 patients had a history of bread baking, four of whom (18.2%) were males. Additionally, 94 subjects had a history of smoking, 86 of whom (91.5%) were males. Moreover, 58 people had a history of addiction, 35 of whom were males (60.3%). The chief complaints of patients during their admission were shortness of breath (97.9%), cough (88.9%), sputum (81.9%), fever (56.6%), hemoptysis (5.7%), and disturbance of consciousness (0.7%).

According to the results of the mentioned study, increasing in the level of serum NT-pro BNP was a prognostic factor, which was in line with our results. The results revealed that there was a significant relationship between the mean serum level of NT-pro BNP and hypoxemia (P=0.0). The mean serum level of NT-pro BNP was higher in the patients with hypoxemia (SpO₂<90%).

In addition, there was a significant relationship between the mean serum level of NT-pro BNP and blood pH. The serum level of NT-pro BNP was higher in patients with blood pH under 7.25 and 7.25-7.30.

The results of the study performed by Andrigovic et al. were in line with the present study. Consistent to the results of the current study, they concluded that several factors such as age, hypoxemia, and serum NT-pro BNP level are prognostic in the mortality of patients (17). Sanchez et al. carried out a study in 2009 and evaluated the serum level of NT-pro BNP in patients with acute attack of COPD(5).

According to the literature, increasing in the serum level of NT-pro BNP was associated with poor prognosis. These results were in line with our ones. Caravita et al. examined the patients

who has pulmonary artery hypertension due to connective tissue diseases. There was a direct correlation between PAP and serum NT-pro BNP (18).

Conclusion

Given the results, the measurement of the serum NT-pro BNP level leads to the diagnosis of COPD exacerbation. According to the rising risk of mortality in patients with high serum NT-pro BNP level, we found out that they need more intense care and must admit to intensive care unit.

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Conflict of Interest

The authors declare no conflict of interest.

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