EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 8
450-454
Year: 2020

B TYPE NATRIURETIC PEPTIDE AS A PREDICTOR OF OUTCOME IN ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASES

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Article Received on 15/06/2020 **Article Revised on 05/07/2020** **Article Accepted on 26/07/2020**

ABSTRACT
Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease associated with significant morbidity and mortality. Exacerbation is defined as acute worsening of respiratory symptoms that results in additional therapy. Exacerbation accelerate the rate of decline of lung function and associated with significant morbidity and mortality. **Aim** To analyze the relationship of Serum B type Natriuretic Peptide (BNP) as predictor of outcome in terms of in hospital mortality, need of intervention during hospital stay and post hospital supportive care in patients admitted with Acute Exacerbation of COPD. **Method** 50 patients with acute exacerbation of COPD above 45 years with no previous history of any independent systemic co-morbidities were recruited for study. Thorough history taking, clinical examination and all relevant investigations were performed. All the patients were treated with standard protocol including oxygen support, nebulisation, systemic antibiotics and corticosteroid . Non-invasive Ventilation and Invasive ventilation support were given whenever required. All the collected data was analysed by SPSS version 16. **Result** Out of 50 patients recruited 9 patients(18%) did not survive. BNP levels were increased in non-survived group when compared with survived group(mean value 1218 vs 318, p value 0.01). It was statistically significant. Mean BNP was higher in patients who required Mechanical Ventillation support in comparison to patients who needed Non Invasive Ventilation support or no intervention(mean value 480 vs 391 vs 115). BNP was also raised in patients who required domiciliary Long Term Oxygen Therapy. **Conclusion** BNP acts as predictors of in hospital mortality. It is positively correlated with, intervention required during hospital stay, need of post hospital supportive measures like domiciliary long term oxygen therapy.

INTRODUCTION
Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease with significant extrapulmonary effects that may contribute to the sesverity in individual patients. COPD is a leading cause of morbidity and mortality worldwide and is associated with a significant economic burden. Exacerbation of COPD is defined as acute worsening of respiratory symptoms that results in additional therapy. Exacerbation accelerate the rate of decline of lung function and associated with significant morbidity and mortality.. In stable COPD, prognostic indices have been thoroughly investigated and tools predicting mortality risk, such as the BODE Score, are well established. However, prognostic research in exacerbations requiring hospitalisation has been limited. No comprehensive data is available in this subject in context of Indian population. Biomarkers may be useful in this scenario. A *biomarker* has been defined as "a biological characteristic that is objectively measured and evaluated as an indicator of a normal or pathogenic biological process or a pharmacological response to a therapeutic intervention". biomarkers are biological molecules that may better reflect disease activity and fluctuate in accordance with disease state. BNP is one of the biomarkers that may be used as prognostic indicator in COPD.

BNP is a cardiac hormone, which is synthesized by the ventricle and secreted into the circulation in response to increased wall stretch and tension during elevations in end-diastolic pressure. BNP seems promising as a marker for pulmonary hypertension and right ventricular dysfunction. Brain natriuretic peptide (BNP) and N-terminal fragment (NT-proBNP) are powerful independent predictors of death and adverse events in HF, a broad range of cardiovascular conditions, and even in asymptomatic individuals in the community. BNP may therefore prove useful in identifying cardiovascular disease, stratifying risk, and guiding therapy in COPD.

However, pulmonary disease itself, pulmonary hypertension, and right ventricular strain are also associated with BNP elevation.

There is a significant inverse correlation between right ventricular ejection fraction and the plasma neurohormones BNP in asymptomatic or minimally symptomatic patients with chronic right ventricular pressure overload and congenital heart disease. Increased plasma BNP concentration in these patients could be a useful early indicator of right ventricular systolic dysfunction, and monitoring changes in plasma BNP may provide quantitative follow up of right ventricular function.

AIM

To analyze the relationship of Serum B type Natriuretic Peptide (BNP) as predictor of outcome in terms of in hospital mortality, need of intervention during hospital stay and post hospital supportive care in patients admitted with Acute Exacerbation of COPD.

MATERIAL AND METHODS

This study was single centre study conducted at a tertiary care centre which caters large population of Eastern Uttar Pradesh, Bihar, Jharkhand, Chattisgarh and Madhya Pradesh. Study was done from August 2016 to May 2018. After approval from institute ethical committee 50 patients were enrolled for this study and their data were analysed. It included patients with acute exacerbation of COPD above 45 years. We excluded the patients who have other systemic diseases viz.; renal disease, hepatic disease, neurological disease, coronary artery disease, multiple organ failure, hemodynamic instability independent cardiac conditions viz.; ischaemic cardiac disease previous episodes of Myocardial infarction etc.

At the time of presentation, thorough history and clinical examination was done. All the patients were aske about history of Cough, Expectoration, Fever, Breathlessness, Chest pain, Smoking – Bidi/ cigarette/ ganja/ hukka/no. of pack years,treatment history,occupational history. Any Previous history of exacebations, hospitalation, NIV application was asked. Thorough physical examination with special reference to cardiovascular. neurological and respiratory examination was done. After that comlete investigational work up was done which include complete blood count. renal and liver function tests, blood sugar level, blood gas analysis, serum bnp level, spirometry, radiography ECG and echocardiograpghy as par requirement.

Clinical Characterstics of Patients

Characteristics	Survived	NonSurvived	P value
Age	62.31±9.35	65.11±7.50	p=0.407
Duration of illness	9.24±4.95	16.44±6.71	p=0.001
Smoking	19.87 ±7.64	24.00±7.64	p=0.254
No. of exacerbations	0.85 ±0.79	1.55±0.72	p=0.030
CAT Score	27.26±2.13	29.77±1.56	p=0.002
Pco2	56.79±9.45	88.65±11.90	p=0.002
pH	7.16±0.92	7.32±0.045	p=0.000
RVSP	28.53± 3.88	32.66± 6.91	p=0.017
BNP	318.32±337.08	1218.10±559.35	p=0.018

Patients were followed through daily rounds till discharge. They were later classified into two groups Survived or Non-survived depending on in hospital mortality. Survived patient were assessed on need for any domiciliary supportive care like Long term oxygen therapy and Non Invasive Ventilation. The data was classified accordingly.

During hospital admission all the patients were treated with standard protocol including oxygen support, oral or intravenous antibiotics and oral or intravenous steroid as recommended by treating physician. Non-invasive Ventilation and Invasive ventilation was done whenever mandated and possible.

Statistical analysis

All the collected data was analysed by SPSS version 16. Independent student-t test was used for comparing the means of two groups. Chi-square test was used for non-parametric variables and p value of less than 0.05 was considered statistically significant and Correlation between variables are derived using Pearson correlation analysis.

RESULT

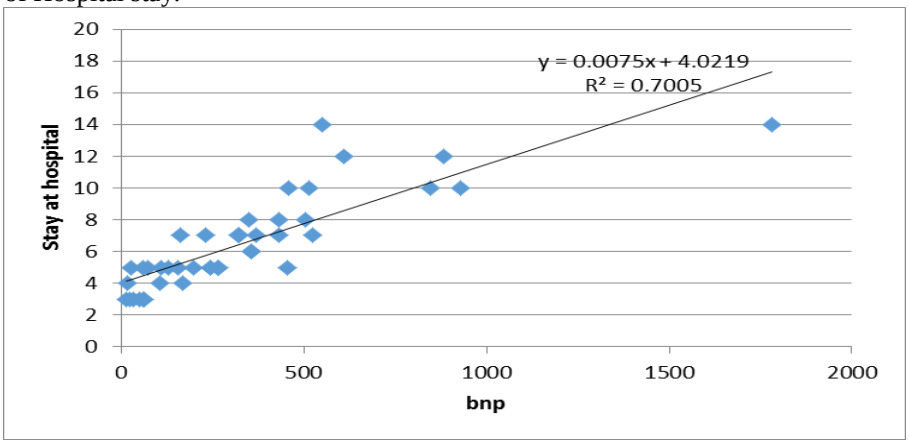
Out of 50 patients recruited 9 patients(18%) did not survive. BNP levels were increased in non-survived group when compared with survived group(mean value 1218 vs 318, p value 0.01). It was statistically significant. Mean BNP was higher in patients who required Mechanical Ventillation support in comparison to patients who needed Non Invasive Ventilation support or no intervention(mean value 480 vs 391 vs 115).

Table 2: BNP(Intervention wise mean).

	Mean±SD	Mann Whitney U-test
Survived	318.32±337.08	Z=2.441
Non survived	1218.10±559.35	p=0.018 (S)

	Mean±SD
No	115.27±57.54
NIV	391.166±136.109
MV	480.28±115.534

BNP vs Duration of Hospital stay.



Graph 1: BNP shows positive correlation with duration of hospital stay.

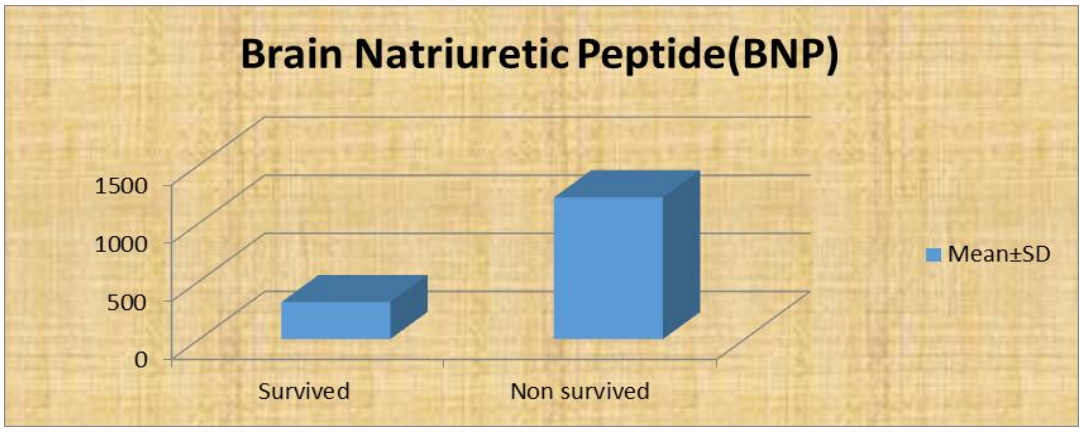


Figure 1: Brain Natriuretic Peptide(BNP)

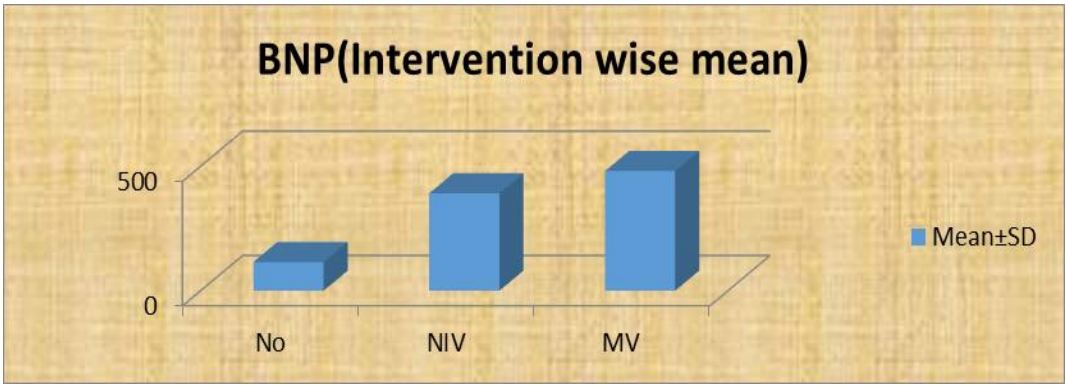


Figure 2: BNP(Intervention wise mean).

DISCUSSION

The annual rate of COPD exacerbations has been estimated from several different studies to be as low as 0.5 to a high of 3.5 exacerbations per patient. In our study it was 0.85 and 1.55 exacerbations in previous one year in survived and non survived groups respectively.

Worsening of clinical signs that represent respiratory distress (Increased respiratory rate, use of accessory muscle, cyanosis) and cor-pulmonale (pedal edema) were found to be significant in our study. 2D echocardiography features like Right atrium or ventricle dilatation, increased right ventricle systolic pressure were found significant in non survived group.

BNP is marker of cardiovascular dysfunction and mortality in acute exacerbation of copd.In our study BNP was raised in non survived groups in comparison to survived groups and it was stastically significant.

Previous study showed BNP independently predicted short term outcomes including intensive care unit admission, inpatient and 30 day mortality. In another study Nishimura K etal showed that Median BNP was also significantly higher in failed (inpatient death or early re-hospitalisation) compared to successful discharges following acute exacerbation of COPD hospitalization. In our study Patient with high BNP needed longer duration of hospital stay. It was also increased in patients who needed Intensive care support.

Some of the demerits of this study are, it is a single centre study with small cohort size. We in this study also did not look at associated co-morbidities and their effect on short term prognosis.

CONCLUSION

BNP was positively correlated with mortality of patients, need of intervention in management during hospital stay. BNP was also positively correlated with need of post hospital support like LTOT. This study provides simple prognostic factor for use in patients with COPD exacerbations presenting to the emergency department. It is very easy to measure at entry in the real-life context and represent powerful predictor of the risk of both death and need for post-hospital support.

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