



Original Research Article

Evaluation of Percentage of Change in Plasma NT-ProBNP Level Following Treatment of Acute Heart Failure Syndromes- A Prospective Clinical Study

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Received: 12/01/2014

Revised: 04/02/2014

Accepted: 13/02/2014

ABSTRACT

Background and aims: N-terminal pro brain natriuretic peptide (NT-proBNP) is known to aid intensive care unit diagnosis of Acutely Heart Failure Syndromes. Our aim was to study the percentage change in Plasma NT-proBNP level following treatment of Acute Heart Failure Syndromes and to establish time basis for measuring the second Plasma NT-proBNP.

Methodology: This study was conducted in 36 patients admitted with Acute Heart Failure Syndromes in Dr B R A M Hospital and Pt J N M Medical College. All the patients underwent comprehensive clinical evaluation and necessary investigations. Plasma NT-proBNP analysis was done twice in each patient, initially at the time of admission and later either at 72 hrs if patient had improved or else at the time of discharge.

Results: In our study, 22 (61.12%) patients showed more than 50% decrease in NT-proBNP values after treatment. While 5 (13.88%) patients showed 30-50% decrease in NT-proBNP values. Remaining 9(25%) patients showed less than 30% change in NT-proBNP values. Also, we found statistically significant reduction in plasma NT-proBNP following treatment at 72 hrs as compared to baseline ($p < 0.0001$).

Conclusion: In our study, majority of patients showed significant reduction in plasma NT-proBNP levels following treatment and majority of them did it within 72 hrs.

Keywords: Plasma N-terminal pro Brain natriuretic peptide, Acute Heart Failure Syndrome.

INTRODUCTION

Plasma NT-proBNP is an established marker for diagnosis and prognosis of Heart Failure patients.^(1,2) Being a quantitative indicator of cardiac wall stress, Plasma NT-proBNP levels decrease rapidly with improvement in Heart Failure.⁽³⁾ Plasma NT-proBNP level at admission or at discharge are considered as useful prognostic indicators for predicting readmission and

mortality at one year. Few studies used a cut off value of >4000 pg/ml at discharge for predicting poor prognosis.⁽⁴⁾ Plasma NT-proBNP is widely variable from patient to patient, because of different combination of underlying pathologies in each patient and intraindividual biological variability of peptide. Considering such large variations in plasma NT-proBNP, percentage reduction is a reliable indicator to assess cardiovascular

morbidity and mortality than levels assessed at either admission or at discharge. Each Heart Failure patient has chronic baseline level of Plasma NT-proBNP. Based on these, our aim was to find the percentage of patients who achieved significant reduction in plasma NT-proBNP following treatment and to establish time basis for measuring the second Plasma NT-proBNP.

MATERIALS AND METHODS

This study was conducted in 36 patients admitted with Acute Heart Failure Syndromes at Dr B R A M Hospital and Pt J N M Medical College, Raipur. Institutional ethics committee approved the study protocol and informed consent was obtained from study participants. All the patients underwent comprehensive clinical evaluation and necessary investigations such as blood tests (complete hemogram, serum creatinine, blood urea, liver function tests, fasting blood sugar, post-prandial blood sugar, fasting lipid profile, Plasma NT-proBNP), ECG, Chest X ray, 2D-Echocardiography and USG abdomen. Acute Heart Failure Syndromes (AHFS) was defined as the new onset or recurrence of gradually or rapidly developing symptoms and signs of heart failure requiring urgent or emergent therapy and resulting in hospitalization. The diagnosis of Acute Heart Failure Syndromes was made using criteria which was taken from the study reported by Rudiger A et al⁽⁵⁾ in the year 2005. The criteria used as follows a) Presence of an underlying heart disease. b) Presence of at least two of the following clinical symptoms and signs: 1) Dyspnea-NYHA grade III or IV, 2) Orthopnea, 3) Respiratory basal rales, 4) Elevated jugular venous pressure, 5) Systolic blood pressure below 90mmHg with decreased end organ perfusion. There has to be a rapid onset or significant worsening of heart failure symptoms within 7 days before admission.⁽⁶⁾

Second sample was taken at discharge if patient had not improved at 72hrs. Following criteria was included for assessment of improvement of acute heart failure in patients after 72 hrs of admission. A) Symptoms of Acute heart failure 1. Improvement in NYHA grade of dyspnea by at least 1 grade. 2. No orthopnea B) Decrease or disappearance of the following signs of Acute Heart Failure had taken as improvement. 1. Respiratory rate < 30 cycles per min 2. Heart rate < or =110 per min if heart rate at admission is >110 per min 3. Improvement in shock -Not on ionotrope support 4. Disappearance of rales 5. Disappearance use of accessory muscles 6. Disappearance of wheeze 7. Disappearance of S3 ,S4 gallop 8. Decreased Jugular venous pressure 9. Disappearance of tender hepatomegaly C) Investigations-. 1. Oxygen saturation-Saturation of 95% or more with room air. 2. Chest x ray-No alveolar pulmonary edema, no interstitial pulmonary edema.⁽⁶⁾ Based on this, second sample was collected at 72hrs in 32 patients and at discharge in remaining 4 patients.

Exclusion criteria were Acute myocardial infarction of less than seven days, Unstable angina, Serum creatinine >2mg/dl, Cirrhosis of liver, Hemoglobin <10g/dl. Patient underwent all the above mentioned investigations. Electrocardiogram was done immediately following admission. Chest X ray was done bedside on the day of admission.

Blood sample collection: Blood sample of about 4-5ml was collected for measurement NT-proBNP. Sample was taken with patient in supine position unless patient was severely orthopnic. The sample was collected into a refrigerated plastic tube, containing EDTA di potassium. The sample was immediately centrifuged within half an hour.

Centrifugation: Centrifugation was done by REMI medico/doctors centrifuges c-854/4

model with a maximum speed of 3500 RPM .The plasma nearly about 2-3mL separated was collected in an eppen drop and stored in deep freezer at minus 70 degree Celsius.

Storage of sample: Sample is stable at temperature of 20-25 degree Celsius for three days at 2-8 degree Celsius for six days at -20 degree Celsius for 24 months. In our study, we stored our samples at minus seventy degree Celsius as studies based on NT-proBNP analysis used storing temperature of minus seventy degree Celsius. Samples were kept in deep freezer in department of biochemistry.

Estimation of NT-ProBNP: We conducted NT-proBNP analysis using Roche Diagnostics cobas e 411 analyzer in the Department of Biochemistry .It is a fully automated, random-access, software controlled system for immunoassay analysis. Kit used for the study was ProBNP II kit. Test is an immunoassay for the in vitro quantitative determination of NT-proBNP in human serum and plasma. It works on the principle of electrochemiluminescence.

Statistical methods: The data entered in the case record forms were transferred to Microsoft Excel spreadsheet 2007. and SPSS version 20. Continuous data were presented as mean, and standard deviation. Categorical data were presented as actual numbers and percentages. Paired student t test was used to compare pre and post plasma NT-proBNP levels following treatment. A two tailed probability of P<0.05 was considered statistically significant.

RESULTS

On evaluation of baseline parameters, patient's mean (SD) age was 57.11(12.4) years, There were 20 males and 16 female patients. 5 patients were in class III NYHA and remaining 31 in class IV NYHA, 13 patients were known diabetic, and 22 patients were known hypertensives.

Parameters	Mean	SD
Age(yrs)	57.11	12.44
Pulse Rate (/min)	106.64	21.30
Systolic Blood Pressure(mmHg)	130.94	33.57
Diastolic Blood Pressure(mmHg)	81.14	19.83
Respiratory Rate(/min)	33.69	5.47
Hemoglobin(gm/dl)	11.57	1.72
Total Count(cell/mm ³)	9303	3163
S. Creatinine(mg/dl)	1.1	0.3
S. Urea(mg/dl)	33.08	20.40
S.Sodium(mEq/L)	135.87	7.34
S.Potassium(mEq/L)	3.848	0.79
Random blood sugar(mg/dl)	170.53	53.51
Fasting Blood Sugar(mg/dl)	113.09	33.56
T.Cholesterol(mg/dl)	146.14	38.87
LV Ejection Fraction(%)	40.47	14.13
NT-proBNP values(Adm)ng/ml	5842	6122
NT-proBNP values Hrs72 ng/ml	2786	4018

Baseline hemodynamic parameters revealed pulse rate 106.64(21.3) per min, Systolic Blood Pressure 130.94(33.5) mmHg, Diastolic Blood Pressure 81.14(19.8) mmHg, and Respiratory Rate 33.69(5.47) per min.

Baseline blood investigations showed Hemoglobin 11.57(1.72) gm/dl, Total Count 9303.14(3163) (cell/mm³), S. Creatinine 1.1(0.3) mg/dl, Urea 33.086(20.4) mg/dl, S. Sodium 135.879 (7.3) mEq/L, S. Potassium 3.848(0.8) mEq/L, Random blood sugar 170.53(53.5) mg/dl, Fasting Blood Sugar 113.09(33.5) mg/dl and T. Cholesterol 146.14(38.8) mg/dl.

Mean Ejection Fraction was 40.47(14.1) %, 15 patients had ejection fraction <40%. Mean NT-proBNP values (at Admission) was 5842.94(6122) ng/ml and NT-proBNP values following treatment (at Hrs72) was 2786.12(4018) ng/ml.(as shown in Table 1). Also, we found statistically significant reduction in plasma NT-proBNP following treatment at 72 hrs as compared to baseline (p<0.0001) as shown in Fig 2.

Fig.1 Percentage of Change in Plasma NT-proBNP Level following Treatment of Acute Heart Failure Syndromes (n=36)

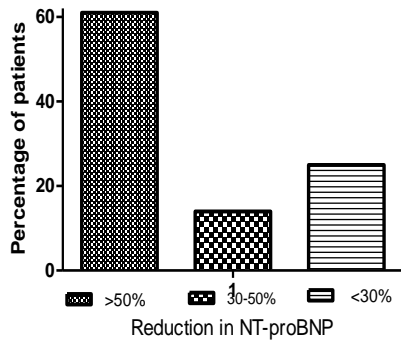
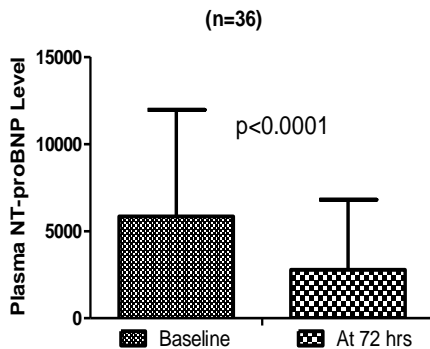


Fig.2 Plasma NT-proBNP level before and after treatment (n=36)



DISCUSSION

In our study, 22 (61.12%) patients showed more than 50% of reduction in plasma NT-proBNP value. In 20 out of these 22 patients, second sample was taken at 72hrs of treatment as they met improvement criteria. Many of the studies demonstrated that plasma NT-proBNP decrease rapidly with treatment and reach the nadir at 48hrs.⁽⁷⁾ Similarly in a study conducted by Noveanu et al, 2011,⁽³⁾ the mean decrease in plasma NT-proBNP was 27% at 24hrs, 45% at 48hrs and 67% at discharge. They showed significant association between reduction in plasma NT-proBNP and survival at 1 year. In a study conducted by Michtalic HJ et al,⁽⁸⁾ 44.70% of patients demonstrated >50% reduction in plasma NT-proBNP at discharge.

Similar to these studies which considered >50% reduction as significant reduction and prognostic feature, there are studies which considered >30% reduction as significant reduction and prognostic factor. In our study, 27(75%) patients showed >30 percent reduction in plasma NT-proBNP levels. Majority of those who achieved >30% reduction did it within 72 hrs. In a study conducted by Bettencourt P et al⁽⁹⁾ >30% reduction in plasma NT-proBNP was noted in 45.05% of patients and plasma NT-proBNP analysis was done at admission and at discharge. Bayes Genis et al⁽¹⁰⁾ studied plasma NT-proBNP at admission, 24hrs, 7 days, 6 months and 12 months. In this study, change in plasma NT-proBNP was noted between 24hrs and 7 days. They considered reduction more than 30% as significant and >30% reduction was considered to be best predictor of cardiovascular death during the follow up period of 1 yr. Based on these studies reduction in plasma NT-proBNP by 30% has been considered as a reasonable goal and patients who show both subjective and objective improvement in heart failure during hospital treatment, without reduction in plasma NT-proBNP are candidates for more intensive medical treatment and follow up.

The limitations of our study are small size of the sample and prognosis was not assessed in our study.

CONCLUSION

We conclude that majority of patients showed significant reduction in plasma NT-proBNP levels following treatment and majority of them do it within 72 hrs. Such reduction in plasma NT-proBNP correlated with improvement in Heart Failure. Hence second sample can be taken at 72hrs of treatment if patient shows improvement.

Conflict of Interest: None

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How to cite this article: Vishnuvardhan BR, Gupta GB, Khare RL et. al. Evaluation of percentage of change in plasma NT-proBNP level following treatment of acute heart failure syndromes- a prospective clinical study. *Int J Health Sci Res*. 2014;4(3):46-50.
