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A REVIEW ON IMPORTANCE OF B-TYPE NATRIURETIC PEPTIDE IN DIAGNOSIS AND MANAGEMENT OF HEART FAILURE IN EMERGENCY DEPARTMENT

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ABSTRACT
Heart failure is the major and increasing cause of death and disability worldwide. Heart failure is often difficult to diagnose with the symptoms and physical findings. Identification of circulatory biomolecules that may provide new windows into the diagnosis and management of cardiovascular diseases. The natriuretic peptide plays an important role in diagnosis and management of heart diseases in present scenario. Misdiagnosis of congestive heart failure can be life threatening, because treatments for congestive heart failure are hazardous to patients with other conditions, such as chronic obstructive pulmonary disease. The natriuretic peptide consists of three peptides, the A type peptide (ANP: Released from atria), the B type peptide (BNP: Released from ventricles) and the C type peptide (CNP: released from endothelial cells). B-type natriuretic peptide is a neurohormone which is released directly from the ventricles in response to volume expansion and pressure overload. In patients with left ventricular dysfunction we can see the elevated levels of BNP. BNP levels are significantly higher in patients with dyspnea because of heart failure than from the cause. The B-type natriuretic peptide has very short half-life i.e. 22 min and thus reflects the current movement of ventricular overload. BNP is more accurate than the ejection fraction or ANP for predicting the diagnosis of congestive heart failure. BNP may distinguish the cardiac and non-cardiac causes of acute dyspnea in emergency department. To provide cost effective treatment for patients with congestive heart failure, rapid and accurate differentiation of congestive heart failure from another causes of dyspnea must be accomplished.

KEYWORDS: Heart failure, Natriuretic peptides, Emergency department, Disability, Ejection fraction, Dyspnea.

INTRODUCTION
Heart failure is the leading cause of hospital admission among patients over the age of 65 yrs and accounts for 3% of the total national health care budget.[1] In the U.S. alone the prevalence of heart failure is 4.6 million, with an incidence rate of 550,000 new cases a year and approximately 957,000 hospitalizations annually.[2] Traditionally the diagnosis of congestive heart failure (CHF) has been done based on the presence of certain signs and symptoms. In chronic out patients, in whom the physical signs are usually prominent, the diagnosis of CHF decompensating is easy. On the other hand, in elderly patients who present to the emergency department (ED) with acute dyspnea, the diagnosis is sometimes challenging. Signs and symptoms may not be sufficiently accurate to make a diagnosis of CHF.[3] Although the echocardiogram is a good method for diagnosing left ventricular systolic dysfunction, it may not reflect an accurate condition. Additionally, as a consequence of population aging, predominant diastolic heart failure is a common finding and thus the presence of a normal systolic function does not rule out the diagnosis of CHF.[4] B-type (or brain) natriuretic peptide (BNP) which was first isolated from the brain of a monkey is a neurohormone secreted mainly from the ventricles as a response to volume expansion and pressure overload. BNP promotes diuresis and vasodilation and has been found to be elevated in patients with CHF and to correlate with New York Heart Association (NYHA) classifications.[5,6,7,8,9]

Physiology of Natriuretic Peptides
BNP and ANP are synthesized in myocytes as larger molecules that are subsequently cleaved to yeald the

active peptide hormone (eg., BNP) and the biologically inactive N-terminal peptide fragment (eg., NT-proBNP). Both ANP and BNP activates the same trans membrane receptor (natriuretic peptide receptor A) on target organs and as a consequence have similar physiologic effects, both hormones promote the renal excretion of sodium (natriuresis) and water (diuresis), cause vasodilation by relaxing vascular smooth muscle cells, improve diastolic relaxation, with ANP acting as the primary circulating natriuretic peptide hormone under normal conditions and BNP being primarily as a result of increased myocardial wall stress.[10] B-type of natriuretic peptide (BNP) is a cardiac neurohormone secreted from membrane granules in the cardiac ventricles as a response to ventricular volume expansion and pressure overload. B-type natriuretic peptide levels have been shown to be elevated in patients with symptomatic left ventricular dysfunction and correlate to left ventricular filling pressure, New York Heart Association (NYHA) classification and prognosis. Falling BNP levels reflect beneficial treatment but, until recently, had the same pitfalls of measurement as other neurohormones and cytokines.[11,13] B- type of natriuretic peptide is a 32-aa polypeptide containing a 17-aa ring structure common to all natriuretic peptides.[14,15] The source of plasma BNP is cardiac ventricles, which suggests that it may be a source more sensitive and specific indicator of ventricular disorders than other natriuretic peptides.[16,17,18]

Measurement of levels of B-type Natriuretic Peptide

During the initial evaluation, a blood sample was collected into a tube containing potassium EDTA. B-type natriuretic peptide was measured with the use of fluorescence immunoassay. Laboratory-based assays and point-of-care assays are available for BNP and NT-pro BNP using fully automated immunoassays. The most commonly used decision threshold for BNP is 100pg/mL; the corresponding values for NT-pro BNP are 125 pg/mL for patients less than 75 years old and 450 pg/mL for those 75 or older.[19] Available data suggest that the BNP and NT-proBNP have similar accuracy in the diagnosis of acute dyspnea.[20] levels of both molecules are elevated with aging and are higher in women than in men.[21] A useful rule of thumb is that the BNP level in a normal person should be less than half their chronologic age.[22] Renal insufficiency affects the levels of both BNP and NT-proBNP. In one large strategy study, BNP had a modest correlation with renal function and levels were increased in patients with a creatinine clearance of less than 60 mL/min/1.73 m^2. The investigators proposed that the reference value for these patients should be 200pg/mL.[23] A similar NT-proBNP study found a moderately strong inverse relation with renal function and the authors recommended a reference value of 1200pg/mL for patients with an estimated clearance below 60 mL/min/1.73m^2.[24] Doust and colleagues identified 19 studies examining the prognostic value of BNP or NT-proBNP in heart failure.[25] The studies using a dichotomous BNP were more variable. The largest of these, the Valsartan Heart Failure Trail (Val-HeFT) using a subset of 3618 patients, reported a doubling of mortality among patients with a BNP level greater than 97pg/mL.[26] Logeart and colleagues examined the prognostic value of serial admission and discharge BNP measurents among 105 patients surviving hospital stay for decompensated heart failure and discharged with either New York Heart Association class II or III disease.[27]

Management of Heart Failure Therapy with BNP

The case for BNP guided therapy depends on several important assumptions. The first, for which there is reasonable evidence, is that therapies that reduce adverse clinical events in heart failure also reduce BNP levels. BNP levels have improved with a variety of drug therapies known to be efficacious in heart failure, including angiotensin-converting-enzymes (ACE) inhibitors[28], angiotensin-receptor blockers[29], beta-blockers[30] and spironolactone.[31] The second assumption, for which there is much less evidence, is that therapies that improve outcomes in heart failure do so primarily through mechanisms that are linked with changes in BNP levels. In an early study involving 20 patients with decompensated heart failure, changes in BNP levels mirrored changes in pulmonary wedge pressures.[32] However, repeated evidence in medicine that surrogate end points often do not behave as expected highlights the necessity of demonstrating in large studies the connection between changes in BNP and patient outcomes. Finally, the concept of BNP-guided therapy presumes that BNP data will direct the clinician to make changes in therapy that could not otherwise be made. For most of heart failure therapy, however, drug dosage is based on patient tolerance and the targets achieved in the pivotal clinical trials, not on response to therapy. Only in the case of diuretic dose is there a major opportunity to alter management by providing additional information about the patients response to therapy.[33]

CONCLUSION

The BNP test had a high level of significance in diagnosis and management of congestive heart failure. However in the clinical setting, BNP testing plays a major role in case of heart failure. In future, the usage of BNP shows impact on socio-economic status of patient. BNP and NT-proBNP are ADCHF biomarkers with well-described diagnostic accuracy that should logically extrapolate to improved patient outcomes within the context of frequently delayed diagnosis in ED patients with multiple confounding comorbidities. Point-of-care analysis of BNP and NT-proBNP help emergency physicians in managing patients with a variety of conditions. They are a strong tool in the ED to differentiate CHF from its various mimics and are also helpful in monitoring of heart failure therapy.

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