Assessment of B-type natriuretic peptide in patients with pneumonia

O. Yetkin, S. S. Hacievliyagil, H. Gunen

Introduction

B-type natriuretic peptide (BNP) was first isolated from the porcine brain and subsequently from the heart of porcine and rats (1). BNP is a 32 amino acid peptide and plays a role on vascular tonus and natriuresis. The mammalian heart synthesises 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. Recent studies described that BNP was acute phase reactant. In this study, we aimed to evaluate BNP levels in patients with pneumonia. Twenty-one patients with pneumonia and 21 healthy control subjects were enrolled in this study. Their serum levels of BNP were measured in addition to the standard evaluations. Leucocyte count [19.3 (13.2–25.7) $10^6$/ml vs. 9.55 (3.7–13.9) $10^6$/ml, p < 0.001], erythrocyte sedimentation rate [73 (57–81) mm/h vs. 35 (4–55) mm/h, p < 0.001], C-reactive protein (CRP) [127.72 (27–290) mg/l vs. 13.19 (3–41) mg/l, p < 0.001] and BNP [53.1 (17–91) pg/ml vs. 16.24 (1–38) pg/ml, p < 0.001] levels significantly decreased after treatment period. Initial BNP levels were significantly higher than control groups (53.10 ± 15.07 pg/ml vs. 18.62 ± 14.05 pg/ml, p < 0.001) and decreased after treatment to the levels comparable with control subjects. BNP levels correlated with CRP levels at admission (r = 0.716, p < 0.001). We have shown that BNP levels show a transient increase in patients with pneumonia and correlate well with CRP.

Methods

Twenty-one consecutive patients admitted with the diagnosis of community acquired pneumonia (CAP) to the outpatient clinics of pulmonary department of Turgut Ozal Research Center, Inonu University, Malatya were included in the study. Twenty-one healthy age-matched volunteers were taken as the control group. The study protocol was approved by the ethics committee of the center. Informed consent was obtained from all participants.

Community acquired pneumonia was defined as the presence of fever (> 38 °C), cough, a new infiltrate on the chest radiograph along with appropriate clinical history and physical signs of lower respiratory tract infection in a patient not hospitalised within the previous month and in whom no alternative diagnosis emerged during follow-up. Sputum samples for gram staining and culture and blood samples for culture were obtained from each patient in a standard fashion. These samples were used to identify the responsible microorganism.

Venous blood samples were drawn for BNP analysis in serum. These samples were taken into a tube
containing potassium EDTA for BNP analysis. BNP was measured immediately with BNP ELISA test (analysis range: 0–4000 pg/ml; Abbott diagnostic, Abbott Park, IL, USA). At the same time blood samples for erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), leucocyte count and bacterial culture were collected. Leucocyte count, ESR, BNP and CRP levels were controlled in a similar way at the 15th day of the treatment. Patients were treated with similar antibiotics according to the recommendations of the national thoracic society which is compatible with the major international guidelines for pneumonia.

Statistical analysis
Continuous variables were presented as mean ± SD and median where appropriate. Mann–Whitney U-test was used to compare the continuous variables between the patient group and the control group. After-treatment comparisons for continuous parameters in the patient group were performed using the Wilcoxon’s signed rank sum test. Spearman rank order correlation coefficient (r) was calculated to measure correlation between CRP and BNP. A two-sided p value < 0.05 was considered to be statistically significant.

Results
The mean ages of the patients and the controls were 37 ± 7 (range, 31–48), (M/F, 13/8) and 35 ± 8 years (range, 32–47), (M/F, 14/7), respectively, (p > 0.05). Initial BNP levels were significantly higher than the control subjects (53.10 ± 15.07 pg/ml vs. 18.62 ± 14.05 pg/ml, p < 0.001), (Figure 1), and there was no statistical difference between BNP levels in the patients and the control subjects at the 15th day control. Initial BNP levels only correlated with CRP levels (r = 0.716, p < 0.001) (Figure 2). Statistically significant decreases were observed between initial and after-treatment levels of leucocyte counts (19.30 ± 6.65 10⁶/ml vs. 9.55 ± 1.58 10⁶/ml, p < 0.001), ESR (73 ± 18 mm/h vs. 35 ± 14 mm/h, p < 0.001), CRP (127.72 ± 63.36 mg/l vs. 13.19 ± 8.51 mg/l, p < 0.001) (Figure 3) and BNP (53.10 ± 15.07 pg/ml vs. 16.24 ± 14.57 pg/ml, p < 0.001) (Figure 4). Median and range values of these parameters are shown in Table 1. In three of the 21 patients, sputum cultures yielded *Streptococcus pneumoniae*.

Discussion
B-type natriuretic peptide is synthesised and secreted constitutively by the ventricles, which is expressed at a low level in adult ventricles except in pathophysiological conditions, such as heart failure, myocardial infarction and severe pulmonary embolism. Recent studies suggest that BNP is over expressed in pneumonia too. However, its role in pneumonia has not been determined clearly yet. Our results have shown that BNP increases transiently in patients with pneumonia, and then it decreases to the normal level with the administration of appropriate antibiotic treatment.

Secretion of BNP increases in proportion to the severity of the ventricular dysfunction, and it is suggested that the secretion is regulated mainly by the
It has been shown that in patients with congestive heart failure, acute myocardial infarction and massive pulmonary embolism, the plasma level of BNP shows a marked increase (9,10).

Community-acquired pneumonia is prevalent worldwide. Community-acquired pneumonia in adults is commonly caused by viruses, bacteria, *Mycoplasma pneumoniae* and *Chlamydia pneumoniae*. Antibiotic treatment for CAP is usually empirical because the causative pathogen is rarely identified. The majority of bacterial infections are caused by *Streptococcus pneumoniae, Haemophilus influenzae* and *Mycoplasma pneumoniae* and beta lactams, macrolids and fluoroquinolons are used frequently for treatment of CAP (11,12). Well-known acute phase reactants are CRP, ESR and leucocyte count. CRP is a protein of the acute phase, synthesised by hepatocytes. Its production is stimulated mainly by interleukin-6 (IL-6), interleukin-1 beta (IL-1β) and tumour necrosis factor alpha (TNF-α) in response to infection or tissue inflammation (13). IL-1β is a potent inflammatory cytokine that is secreted by a variety of cells and affects nearly every tissue and organ system (14). Increased levels of circulating IL-1β is found in patients with congestive heart failure and circulating levels of IL-1β correlates with myocardial injury and dysfunction (15). Proinflammatory cytokines, such as IL-6, IL-1β and TNFα, are secreted predominantly by alveolar macrophages, which represent the first line of defence in the host response against pulmonary pathogens, and are known to be potent triggers for an effective immune response (16). Circulating levels of proinflammatory cytokines, IL-1β, IL-6 and TNFα, are usually elevated in pneumonia (17,18). However, the relationship of pro-inflammatory cytokines to disease severity is not clear (19). According to this knowledge, IL-1β might increase plasma BNP from ventricles and CRP from liver in pneumonia. It has been reported that BNP levels might be affected by increased pulmonary artery pressure and the proinflammatory cytokines released from the lung tissue (20,21). Recent studies have shown significant correlation between CRP and BNP in patients with chronic renal failure and heart failure (22,23). In our study, CRP levels significantly correlated with BNP, and both of them significantly decreased at the end of the treatment period. As the significant correlation has been shown between BNP and IL-1β in patients with myocardial dysfunction, it can be speculated that IL-1β released from the alveolar macrophages might play a role in secretion of CRP and BNP. It is reasonable to expect that the correlation between CRP and BNP exists in patients with pneumonia.

These findings have suggested that BNP might play an indirect role like acute phase reactant in pneumonia. Previous studies demonstrated that BNP levels negatively correlated with hypoxaemia in patient with COPD (24). Moine et al. (25) reported...
that decreased level of partial arterial oxygen pressure correlated with severity of pneumonias. Mauller et al. (21) detected higher BNP levels in severe pneumonia, and the highest levels of BNP were obtained in subjects who died of pneumonia. The sympathetic nervous system and proinflammatory cytokines stimulate BNP secretion. Initial high levels and decreased levels of BNP after antibiotic treatment may be explained by proinflammatory cytokines.

In conclusion we have shown that BNP levels show a transient rise in patients with pneumonia, and this condition correlates well with CRP. We think that further clinical studies are needed to define the clinical implications of increased BNP in pneumonia and its relationship with cardiopulmonary hemodynamics.

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