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## Effect of diuretics on the plasma brain natriuretic peptide (BNP) level in patients with an acute exacerbation of COPD

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## ABSTRACT

**Background:** Brain natriuretic peptide (BNP) is a cardiac biomarker originates from the stretched myocardium.

**Aim of the work:** To evaluate the effect of mild diuretic treatment on the plasma BNP level in patients with an acute exacerbation of COPD without clinical findings of cor pulmonale.

**Material and methods:** 31 patients with acute exacerbation of COPD without any clinical evidence of cor pulmonale who had elevated plasma BNP concentrations (group I) and 10 patients with stable COPD as controls (group II) participated in this study. A mild diuretic treatment in addition to the standard treatment for an acute attack of COPD was randomized to 16 patients in group 1 (group IA) and the remaining patients in group I only took standard treatment for acute COPD exacerbation (group IB). Plasma BNP concentrations were measured on admission and repeated on the 8th day post therapy.

**Results:** Plasma BNP levels (mean  $\pm$  SD in pg/ml) were significantly elevated in acute exacerbation of COPD than in stable patients ( $187.01 \pm 62.7$  vs  $96.17 \pm 26.97$ ,  $p = 0.0001$ ). There was a significant decrease in plasma BNP level in AECOPD patients post therapy, which was more striking in group IA than IB ( $179.09 \pm 52.55$  pre-treatment vs  $77.43 \pm 15.46$  post-treatment with  $p = 0.0001$  and  $195.48 \pm 72.93$  pre-treatment vs  $118.84 \pm 45.19$  post-treatment with  $p = 0.0001$ ) respectively. There was a significant correlation between plasma BNP level and right ventricle end diastolic diameter ( $r = 0.5$ ,  $p = 0.001$ ) and pulmonary artery systolic pressure ( $r = 0.3$ ,  $p = 0.04$ ).

**Conclusion:** Adding mild diuretics to the standard treatment for an acute attack of COPD may rapidly reduce plasma BNP levels in COPD patients with acute exacerbations who have high plasma BNP levels without any clinical evidence of cor pulmonale.

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## Introduction

COPD is often associated with exacerbations of symptoms [1]. An exacerbation of COPD is defined as an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD [2,3]. Early diagnosis and treatment of COPD increases survival rate and improves the patients' quality of life. Cardiac biomarkers are

tools that should aid the physician in the following: diagnosis, guiding selection of therapy and in some cases, serving as a target for therapy [4]. Brain natriuretic peptide (BNP) as a cardiac biomarker, was first extracted from the porcine brains in 1988 by Sudoh of Japan [5]. It originates from the ventricular myocardium and is secreted as a response to increased ventricular pressures and/or volume overload. It plays a role in the control of sodium excretion and blood pressure, and has a compensatory role in cardio renal homeostasis [6–8]. BNP has been shown to increase in hypoxemic patients with chronic obstructive pulmonary disease (COPD) and it is significantly increased in patients with cor pulmonale when compared to patients with COPD alone. It is especially increased in proportion to the degree of right ventricular (RV) dysfunction [7,9]. BNP can be used as a diagnostic and prognostic tool in patients with COPD as elevated plasma BNP concentrations can

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be a useful early indicator of RV dysfunction and monitoring changes in plasma BNP, it also may provide a quantitative method for assessing RV function in COPD patients during follow-up [10].

### Aim of the work

To evaluate the effect of mild diuretic treatment on the plasma BNP level in patients with an acute exacerbation of COPD without clinical findings of cor pulmonale.

### Patients and methods

This study included forty-one male COPD patients, thirty-one with acute exacerbation (group I) without clinical manifestation of cor pulmonale; and ten stable COPD patients (group II).

The echo was done in the cardiology department, Beni-suef University.

The BNP was done in the clinical pathology department, Beni-suef University.

### Selection criteria

- 1) COPD patients were diagnosed according to GOLD guidelines 2013 [11].
- 2) Age over 40 years;
- 3) A history of smoking;
- 4) A forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) < 0.7 on or before the first day of admission;
- 5) Presence of acute exacerbation of COPD without clinical manifestation of cor pulmonale according to the criteria of the Global Initiative for Obstructive Lung Diseases (GOLD, 2013) [11].

### Exclusion criteria

- Chronic chest diseases other than COPD as asthma or others.
- Clinically evident cor pulmonale.
- Pneumonia,
- Any chronic renal, endocrinal or hepatic disease,
- Lung cancer,
- Atherosclerotic,
- Congenital cardiac disease,
- Left ventricular failure,
- Systemic hypertension,
- Primary myocardial disease,
- Patients already on diuretics.

Every patient was submitted to the following:

- Full history taking.
- Full clinical examination.
- Radiological examinations.
- Spirometry-before and after bronchodilation-were performed using (Master screen-Jaeger-Hochberg, Germany).
- Doppler echocardiography using (GE vivid S5-USA) examination with assessment of:
  - Right ventricle dimensions and myocardial performance index (RV MPI).
  - Left ventricle systolic and diastolic function.
  - Systolic pulmonary artery pressure.
  - Main pulmonary artery dimensions.
- Measurement of BNP

### Study design

Three cm of venous blood were collected from the studied patients for the determination of BNP using Human brain

natriuretic peptide, BNP ELISA Kit. Peripheral blood samples were collected in tubes containing 1.5 mg/ml ethylene diaminetetra acetic acid (EDTA). Group I: divided into Group IA and Group IB according to treatment given: All patients in group I received the standard conventional treatment for acute COPD exacerbation as defined below: All patients who needed oxygen received it through nasal cannula to maintain a target oxygen saturation of 88 to 92%. Nebulized salbutamol (5 mg/4 h) and nebulized ipratropium bromide (500 mg/6 h) were preferred as bronchodilators. Methylxanthines (aminophylline, 5–6 mg/kg as loading dose; 0.5 mg/kg/h infusion as maintenance), corticosteroids (dexamethasone equivalent to 1 mg/kg/day prednisolone intravenously; then decreasing doses of oral prednisolone for 15 days) and antibiotics (when signs of bacterial infection were present) were given to all patients. A mild diuretic treatment (20 mg furosemide IV once daily) in addition to the standard acute attack treatment was randomized to 16 patients only of group I who were categorized as group IA. The remaining 15 patients in group I, who were not received mild diuretic treatment, were categorized as group IB. Group II: Patients in group II (ten patients with stable COPD) were on conventional treatment of stable COPD (different types of inhaled steroids and bronchodilators). After the First samples for BNP were taken on the day of admission from both patient groups Group I and group II. Another blood samples for measuring BNP were collected from patients in Group I (exacerbation group) after their recovery around their discharging day (average on 8th day of admission).

### Statistical analysis

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation, analysis of variance [ANOVA] test and chi-square test by SPSS V.11.

### Results

This study was performed on thirty-one [31] patients with acute exacerbation of COPD (group I) and [10] stable COPD patients as a control group (group II) without clinical manifestation of cor pulmonale but have high level of plasma BNP to be included in the study. The detailed baseline characteristics of the study population are summarized in Table 1. The plasma BNP levels measured during acute exacerbation of COPD were statistically significantly elevated in comparison to stable COPD patients  $p = 0.0001$  (Table 2). There was statistically significant decrease in plasma BNP levels after treatment of the acute exacerbation in both groups IA and IB  $p = 0.0001$  and. The decrease in post-treatment BNP concentration in the group that received diuretics was more than that in patients treated with the conventional treatment only and was statistically significant ( $p = 0.002$ ) (Table 3). When evaluating cardiac function in all patients (stable and AECOPD) by trans-thoracic echocardiography, it revealed dilated right ventricle end diastolic dimensions (RVEDD) in 29 patients, their values in COPD exacerbations group (group1) and control group (group 11), with no statistical significant difference between the two group  $p = 0.46$  but there is statistically significant increase in the Systolic pulmonary artery pressure (sPAP) during acute exacerbation of COPD (group I) in comparison with stable COPD (group II) ( $p = 0.02$ ) (Table 4).

### Discussion

The aim of the present study is to evaluate the effect of adding mild diuretic treatment to the conventional treatment of AECOPD in patients with no clinical manifestations of cor pulmonale but have high plasma concentration of BNP. Since high plasma concentration of BNP is associated with increased strain on the ventricles,

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