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NT-ProBNP as a Diagnostic and Prognostic Marker in Case of NSTEMI Patients

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ABSTRACT

Background: *Till date, myocardial infarction presents an alarming situation resulting in high morbidity and mortality. Non-ST elevation myocardial infarction (NSTEMI), becomes quite critical to diagnose from a specific biomarker. In this regard role of NT-proBNP as a prognostic marker in NSTEMI patients could be well considered.*

Aim: *Objective of this study is to highlight diagnostic and prognostic value of NT-proBNP in treatment of NSTEMI patients.*

Methods: *60 NSTEMI patients from outpatient department at Institute of Post graduate Medical Education and Research, Kolkata for a period of six months starting from January 2014 to June 2014 along with 60 age matched controls were included in the study. Serum was collected by centrifugation of the samples at 1500g and stored at -80°C for further analysis. Within first 48 hrs of admission, a level of NT-proBNP was measured. Results were presented as mean ± SEM or number or percentages and further analysis was done by SPSS software.*

Results: *Among 60 NSTEMI patients, 7 patients expired. Rest 53 patients recovered after treatment and showed significant decline in the NT-proBNP level after treatment (3565 ± 4261 pg/ml vs* 11,424 ± 12,460*pg/ml P<.0001).*

Conclusion: *It can be aptly stated that for early diagnosis and further prognosis in NSTEMI patients, NT-proBNP plays a crucial role.*

Keywords: *NSTEMI, NT-proBNP, BNP, myocardial infarction, prognosis*

INTRODUCTION

Throughout the world, myocardial infarction presents an alarming situation that ultimately leads to high morbidity and mortality. Non-ST elevation myocardial infarction (NSTEMI), the condition of myocardial infarction where the ECG tracing corresponds with the baseline, becomes quite elusive to diagnose from a specific biomarker. Hence, search for a definite diagnostic as well as prognostic marker is still on.

The N-terminal fragment of the prohormone B-type natriuretic peptide (NT-proBNP), a endogenous neurohormone, is known to get elevated as a cardiac stress response. NT-proBNP, the inactive form of BNP which is more stable than the active hormone BNP, is widely used in the diagnosis of cardiac stress [1]. Though, NT-proBNP and BNP are equivalent predictors of heart failure at all levels of renal function, NT-proBNP is far more superior indicator of mortality [2]. But definite prognostic role of NT-proBNP is still not characterized.

Increased plasma concentrations of NT-proBNP have been shown in several studies, to be an independent predictor of mortality in heart failure patients [3]. NT-proBNP elevations >450 pg/mL leads to a two- to six-fold increase in risk for cardiac mortality and/or morbidity.

In several studies, diagnostic role of NT-proBNP has been investigated and positively reported [4,5]. However, the role of NT-proBNP as a prognostic marker in NSTEMI remains elusive till date.

Thus, the main objective of this study is to highlight diagnostic and prognostic value of NT-proBNP in treatment of NSTEMI patients.

METHODS

Study Design

The study population comprises of 60 NSTEMI patients from outpatient department at Institute of Post graduate Medical Education and Research, Kolkata for a period of six months starting from January 2014 to June 2014. The study was approved by Institutional Human Ethical Committee and consents were duly taken from each patient. Few patients were excluded for not complying with the inclusion criteria. Patients were diagnosed to have acute myocardial infarction when level of creatine kinase-MB was elevated to twice the normal level with more than 20 mins duration of chest pain [6]. Diagnostic

serial electrocardiographic changes comprising of pathological Q waves or ST-segment and T-wave changes were studied [7] and thus 62 NSTEMI cases were chosen to be included in this present study. A minimum of 3 months follow-up [8] was undertaken which included measurement of NT-proBNP and exercise capacity estimations.

60 control cases were selected in the same age group (50-75) matching with the NSTEMI patients group. Smoking, cardiogenic shock, revascularisation, beta blocker intake of the controls were taken in accordance with the patient samples. Reported malignancy and recent surgery were considered as exclusion criteria.

Blood samples were obtained while patients were at rest. Serum was collected by centrifugation of the samples at 1500g and stored at -80°C for further analysis. Within first 48 hrs of admission, levels of NT-proBNP was measured by elctrochemiluminescence (Roche, Cobas e411).

Statistical Analysis

All the statistical analyses were done by SPSS software. Results were presented as mean ± SEM or number or percentages. Student's t test and non-parametric Wilcox test were employed to evaluate differences between groups. A p-value of <0.05 was considered to be significant.

RESULTS

On admission 60 patients presented signs of acute myocardial infarction without ECG change. It was found that in patients with acute myocardial infarction without ECG change (the patients were stamped as NSTEMI by CPK-MB and other clinical sign). NT-proBNP levels was significantly elevated than control (11,424±12,460 pg/ml vs 650±88 pg/ml, p <0.0001).

Patient characteristics were presented in Table 1. 55% of the patients in the study population were males and hypertension was present in 60% patients. 35% showed the characteristics of diabetes mellitus and previous medical records of coronary artery disease were 20% and myocardial infarction were 10%. On admission, 5% of the patients presented significant heart failures and 5% patients showed mitral regurgitation.

Previous medical history of the study population has been documented in Table 2.

60 Patients as Control and 60 NSTEMI patients taken both from same (50-75)yrs age group.20% control were smokers where as 25% NSTEMI Patients were smokers.1% control had cardiogenic shock but no control had previous history of revascularization where as 2% NSTEMI patients had history of both cardiogenic shock as well as revascularization.40% control were taking beta blocker where as 42% NSTEMI patients were taking beta blocker. Though no control had history of angina pectoris 1% NSTEMI patients had history of angina pectoris.

During treatment 7 NSTEMI Patients expired. Rest 53 NSTEMI Patients recovered after treatment. These 53 patients show tremendous decline in the pro BNP level after treatment (3565 ± 4261 pg/ml vs 11,424 ± 12,460 pg/ml P<.0001)

Table 1: Demographic and clinical data of study population

Parameter	Percentage
Hypertension	60
Male gender	55
Diabetes mellitus	35
Previous coronary artery diseases	20
History of myocardial infarction	10
Significant heart failure during admission	05
Mitral regurgitation on admission	05

Table: 2 Characteristics of the patients

Parameters	Normal patients	NSTEMI patients on admission
Number	60	60
Age group	50-75	50-75
	Previous medical records	
Smokers	20%	25%
Cardiogenic shock	1%	2%
Revascularisation	0%	2%
Beta blockers	40%	45%
Angina pectoris	0%	1%

Table 3. Level of NT-proBNP in normal and NSTEMI patients

Normal patients	NSTEMI patients on admission	NSTEMI patients on treatment
650 ± 88	11,424 ± 12,460	3565 ± 4261

DISCUSSION

Clinicians still face great difficulties in proper diagnosis and prognosis of NSTEMI as there is no help from ECG; also prognosis is also hard to predict in NSTEMI as revascularisation is contraindicated here [9]. By early and definite prediction of NSTEMI unnecessary medication that may lead to various harmful side effects may be avoided. However there exists high insufficiency in this area. Hence there is a immediate need for a definite diagnostic and prognostic marker of acute coronary diseases, so that initiation of treatment or change of medicines could be undertaken without much delay. PTCA which is life saving should be promptly considered depending on it and condition of the patient after PTCA could be reassessed by pro BNP.

Generally troponin, CK-MB has been the most commonest biochemical markers for AMI patients but there specificity is low [10]. Several recent studies, have reported newer biomarkers like BNP [11].

In this present study, we confirmed NT-pro BNP, more stable counterpart of BNP as both diagnostic and prognostic marker that can largely influence decision making in framing treatment regimens for patients. NT-proBNP, 76 amino acid biologically inert molecule is generated by proteolytic cleavage by furin and corin, produced due to cardiomyocyte stress [12]. 125/450 pg/ml cutpoints of FDA approved NT-pro BNP are effective to consider for early diagnosis of heart failure. Thus, NT-proBNP can be well established as an independent, additive as well as prognostic

marker in case of non-ST elevation myocardial infarction [13, 14].

This will enable clinicians to start early and more specifically targeted treatment regimen. In addition to clinical judgement, NT-proBNP measurement may lead to a more effective combinational therapy.

NT-proBNP has been reported to be a predictor of long duration mortality [15]. Omland et al reported 4 years mortality also in patients without heart failure by measurement of NT-proBNP [16].

In previous studies, NT-proBNP has shown a relationship with age and previous heart failure [17]. NT-proBNP maintained a higher than reference value level after 3 months of heart failure.

It has been proposed in [18] that more elevated level of NT-proBNP may occur due to presence of larger ischemic to necrotic zone ratio in early phase of NSTEMI, but afterwards necrosis and ischemia together leads to superimposition of NT-proBNP curves.After treatment of NSTEMI when ischemia resolves ProBNP level decline. Thus it can be aptly stated that for early diagnosis and further prognosis in NSTEMI patients, NT-proBNP plays a crucial role.

NT-proBNP level provide further implications in older patients [19]. High serum NT-proBNP in older patient group, being indicative of increased risk of future sudden cardiac dysfunction (arrhythmia and fibrillation) may enable clinicians to streamline more target oriented treatment, later followed by regular monitoring of clinical parameters.

CONCLUSION

NT-proBNP is thus can be accepted as a very powerful tool for NSTEMI patients. Not only infraction, in case of other cardiac emergency such as heart failure [20]. it proves its efficacy. Other than cardiac problem in COPD it has diagnostic and prognostic value [21]. Main advantage of NT-proBNP is that it is more specific as well as sensitive than traditional cardiac biomarkers [22]. The success of intervention such as PTCA can be predicted by it. The rate of fall or rise of NT-ProBNP in NSTEMI patients needs to be further investigated. Probably it is going to be a very useful marker of global dyskinesia of heart.

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REFERENCES

1. Hama N, Itoh H, Shirakami G, et al. Rapid ventricular induction of brain natriuretic peptide gene expression in experimental acute myocardial infarction. *Circulation* 1995: 92: 1558-64.
2. Kragelund C, Grønning B, Køber L, et al. N-terminal pro-B-type natriuretic peptide and long-term mortality in stable coronary heart disease. *N Engl J Med* 2005: 352: 666-75.
3. De Winter RJ, Stroobants A, Koch KT, et al. Plasma N-terminal pro-B-type natriuretic peptide for prediction of death or nonfatal myocardial infarction following percutaneous coronary intervention. *Am J Cardiol* 2004: 94: 1481-5.
4. Gardner RS, Ozalp F, Murday AJ, Robb SD, McDonagh TA. N-terminal pro-brain natriuretic peptide. A new gold standard in predicting mortality in patients with advanced heart failure. Eur Heart J 2003: 24(19):1735-43.
5. Darbar D, Davidson NC, Gillespie N et al. Diagnostic value of B-type natriuretic peptide concentrations in patients with acute myocardial infarction. Am J Cardiol 1996: 78(3):284-7.
6. McCarthy BD, Wong JB, Selker HP. Detecting acute cardiac ischemia in the emergency department: a review of the literature. J Gen Intern Med 1990; 5:365–373.
7. Shiran A, Adawi S, Dobrecky-Mery I, et al. Echocardiographic predictors of late mortality in elderly patients with acute coronary syndromes. *Isr Med Assoc J* 2007: 9: 247-51.
8. Eagle KA, Lim MJ, Dabbous OH, Pieper KS, Goldberg RJ, Van de Werf F, Goodman SG, Granger GB, Gabriel Steg P, Gore JM, Budaj A, Avezum A, Flather MD, Fox KAA. A validated prediction model for all forms of acute coronary syndrome. Estimating the risk of 6-month postdischarge death in an international registry. JAMA 2004: 291:2727–2733.
9. Hoekstra JW, Pollack CV Jr, Roe MT, Peterson ED, Brindis R, Harrington RA, Christenson RH, Smith SC, Ohman EM, Gibler WB. Improving the care of patients with non-ST-elevation acute coronary syndromes in the emergency department: the CRUSADE initiative. Acad Emerg Med 2002; 9:1146–1155.
10. Kistorp C, Raymond I, Pedersen F, Gustafsson F, Faber J, Hildebrandt P. N-terminal pro-brain natriuretic peptide, C-reactive protein, and urinary albumin levels as predictors of mortality and cardiovascular events in older adults. JAMA 2005: 293(13):1609-16
11. Seino Y, Ogawa A, Yamashita T et al. Application of NT-proBNP and BNP measurements in cardiac care: a more discerning marker for the detection and evaluation of heart failure. Eur J Heart Fail 2004: 6(3):295-300.

12. Wojciech Drewniak, Grażyna Snopek, Magdalena Zarukiewicz, Marcin Borys, Marek Dąbrowski. Prognostic value of the N-terminal pro-B-type natriuretic peptide in the elderly with acute myocardial infarction. Kardiol Pol 2008: 66: 750-755.
13. Latini R, Masson S, Wong M et al. Incremental prognostic value of changes in B-type natriuretic peptide in heart failure. Am J Med 2006: 119(1):70-30.
14. Olsson LG, Swedberg K, Cleland JG et al. Prognostic importance of plasma NT-pro BNP in chronic heart failure in patients treated with a beta-blocker: results from the Carvedilol Or Metoprolol European Trial (COMET) trial. Eur J Heart Fail 2007: 9(8):795-801.
15. McKie PM, Rodeheffer RJ, Cataliotti A et al. Amino-terminal pro-B-type natriuretic peptide and B-type natriuretic peptide: biomarkers for mortality in a large community-based cohort free of heart failure. Hypertension 2006: 47(5):874-80.
16. Omland T, Persson A, Ng L, et al. N-terminal pro-B-type natriuretic peptide and long-term mortality in acute coronary syndromes. *Circulation* 2002: 106: 2913-8.
17. Hogenhuis J, Voors AA, Jaarsma T, et al. Influence of age on natriuretic peptides in patients with chronic heart failure: a comparison between ANP/NT-ANP and BNP/NT-proBNP. *Eur J Heart Fail* 2005: 7: 81-6.
18. Heeschen C, Hamm CW, Mitrovic V, et al. N-terminal pro-B-type natriuretic peptide levels for dynamic risk stratification of patients with acute coronary syndromes. *Circulation* 2004: 110: 3206-12.
19. Bettencourt P, Azevedo A, Pimenta J, Frioes F, Ferreira S, Ferreira A. N-terminal-pro-brain natriuretic peptide predicts outcome after hospital discharge in heart failure patients. Circulation 2004: 110(15):2168-74.
20. Davidson NC, Naas AA, Hanson JK, et al. Comparison of atrial natriuretic peptide B-type natriuretic peptide, and N-terminal proatrial natriuretic peptide as indicators of left ventricular systolic dysfunction. *Am J Cardiol* 1996: 77: 828-31.
21. Rubinsztajn R, Nasiłowski J, Przybyłowski T, Karwat K, Chazan R. Usefulness of NT-proBNP serum level in the diagnosis of dyspnea in COPD patients *Pneumonol. Alergol.* Pol. 2013: 81, 1: 24–29.
22. Hall C. NT-ProBNP: the mechanism behind the marker. J Card Fail 2005: 11(5 Suppl):S81-S83.