Study of Serum B-Type Natriuretic Peptide (BNP) Levels as a Prognostic Marker in Acute Exacerbation of COPD in HSK Hospital, Bagalkot, Karnataka

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ABSTRACT

BACKGROUND

Pulmonary hypertension (PH) and heart failure are common comorbidities in 20 – 30 % of chronic obstructive pulmonary disease (COPD) patients with acute exacerbation. Similarities in signs and symptoms and lack of objective measures to stratify them at emergency department makes the management difficult. Echocardiography though useful requires specialised training. Hence, B-Type Natriuretic Peptide (BNP) is a simple test that can prognosticate the severity and can influence management in such patients. The purpose of the study was to estimate the significance of BNP during acute exacerbation of chronic obstructive pulmonary disease (AECOPD) as an important marker of severity and to study its correlation with duration of hospital stay, place and mode of management in patients with severe and life-threatening exacerbation of COPD.

METHODS

This is a prospective longitudinal observational study conducted on 50 patients of severe and life-threatening COPD exacerbation admitted to General Medicine department of HSK hospital, Bagalkot and their outcomes were noted based on the BNP levels.

RESULTS

The study showed higher levels of BNP in patients admitted to ICU as compared to emergency ward (P = 0.001). Greater values among those on invasive mechanical ventilation vs. non-invasive ventilation (NIV). There was a positive correlation and statistical significance of BNP values with arterial blood gases (ABG) parameters like pulmonary hypertension (PH), partial pressure of carbon-di-oxide ($PaCO_2$), partial pressure of oxygen (PaO_2), echo parameters like right ventricle (RV) diameter and pulmonary artery systolic pressure (PASP) and duration of hospital stay.

CONCLUSIONS

BNP is a simple, low cost and easily available blood test that can prognosticate oxygen requirement, mode of ventilation, place of management and can grade and reflect the severity in acute exacerbation of COPD.

KEYWORDS

AECOPD, BNP, Prognostic Marker, Outcome

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BACKGROUND

Chronic obstructive pulmonary disease (COPD) is one of the major causes of mortality for which death rates continue to rise.[1] Pulmonary hypertension and heart failure are common comorbidities in 20 – 30 % of COPD patients. Cardiac dysfunction may trigger exacerbation in up to 25 %.[2] Similarities in signs and symptoms and lack of objective measures to risk- stratify patients, standardized management of comorbidities and therapies that prolong life pose a challenge.

Though echocardiography is useful, specialised training is required owing to poor echo window due to tachypnoea and hyperinflation. Moreover, it is not ideal in primary care where its availability is a question.[3] Measurement of plasma B - type natriuretic peptide (BNP) which is secreted from the myocardium in response to stretch, volume overload and increased filling pressures, with higher levels seen in pulmonary hypertension or cor pulmonale, facilitate the diagnosis of acute dyspnoea in patients known to have both COPD and chronic heart failure.[4]

Thus, BNP correlates to the functional impairment, severity and hemodynamic sequelae due to chronic heart failure.[5] However, BNP is elevated in COPD without heart failure as well.[2] The BNP levels are greater in acute exacerbation than that in stable COPD patients which may be multifactorial. Hence, it may reflect and predict the severity of acute exacerbation.[6]

Objectives

1. To estimate the significance of BNP during AECOPD as an important marker of severity.
2. To study the correlation of serum BNP levels with duration of hospital stay, place and mode of management in patients with severe and life-threatening exacerbation of COPD

METHODS

This is a prospective longitudinal observational study that explored the role of BNP in predicting the duration of hospital stay among 50 patients admitted to General Medicine Department of H.S.K hospital, Bagalkot. Conducted after carefully fulfilling the inclusion and exclusion criteria as given by Global Initiative for Obstructive Lung Diseases[7] from January 2019 to January 2020.

At admission, all patients were assessed clinically noting their respiratory rate, use of accessory muscles, mentation, past history, smoking index. Every patient's BNP, ABG, chest X - ray, electrocardiogram, 2D - echocardiogram, Troponin I, complete hemogram and other relevant biochemical and radiological investigations were done.

Those with severe exacerbation with or without acute respiratory failure were admitted to emergency ward while those with life threatening exacerbation were admitted to intensive care unit (ICU) on the basis of inclusion criteria and their outcomes were noted based on the values of BNP.

Statistical Analysis

Statistical analysis was done using SPSS software 19.0. Data obtained was tabulated in the Excel sheet and later analysed. Quantitative data was expressed as mean and standard deviation and non-parametric data was expressed as median and min-max values. Percentages are used for representing qualitative data.

Chi - square test for proportions in qualitative data was done. Pearson's correlation coefficient for the parameters was done. ROC (Receiver operating characteristics curve) curve analysis was for determining the optimum cut off of BNP for the outcomes, with maximum sensitivity and specificity being calculated. $P < 0.05$ was considered statistically significant.

Inclusion Criteria

According to the guidelines of the Global Initiative for Obstructive Lung Diseases[7]

1. Severe exacerbations: include two categories as follows.
   a. Patients without acute respiratory failure: Respiratory rate 20 – 30 / min, hypoxemia improved with venture mask 28 – 35 %, with no hypercapnia.
   b. Patients with acute respiratory failure but non- life threatening: respiratory rate more than 30 / min, using accessory respiratory muscles, no mental changes, hypoxemia improved via Venturi mask 25 – 30 % FiO_2, hypercarbia ($PaCO_2$ increased compared with baseline or elevated 50 – 60 mm Hg).
2. Life-threatening exacerbations: Respiratory rate more than 30 / min, acute mental changes, using of accessory respiratory muscles, hypoxemia not improved with oxygen via Venturi mask or requiring fraction of inspired oxygen (FiO_2) more than 40 %, $PaCO_2$ elevated in comparison to baseline or higher than 60 mmHg or acidosis (pH < 7.25).

Exclusion Criteria

1. Patients with mild and moderate COPD exacerbation that did not require hospital admission.
2. Other conditions that affect the BNP level e.g. thromboembolic disease, impaired renal function, coronary artery diseases, congestive cardiac failure, cardiac arrest before admission, liver cirrhosis.
3. Patients with interstitial lung fibrosis, active pulmonary tuberculosis and other chronic lung conditions.

RESULTS

Table 1 demonstrates the baseline characteristics of the study population. This study included a total of 50 patients, of which 44 (88 %) were male and 6 (12 %) were females with a mean age of 66.2 ± 7.8. The median BNP was 670. Twenty - four out of 50 were admitted to ICU while 26 were admitted and managed in emergency ward, fulfilling the inclusion and exclusion criteria. 32 % of the patients required invasive mechanical ventilation, 20 % were on NIV

in view of Type 1 respiratory failure and remaining 48 % of the patients were on inhaled oxygen with FiO2 requirement of less than 40 %. Troponin I was negative in all 50 patients ruling out coexisting coronary artery diseases. The mean duration of hospital stay was 4.2 ± 2.0 days.

Baseline Variables		Patient (N = 50)
Mean Age		66.2 ± 7.8
Gender	Male	44 (48)
	Female	6 (12)
HTN		16 (32)
DM		24 (48)
SOB grade	1	2 (4)
	2	25 (50)
	3	12 (24)
	4	11 (22)
BNP	100 - 200	11 (22)
	200 - 500	11 (22)
	500 - 5000	28 (56)
Smoking	Yes	23
	No	27
Management place	ICU	24 (48)
	ward	26 (52)
Mode of treatment	MV	16 (32)
	NIV	10 (20)
	Inhaled O2	24 (48)
Trop-i		0.01 ± 0.2
BNP		1113.0 ± 1253.7
PH		7.3 ± 0.1
Pa02		55.1 ± 8.5
PaCO2		53.8 ± 17.5
SaO2		81.0 ± 5.2
RVD		3.4 ± 0.6
PASP		30.3 ± 10.9
Duration of stay		4.2 ± 2.0
Smoking index		38.9 ± 11.9

Table 1. Baseline Characteristics of the Study Population

Variables	r Value	P Value	Significance
Age	- 0.137	0.341	Not significant
Trop-I	0.255	0.077	Not significant
PH	- 0.738	0.000	Highly significant
PaO2	- 0.638	0.000	Highly significant
PaCO2	0.798	0.000	Highly significant
SaO2	- 0.796	0.000	Highly significant
RVD	0.635	0.004	Highly significant
PASP	0.795	0.000	Highly significant
Duration of stay	0.580	0.000	Highly significant

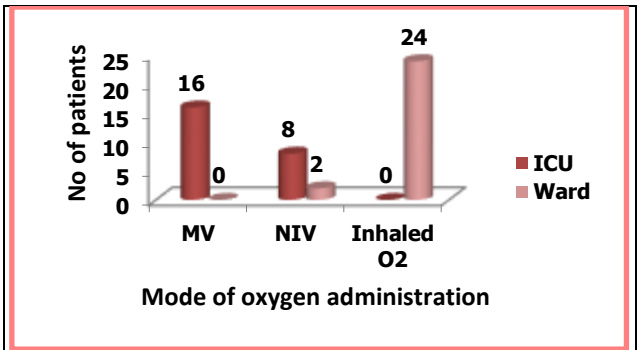
Table 2. Correlation of BNP with ABG, ECHO and Duration of Hospital Stay

Mode of Treatment	Management Place		Total
	ICU	Ward	
MV	16	0	16
NIV	8	2	10
Inhaled O2	0	24	24
Total	**24**	**26**	**50**

Table 3. Correlation of BNP with Mode of Ventilation and Place of Management

P<0.000, Highly Sig

All patients were subjected to 2D echo to note the right ventricular diameter and to calculate the pulmonary artery systolic pressure with mean values of 3.4 ± 0.6 mm and 30.3 ± 10.9 mmHg respectively. None of the patients had left ventricular dysfunction. Other conditions that falsely elevate the BNP levels such as renal failure, cirrhosis of liver, sepsis secondary to pneumonia, active pulmonary tuberculosis, interstitial lung disease and connective tissue disorders were ruled out with relevant radiological and biochemical investigations. In our study, we observed that serum BNP levels were significantly elevated in AECOPD patients who were admitted to ICU as compared to those in emergency medical ward. (1987 ± 1331.0 vs. 306.2 ± 188.2 pg. / ml, P < 0.001). There was a significant correlation and high statistical significance of BNP level with arterial blood gas parameters such as pH, PaO2, PaCO2 as well as echocardiographic data (RVD, PASP) and the duration of hospital stay as depicted in table (2). Hence proving that BNP could be considered as an independent predictor of severity as demonstrated in table (3) with BNP cut offs to predict ICU admission as shown in table (4) receiver operating characteristic (ROC) curve.

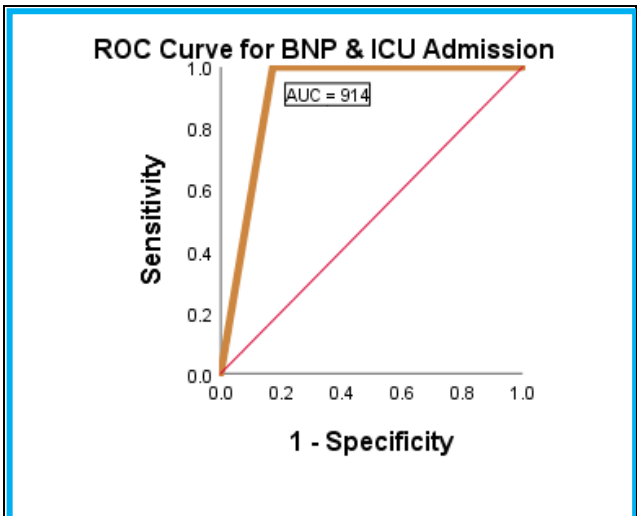


Graph 1. Correlation of BNP with Mode of Oxygen Administration and Place of Management

Receiver Operating Characteristic Curves Result of BNP Levels to Predict ICU Admission

Cut off point	Sensitivity	Specificity	PPV	NPV	Accuracy	95% CI	P Value
425	100 %	81 %	83 %	100 %	90 %	0.078 - 0.383	P < 0.001
780	87.50 %	100 %	100 %	90 %	94 %	3.311 - 28.22	P < 0.001
980	79 %	100 %	100 %	84 %	90 %	2.778 - 13.84	P < 0.001
1345	50 %	100 %	100 %	68 %	76 %	1.983 - 5.06	P < 0.001

Table 4. Receiver Operating Characteristic Curve Results of BNP Levels in ICU Admitted Patients



Graph 2. Receiver Operating Characteristic Curve Results of BNP Levels in ICU Admitted Patients

DISCUSSION

Pulmonary hypertension in COPD develops due to pulmonary

arterioles vasoconstriction, endothelin secretion, inflammation and capillary destruction associated with hyperinflation. In acute exacerbation of COPD, acute hypoxemia and RV dysfunction causing acute hemodynamic instability, it leads to elevation in serum BNP levels.[1] COPD comorbidities include respiratory acidosis, ischemic heart disease, cardiomyopathy, and heart failure with cor pulmonale.[8]

Our study outcomes are consistent with the results of Nasser K et al 2019[2] and Stolz et al[9] which showed that BNP was greater during the exacerbation as compared to that following treatment which explains the drop in BNP with improvement of hypoxemia. The results are also in agreement with Chi et al.[10] and Nasser K et al. 2019[2] who reported high significant correlation between BNP serum level and systolic PAP and PaCO2 while Lang et al.[11] found significant inverse correlation between BNP and the PaO2 only. It is thus evident from our study that assessing through BNP though simple, is a cost-effective strategy to prognosticate the outcome of COPD exacerbation and stratify the management of patients accordingly.

CONCLUSIONS

BNP is a low-cost, easily available blood investigation to grade the severity of acute exacerbation of COPD. It may also be considered as a predictor for ICU admission, indication for invasive mechanical ventilation, and reflects the length of hospital stay. Hence, BNP can prognosticate the oxygen requirement and outcome of acute exacerbation of COPD patients.

Limitations and Recommendations

Small number of patients, no follow-up, reduced statistical power, complications of invasive ventilation, and hospital-acquired infections are some of the limitations of our study. Hence, larger studies to evaluate the value of BNP in the management of AECOPD patients are needed. Screening for LV dysfunction owing to reverse Bernheim effect, at subsequent follow up in long standing COPD patients is advised.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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