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B-TYPE NATRIURETIC PEPTIDE(BNP) LEVELS AND ITS PROGNOSTIC VALUE IN ACUTE CORONARY SYNDROMES(ACS)

Medicine

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ABSTRACT

OBJECTIVES: This study was designed to evaluate the prognostic value of B-type natriuretic peptide (BNP) in patients across the entire spectrum of acute coronary syndromes (ACS). **METHOD:** We measured BNP levels at baseline in 100 consecutive patients between 24-96 hours after the onset of ischemic symptoms in patients of acute coronary syndromes. We did comparison between BNP levels and established prognostic markers Trop-T to determine short term morbidity and mortality. **RESULTS:** Patients with baseline BNP levels (> 80pg/ml, n=28) were at higher risk of new or progressive congestive heart failure (CHF) [17.8% vs. 1.39%, P = 0.002), new or recurrent myocardial infarction [17.8% vs. 2.8, P = 0.008) and death [17.8% vs. 1.39%, P= 0.002) within a period of 30 days. The mortality within 30 days in patients with BNP > 80pg/ml was 17.9% (P=0.002)compared to 5.7%(P=0.718) in patients with positive Trop-T (> 0.1ng/ml). **CONCLUSION:** A single measurement of BNP obtained between 24-96 hours after the onset of ischemic symptoms provides predictive information for use in risk stratifications across the spectrum of acute coronary syndromes. Cardiac neurohormonal activation may be a unifying feature among patients at high risk for death after acute coronary syndromes. BNP levels should be measured in all patients of Acute coronary syndromes.

KEYWORDS

BNP, ACS, CHF, Trop-T, STEMI,NSTEMI,UA,MI

INTRODUCTION

BRAIN (B-type) natriuretic peptide is a Cardiac neurohormone synthesized in ventricular myocardium and released into the circulation in response to ventricular dilatation and pressure overload.[1-3] BNP is synthesized in bursts and constitutively released from ventricular myocytes as a 76-amino acid N- terminal fragment (N-terminal BNP) and a 32-amino acid active harmone (BNP)[4]. The actions of brain (B-type) natriuretic peptide, include natriuresis, vasodilatation, inhibition of the renin-angiotensin–aldosterone axis, and inhibition of sympathetic nerve activity.[5] The natriureteric peptides relax vascular smooth muscles,causing arterial and venous dilation and leading to reduced blood pressure and ventricular preload [6-7].The plasma level of B-type natriuretic peptide is elevated in patients with congestive heart failure and increases in proportion to the degree of left ventricular dysfunction and the severity of symptoms of heart failure.[2,8]

After acute myocardial infarction, levels of B-type natriuretic peptide(BNP) rise rapidly during the first 24 hours and then tend to stabilize.[9-12] Measurement of the level of B-type natriuretic peptide(BNP) between one and four days after a transmural infarction provides prognostic information that is independent of the left ventricular ejection fraction and other important base-line variables [11,13-17] First studied as a diagnostic and prognostic marker among patients with congestive heart failure (CHF)[18], BNP was subsequently found to predict outcomes in patients with acute transmural myocardial infarction (MI)[19]. We extended these findings across the spectrum of patients with acute coronary syndromes (ACS) including those with unstable angina

AIMS AND OBJECTIVES :

1. To measure the plasma level of brain natriuretic peptide (BNP) in patients of acute coronary syndromes (ACS) .

2. Follow up of the patients of acute coronary syndromes (ACS) through 30 days to determine short term morbidity and mortality and their relation with BNP levels.

MATERIAL AND METHOD:

A total of 100 consecutive patients of acute coronary syndromes admitted in medical intensive coronary care unit (MICCU) of Govt Medical college Srinagar fulfilling the inclusion criteria were included in this study.

Study Design: Prospective, cross-sectional-analytical study

Inclusion Criteria[20]: Patients were included if they presented within 72 hours after the onset of ischemic discomfort and met one or more of the following criteria:
Electrocardiographic changes (ST-segment depression or elevation of at least 0.5 mm,T-wave inversion of at least 3 mm in at least three leads, or left bundle-branch block), elevated levels of cardiac markers, a history of coronary disease, or an age of at least 65 years in patients with diabetes or vascular disease.

Exclusion Criteria :
Age >80 years
Death within 24 hours after acute coronary syndromes
Cardiogenic shock
Serum creatinine>2.5mg/dl

A detailed history and clinical examination of all the patients fulfilling above criteria with baseline investigations was done as per the proforma attached . Heart failure was diagnosed on the basis of Framingham's criteria for diagnosis of congestive heart failure[21].

Biochemical Analysis: Blood sample (2ml) were taken between 24 to 96 hours of the onset of the symptoms. B-type natriuretic peptide (BNP) was measured in EDTA. Anticoagulated plasma using two site sandwich immunoassay by direct chemiluminescence technology using ADVIA-CENTAUR from SIEMENS).This assay has a minimal detectable concentration of 2.0pg/ml.

Cardiac Troponin-T was measured using Trop-T kit by Roche. A positive result (> 1.0ng/ml) is evidence of cell damage in myocardium. CK-MB was measured using CK-MB isoenzyme reagent catridge manufactured by Dad Behring USA with normal range from 0.7 U/L on Dad Behring analyzer. Any value more than higher limit of normal was taken as positive.

RESULTS:

Baseline characteristics of the patients included in the study

Patient characteristics		No. of patients	Percentage (%)
Gender	Male	69	69 %
	Female	31	31%

Age	≤65	60	60%
	>65	40	40%
Heart rate (mean±SD)	84.9±14.3(62-136)		
Systolic blood pressure (mean±SD)	132.3±21.0(90-190)		
Killip class	Class 1	83	83%
	Class 2	14	14%
	Class 3	03	03%
MEDICAL HISTORY			
Cigarette smoking		67	67%
Diabetes mellitus (DM)		26	26%
Hypertension		62	62%
Congestive heart failure (CHF)		05	5%
Previous Angina		42	42%
Cerebrovascular Disease (CVD)		05	5%

Acute coronary syndromes (ACS) in patients included in the study

Acute coronary syndromes	No. of patients	Percentage (%)
STEMI	59	59
NSTEMI	29	29
Unstable Angina	12	12

Brain natriureteric peptide (BNP) levels (pg/ml) in patients included in the study

		No. of patients	Percentage(%)
Brain natriureteric peptide (BNP)levels (mean±SD)		68.7± 48.5(2,634)	
Brain natriureteric peptide (BNP)	>80	28	28
	≤80	72	72

Table 1 : Brain Natriuretic Peptide levels in relation with Age and Gender of Acute Coronary Syndromes Patients included in the study

		> 80		≤ 80		Results
		N	%	N	%	
Age	> 65	18	45.0	22	55.0	OR=4.1: p = 0.002 (Sig)
	≤ 65	10	16.7	50	83.3	
Gender	Male	16	23.2	53	76.8	OR= 2.1: p = 0.112 (NS)
	Female	12	38.7	19	61.3	

Table 3: Brain Natriuretic Peptide in relation with Past Cardiovascular History in the patients included in the study

Past History		> 80		≤ 80		Results
		N	%	N	%	
Congestive Heart Failure	Present	4	80.0	1	20.0	OR= 11.8: p = 0.000 (Sig)
	Absent	24	25.2	71	74.7	
Previous angina	Present	22	78.6	21	29.2	OR= 8.9: p = 0.000 (Sig)
	Absent	6	21.4	51	70.8	
Cerebro- vascular Disease	Present	4	80.0	1	20.0	OR= 11.8: p = 0.008 (Sig)
	Absent	24	25.3	71	74.7	

Table 5: Brain Natriuretic Peptide in relation with acute coronary syndrome in the patients included in the study

Acute coronary syndrome	> 80		≤ 80	
	N	%	n	%
STEMI	19	32.2	40	67.8
NSTEMI	7	24.1	22	75.9
U/A	2	16.6	10	83.4
Overall chi square (x^2) = 1.496; p = 0.473				

Table 6: Brain Natriuretic Peptide levels in relation with Cardiac Bio-Markers in the patients included in the study

Bio-Marker		> 80		≤ 80		Results
		N	%	N	%	
Trop T	Positive	27	30.6	61	69.4	OR= 4.9: p = 0.351 (NS)
	Negative	1	8.3	11	91.7	
CK- MB	Positive	26	31.3	57	68.7	OR= 3.42: p = 0.297 (NS)
	Negative	2	11.7	15	88.3	

Table 11 : Relationship between Elevated Bio Markers and Mortality within 30 days in the patients included in the study

		Died		Survived		p value
		n	%	n	%	
BNP	> 80	5	17.9	23	82.1	0.002 (Sig)
	< 80	1	1.4	71	98.6	
Trop T	Positive	5	5.7	83	94.3	0.718 (NS)
	Negative	1	8.3	11	91.7	

Table 10: Incidence of new or progressive congestive heart failure, new or recurrent myocardial infarction and mortality in the patients included in the study at 30 days

Follow Up		> 80		≤ 80		Results
		> 80	%	n	%	
New or Progressive CHF	Present	5	17.8	1	1.39	OR= 15.4: p = 0.002 (Sig)
	Absent	23	82.2	71	98.6	
New or recurrent MI	Present	5	17.8	2	2.8	OR= 7.6 : p = 0.008 (Sig)
	Absent	23	82.2	70	97.2	
Mortality	Present	5	17.8	1	1.39	OR= 15.4 : p = 0.002 (Sig)
	Absent	23	82.2	71	98.6	

DISCUSSION:

This is the first ever study of its kind conducted in which we evaluated the the prognostic value of BNP,a cardiac neuroharmone across the entire spectrum of ACS. Patients with BNP levels of more than 80 pg/ml were significantly more likely to die, have new or recurrent myocardial infarction,or have new or progressive heart failure than those with with BNP less than 80 pg/ml[20]. After adjustment for other independent predictors of long term risk of death, a BNP threshold of more than 80 pg/ml was taken as cut off for evaluation in this study.

Among 100 patients of ACS index diagnosis was ST-segment elevation myocardial infarction (STEMI) in 59%,non-ST-segment elevation myocardial infarction (NSTEMI) in 29% and unstable angina (UA) in 12%.in our study 32.2% of the patients with STEMI, 24% of the patients with NSTEMI and 16.6% of the patients with UA had BNP levels> 80pg/ml. this shows that BNP levels were raised among all the three subgroups of ACS patients, with STEMI patients more likely to have raised BNP > 80pg/ml.

Among patients with positive Trop-T(>0.1ng/ml) and raised CK-MB, BNP levels >80pg/ml were found in more number of patients compared those with negative Trop-T and normal CK-MB levels.

In our study, 17.8% of the patients with BNP>80pg/ml had new or progressive congestive heart failure as compared to 1.3% with BNP<80pg/ml (P=0.002). similarly new or recurrent MI was 17.8% with BNP>80pg/ml as compared to 2.78% with BNP≤80pg/ml (P=0.008). Five patients (17.8%) who had BNP levels> 80pg/ml died with in 30 days while only one patient (1.39%) with BNP≤80pg/ml(P=0.002) during the follow up period of one month.

Among established cardiac biomarkers, BNP is the most robust prosnostic mrker as evident by the fact that 17.9%(P=0.002)of the patients with BNP levels >80pg/ml died with 30 days compared to 5.7% (P=0.718) with positive Trop-T test.

We have demonstrated that a single measurement of B-type natriuretic peptide, obtained between 24-96 hours of the onset of ischemic symptoms provides powerful information for use in risk stratification across the entire spectrum of acute coronary syndromes. Despite heterogenecity in pathophysiology, clinical presentation and risk among patients who had myocardial infarction with ST-segment elevation, patients who had myocardial infarction in the absence of ST-segment elevation, and patients who had unstable angina, increasing levels of B-type natriuretic peptide were predictive of an increased risk of morbidity and mortality in each of these subgroups.

The association between BNP and the short term risk of death was independent of presence or absence of clinical evidence of heart failure, the troponin T, electrocardiographic changes, and other known predictors of the risk of death in patients with acute coronary syndromes. In addition a high level of BNP was associated with an increased risk of non-fatal end points, including new or progressive heart failure and myocardial infarction. Finally it appears that the

previously defined BNP threshold of 80pg/ml, indicative of neurohormonal activation in patients with heart failure[11] is also an appropriate threshold among patients with acute coronary syndromes.

CONCLUSION:

For a cardiac biomarker to be clinically useful, it must help clinicians select an appropriate therapeutic regimen. Patients with elevated levels of B-type natriuretic peptide after an acute coronary syndrome are at high risk for death, a new myocardial infarction, and heart failure and may benefit from intensive antiplatelet and antithrombotic therapies, neurohormonal antagonism with agents such as beta-blockers and angiotensin-converting-enzyme inhibitors, and early revascularization. Further studies should be conducted on larger scale to assess the role of BNP in identifying patients who would benefit from various treatment strategies.

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