CLINICAL EVALUATION AND ROLE OF BNP IN THE DIAGNOSIS OF HEART FAILURE IN PATIENTS WITH ACUTE SHORTNESS OF BREATH- AN OBSERVATIONAL STUDY

Sidharth Kapoor[1]

[1]*Associate Professor, Department of Medicine, Acharya Shri Chander College of Medical Sciences, Sidhra, Jammu.*

ABSTRACT

BACKGROUND

Acute dyspnoea is a common clinical finding in the emergency department. A rapid and accurate investigation of acute dyspnoea is vital since treatment of dyspnoea can differ markedly depending on the initial clinical impression. Distinguishing between cardiac and noncardiac causes of dyspnoea is often challenging. Measuring blood, BNP levels rapidly and accurately confirms or excludes the diagnosis of CHF in the urgent care setting making it a valuable clinical tool.

MATERIALS AND METHODS

This observational study was conducted on 100 patients who had presented with acute shortness of breath to the Emergency Department of Acharya Shri Chander College of Medical Science and Hospital with effect from November 2006 to November 2007. 5 mL of sample blood was collected for measurement of Brain Natriuretic Peptide (BNP), which was estimated quantitatively chemiluminescence method.

RESULTS

In this study of 100 patients, final diagnosis of CHF was present in 60 patients, which was based on echocardiographic results. Cutoff of <100 pg/mL, BNP levels was taken to exclude heart failure. It was observed that according to BNP levels alone 62 patients had heart failure (BNP levels of >100 pg/mL). BNP levels for diagnosing CHF had a sensitivity of 90% and a specificity of 80%. It was also found that BNP was helpful in detecting diastolic heart failure in presence of normal left ventricular systolic function. 7 patients had BNP levels at the time of admission higher than 1000 pg/mL and died within a week of hospital stay indicating the correlation of BNP levels with severity of CHF and also its prognostic significance.

CONCLUSION

The dramatic rise in incidence and prevalence of Congestive Heart Failure (CHF) can be attributed to a drastic increase in cardiovascular risk factors such as obesity and diabetes and improved survival rate after acute myocardial infarction and subsequent development of CHF in the last 25 years. Misdiagnosis can lead to increased mortality. BNP assay is a simple and reliable tool to improve the diagnostic accuracy of CHF.

KEYWORDS

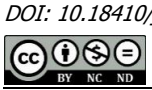
Congestive Heart Failure, B-Type Natriuretic Peptide, Amino Terminal ProBNP, Left Ventricular Ejection Fraction, Myocardial Infarction.

HOW TO CITE THIS ARTICLE: Kapoor S. Clinical evaluation and role of BNP in the diagnosis of heart failure in patients with acute shortness of breath- An observational study. J. Evid. Based Med. Healthc. 2017; 4(44), 2706-2709. DOI: 10.18410/jebmh/2017/538

BACKGROUND

Dyspnoea is defined as an abnormally uncomfortable awareness of breathing; it is one of the principal symptoms of cardiac and pulmonary disease and ranges from an increased awareness of breathing to intense respiratory distress (Schwartzstein and Thibault, 1998).[1] After evaluating patient's symptoms conducting a physical examination and performing electrocardiography and chest radiography, the clinician is often left with considerable diagnostic uncertainty, which results in misdiagnosis and delays the initiation of appropriate therapy. Misdiagnosis causes morbidity, increases the time to discharge and the cost of treatment. The use of a treatment strategy for other conditions such as chronic obstructive pulmonary disease may be hazardous to patients with heart failure and vice versa (Maisel et al, 2002).[2]

Financial or Other, Competing Interest: None.
Submission 22-05-2017, Peer Review 27-05-2017,
Acceptance 31-05-2017, Published 01-06-2017.
Corresponding Author:
Dr. Sidharth Kapoor,
Associate Professor, Department of Medicine,
Acharya Shri Chander College of Medical Sciences,
Sidhra, Jammu.
E-mail: sidkap10@gmail.com
DOI: 10.18410/jebmh/2017/538



Aims and Objectives

The Framingham criteria is one of the most commonly used tools to predict CHF on the basis of history and physical examination results. They use major and minor criteria based on history, physical examination results and ancillary test results to categorise patients as having definite, probable and questionable CHF (Ho, 1993).[3]

Although, having a high specificity for increased filling pressures, jugular venous distention and an S3 gallop have sensitivities of only 30% and 24%, respectively (Collins et

al, 2003)[4] endothelin. As any pressure and/or volume overload of the cardiac chambers would stimulate production and release, increased natriuretic peptides reflect a common pathology present in patients with left ventricular dysfunction, volume overload or heart failure regardless of aetiologies (Moe, 2006).[5]

Although, its clinical utility of BNP as a biochemical marker of left ventricular systolic dysfunction has been reported, elevation of plasma BNP is one of the characteristics of patients with or at risk of diastolic heart failure among subjects with preserved left ventricular systolic function (Hitoshi Y et al, 2004).[6]

BNP has been shown to be a powerful prognostic marker in both chronic and acute heart failure independent of standard echocardiographic parameters. At best, BNP testing may provide better titration of the diuretic dose, allow earlier discharge when the BNP levels do fall satisfactorily and identify those patients who should have more intensive therapy (if it is possible) and closer observation (John E S, 2004).

It is found that when used in conjunction with other clinical information, rapid measurement of BNP levels in the emergency department improves the care of patients with acute dyspnoea and thereby reduces the time to discharge and the total cost of treatment (Mueller et al, 2004).[7]

MATERIALS AND METHODS

This observational study was conducted on patients attending the emergency department of Acharya Shri Chander College of Medical Science (ASCOMS) and hospital with effect from November 2006 to November 2007. ASCOMS is a 500 bedded multispeciality hospital located on national highway bypass, Sidhra, Jammu, and caters to patients either seeking treatment directly or referred from other healthcare institutions in the State of Jammu and Kashmir. In the present study, 100 patients of different age groups were studied whose predominant symptom was dyspnoea of acute onset. Because of increased awareness of heart failure and dyspnoea being so distressing complaint, patients and their attendants could be easily motivated for this.

A definitive CHF diagnosis is often based on right heart catheterisation or indirect measurement of ejection fraction by means of radionuclide scanning or echocardiography. Lack of immediate availability and high cost make these studies prohibitive as emergency department screening tests. As a result, an emergency department diagnosis of CHF is often based on history and physical examination findings along with results of ancillary tests such as chest radiography and Electrocardiography (ECG) (Collins et al, 2003).

It has been known for about 50 years that the heart is cardiorespiratory and an endocrine organ. Left ventricular dysfunction results in haemodynamic changes and neurohormonal activation. The sympathetic nervous system, renin-angiotensin-aldosterone system and endothelin pathway are activated to maintain blood pressure, improve perfusion and increase chronotropy and inotropy (Collins et al, 2003). But, prolonged activation of these systems might lead to deleterious effects such as hypertrophy, fibrosis and apoptosis. Subsequently, there is release of natriuretic peptides, which act as counter regulatory system by suppressing the renin-angiotensin-aldosterone system and endothelin. The natriuretic peptide family consists of Atrial Natriuretic Peptide (ANP), Brain Natriuretic Peptide (BNP), and three other structurally similar peptides- C-type Natriuretic Peptide (CNP) mostly of central nervous system and endothelial origin, urodilatin from the kidney and Dendroaspis Natriuretic Peptide (DNP), which is of unknown significance (Levin et al, 1998).[8]

It has been seen that significant amounts of ANP can be released in response to minor stimuli such as exercise, but BNP is synthesised in bursts and is released predominantly in response to stretching of the ventricular wall and volume overload. The biologic actions of BNP include vasodilatation, diuresis, natriuresis and inhibiting or antagonising the actions of the renin-angiotensin aldosterone system, the sympathetic nervous system, arginine vasopressin and cardiomegaly, acute pulmonary oedema, S3 gallop and hepatojugular reflux.

Minor Criteria

Bilateral ankle oedema, nocturnal cough, dyspnoea on ordinary exertion, hepatomegaly, pleural effusion and tachycardia (>120 beats/min.).

Diagnosis of congestive cardiac failure required two major or one major and two minor criteria to be present concurrently.

Patients were categorised into 2 groups- After complete clinical evaluation, those patients fulfilling the Framingham's criteria were classified as CHF group and those not meeting the criteria as NO CHF group as diagnosed initially on the basis of clinical assessment.

Final diagnosis of CHF being present or absent was made by a cardiologist whose diagnosis was also supported by echocardiography. Systolic heart failure was diagnosed based on determination of Left Ventricular Ejection Fraction (LVEF). Patients with LVEF <50% were categorised as having systolic failure. Diastolic failure was made on the basis of exclusion, which includes clinical signs and symptoms of CFIF, but with normal LVEF.

Statistical Analysis

The data was analysed with the help of computer software Epi-Info version 6.0. Brain natriuretic peptide levels were presented as mean and Standard Deviation (SD) with corresponding 95% confidence intervals. Diagnostic accuracy of BNP was evaluated by calculating sensitivity, specificity with 95% confidence intervals. Predictive value of the BNP was also calculated. Different cutoff of the BNP levels were used for this purpose.

Inclusion Criteria

Acute shortness of breath or dyspnoea was defined as an abnormally uncomfortable awareness of breathing of less than 7 days duration. Those patients primarily presenting

with acute shortness of breath (NYHA class III-IV) constituted the study group.

Exclusion Criteria

1. Patients with history of renal disease (defined by serum creatinine level of more than >2.8 mg/dL).
2. Patients of cirrhosis with ascites.
3. Patients of thyroid dysfunction.
4. Patients with history of trauma, chest wall.
5. Patients of acute myocardial infarction.
6. Patients on chronic use of β-blockers, diuretics and digoxin, angiotensin-converting enzyme inhibitors.
7. Patients with unstable angina were excluded from the study unless their predominant symptom at presentation was acute dyspnoea.

Patients of dyspnoea were clinically evaluated, which included complete history and examination, electrocardiography and x-ray chest.

Measurement of Brain Natriuretic Peptide (BNP) levels- Before patient was given any medication 5 mL of venous blood was withdrawn from a peripheral vein by a plastic disposable syringe and collected in an air-tightened lavender top EDTA (ethylenediaminetetraacetic acid) plastic tube. Blood was frozen after it is centrifuged. BNP level was estimated quantitatively by chemiluminescence method. Cutoff of <100 pg/mL, BNP levels was taken to exclude heart failure.

Diagnosis of heart failure- To establish a clinical diagnosis of congestive heart failure following the Framingham's criteria were used.

Major Criteria- Paroxysmal nocturnal dyspnoea, neck vein distention, rales, radiographic, 18 patients with CHF were missed by initial clinical evaluation.

It was also observed that in majority of patients with CHF, BNP levels was >400 pg/mL. Higher mean BNP levels was observed with advancing age particularly in patients with CHF with highest mean BNP levels of 770.02 pg/mL in age group of >75 years with CHF. Lower BNP Levels was observed in patients without CHF with lowest mean BNP level of 51.05 pg/mL in age group of 56-65 years without CHF.

Furthermore, it was seen, 7 patients had BNP levels at the time of admission higher than 1000 pg/mL. These patients had severe heart failure, majority had markedly reduced ejection fraction on echocardiography. All these patients died within 7 days of hospital stay. 6 patients had BNP <100 pg/mL, but had CHF as final diagnosis. 8 patients had BNP >100 pg/mL, but had no diagnosis.

It was also observed that out of 100 patients 9 patients which included 7 males and 2 females had normal systolic functions (LVEF >50%), but were included in the final diagnosis of diastolic heart failure by the cardiologist based on diastolic filling abnormalities on echocardiography. All these 9 patients had BNP levels >100 pg/mL (mean BNP level of 523.9 pg/mL). Out of these 9 patients, 3 patients had initial clinical diagnosis of heart failure.

RESULTS

The study sample was comprised of 100 patients, which included 55 males and 45 females. 47 patients met the clinical criteria of heart failure out of whom, 41 patients had BNP levels of >100 pg/mL.

60 patients had final diagnosis of CHF, which was also supported by echocardiography, out of whom only 6 patients had BNP levels of <100 pg/mL, whereas rest of 54 patients had BNP levels of >100 pg/mL test, which could help in finding out the cause of dyspnoea. Patients with acute shortness of breath fulfilling the criteria mentioned below were part of the study.

Final Diagnosis of CHF Based on Echocardiography	Based on Serum BNP Level		Based on Clinical Evaluation	
	>100 pg/mL	<100 pg/mL	CHF Present	CHF Absent
CHF present	54	6	42	18
CHF absent	8	32	5	35

Table 1. Diagnosis of CHF

Age (Years)	Males	Females	Total	Mean Serum BNP in (pg/mL) in Patients With CHF		Mean Serum BNP (pg/mL) in Patients Without CHF	
				Males	Females	Males	Females
15-25	5	3	8	140	134	57.6	63.06
26-35	4	8	12	243	206.5	59.2	70.58
36-45	9	7	16	408.4	366.5	53.06	125.6
46-55	10	8	18	550.17	343	200	109.12
56-65	8	7	15	404.35	480.75	51.05	102
66-75	6	6	12	394.32	706	63.9	65.2
>75	13	6	19	770.02	628	78	84
Total	**55**	**45**	**100**				

Table 2. Serum BNP Levels in Patients With or Without CHF in Both Sexes with Respective to Their Age Groups

BNP Level (in pg/mL)	With CHF	No CHF	Total
<100	6	32	38
100-199	1	3	4
200-299	5	3	8
300-399	10	1	11
400-699	20	0	20
>700	18	1	19
Total	**60**	**40**	**100**

Table 3. Serum BNP Levels in Patients With or Without Final Diagnosis of CHF

Diagnostic Accuracy	Serum BNP Levels (pg/mL)	Clinical Assessment
Sensitivity	90% (78.83-95.86)	70 (56.62-80.79)
Specificity	80% (63.86-90.38)	87.5 (72.39-95.30)
Positive predictive value	87.09% (75.59-93.38)	89.36 (76.10-96.01)
Negative predictive value	84.21% (68.07-93.41)	66.03 (51.64-78.11)

Table 4. Diagnostic Accuracy of Serum BNP Levels Versus Clinical Evaluation

DISCUSSION

In this study, it was observed that clinical examination have a sensitivity of 70%, specificity of 87.5%, positive predictive value of 89.36%, negative predictive value of 66.03%, positive likelihood ratio = 5.6% and negative likelihood ratio of 0.34% for diagnosing CHF.

It was observed in this study that BNP levels for diagnosing CHF has a sensitivity of 90%, specificity of 80%, positive predictive value of 87.09, negative predictive value of 84.21, positive likelihood ratio of 4.5 and negative likelihood ratio of 0.125 for diagnosing CHF-BNP can reliably detect diastolic heart failure in presence of normal left ventricular systolic function. Therefore, BNP assay can reinforce the diagnosis of diastolic heart failure in such patients.

CONCLUSION

Furthermore, patients with higher BNP levels, e.g. >1000 pg/mL had higher mortality rates indicating that these patients had severe heart failure, majority had markedly reduced ejection fraction on echocardiography. This indicates that BNP has not only diagnostic, but prognostic significance as well. These observations emphasise the importance of measuring BNP levels on initial presentation in patients with suspected heart failure, so that vigorous and appropriate therapy could be instituted.

REFERENCES

[1] Schwartzstein RM, Thibault GE. Approach to the patient with dyspnea. In: Goldman L, Braunwald E, eds. Primary cardiology. Philadelphia: WB Saunders 1998:98-111.

[2] Maisel AS, Krishnaswamy P, Nowak RM, et al. Rapid measurement of B- type natriuretic peptide in the emergency diagnosis of heart failure. N Engl J Med 2002;347(3):161-167.

[3] Ho KL, Prinsky JL, Kannel WB, et al. The epidemiology of heart failure: the Framingham study. J Am Coll Cardiol 1993;22(Supp A):6A-13A.

[4] Collins SP, Ronan-Bentle S, Storrow AB. Diagnostic and prognostic usefulness of natriuretic peptides in emergency department patients with dyspnea. Ann Emerg Med 2003;41(4):532-545.

[5] Moe GW. B-type natriuretic peptide in heart failure. Current Opinion in Cardiology 2006;21(3):208-214.

[6] Yamaguchi H, Yoshida J, Yamamoto K, et al. Elevation of plasma brain natriuretic peptide is a hallmark of diastolic heart failure independent of ventricular hypertrophy. J Am Coll Cardiol 2004;43(1):55-60.

[7] Mueller C, Scholer A, Laule-Kilian K, et al. Use of B-type natriuretic peptide in the evaluation and management of acute dyspnea. N Engl J Med 2004;350(7):647-654.

[8] Levin ER, Gardner DG, Samson WK. Natriuretic peptides. N Engl J Med 1998;339(5):321-328.