ABNORMAL LABORATORY RESULTS

B-type natriuretic peptide: a new diagnostic tool for congestive heart failure

Ben Ewald, Lecturer in Epidemiology, and General Practitioner, Centre for Clinical Epidemiology and Biostatistics, University of Newcastle, Newcastle, New South Wales

SYNOPSIS

B-type natriuretic peptide is released from the ventricle of patients with heart failure. High concentrations help to distinguish heart failure from other causes of dyspnoea. The test is sensitive in congestive heart failure but it cannot distinguish if the dysfunction is diastolic or systolic. B-type natriuretic peptide is not used as a routine test in Australia, but if it becomes available it may be helpful in ruling out the diagnosis of congestive heart failure. It is also being investigated as a screening tool for heart disease in the community.

Index words: echocardiography, dyspnoea, screening.

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Introduction

The diagnosis of congestive heart failure rests on three elements. These are suitable signs and symptoms, objective evidence of ventricular dysfunction, and response to treatment. While the diagnosis is generally clear when the patient has obvious clinical or radiological pulmonary oedema, it can be difficult to make when the condition is less advanced or the patient has comorbidities such as lung disease. The Framingham criteria are a way of scoring symptoms and clinical signs, but cannot be regarded as giving a definitive diagnosis of congestive heart failure. In one recent study the Framingham criteria were compared with the diagnosis made by two cardiologists with access to echocardiographic results for 1586 acutely dyspnoeic patients presenting to emergency wards. The criteria and the final diagnosis were concordant in only 73% of patients.[1] Improved ways of detecting congestive heart failure would therefore be of great clinical benefit.

Objective evidence of ventricular dysfunction is currently obtained from echocardiography, catheter studies, or nuclear medicine studies. Catheter studies and nuclear medicine are invasive, quite expensive and not widely available. Echocardiography is more widely available, however it still requires waiting for, and travel to, an appointment. This can be a problem for the frail aged or patients in rural areas. Detection of ventricular dysfunction by a simple blood test would therefore be a very attractive alternative.

Physiology

Four neurohormonal systems are activated by ventricular dysfunction. These are the sympathetic nervous system, the renin-angiotensin-aldosterone system, the endothelin pathway, and the natriuretic peptides. All these systems maintain systemic tissue perfusion and the first three also maintain blood pressure, which is advantageous in the short term but deleterious to the heart in the long term.

The natriuretic peptides produce diuresis, natriuresis and vasodilatation. These effects reduce the load on the heart, and work in opposition to the renin-aldosterone system and the sympathetic nervous system. Although natriuretic peptides are increased in heart failure, their effects are overwhelmed by the activated renin-angiotensin-aldosterone system and sympathetic nervous system. Three peptides have been identified:

- A (or atrial) natriuretic peptide is secreted by the atrium in response to dilatation
- B natriuretic peptide (BNP, originally called 'brain natriuretic peptide' as it was found in the brains of pigs) is produced by the ventricle in response to increased end diastolic pressure or volume
- C natriuretic peptide is produced widely by endothelial cells in response to shearing stresses.

B-type natriuretic peptide

When stimulated by stress or stretch, ventricular myocytes activate transcription of the relevant gene and produce a 108 amino acid peptide (Pro BNP). Before excretion by the myocyte this peptide is cleaved to produce an inactive 76 amino acid N-terminal fragment and the C-terminal 32 amino acid with hormonal activity (BNP).[2] Plasma half-life of BNP *in vivo* is 18 to 22 minutes so concentration promptly reflects changes in cardiac status.

Available assays measure either the inactive N-terminal fragment or the active 32 amino acid peptide. There are currently several assays available that do not give directly comparable results. Individual laboratory reference ranges should therefore be used.

Of all the neurohormones, BNP is the best candidate for use as a diagnostic test. When BNP rises it tends to go very high,

which gives it good discriminatory power in separating ventricular causes of dyspnoea from other causes. In one series of patients presenting to an emergency ward with shortness of breath, those without heart failure had a mean BNP concentration of 38 pg/mL while in those with heart failure it averaged 1076 pg/mL. [3]

Four studies* (totalling 1994 patients) have compared the test performance of BNP with the diagnosis of congestive heart failure made by echocardiography and consideration of all clinical details.[1,3,4,5] The results show BNP has a sensitivity of 90–97% and a specificity of 76–92%. There have also been four studies* (totalling 6109 people) which investigated using BNP to screen for pre-clinical heart disease in the community.[6,7,8,9] Three of these studies showed good test performance with sensitivities ranging from 77% to 100% and specificities from 70% to 96%. Recent results[9] contradict these findings and show sensitivity in detecting any left ventricular systolic dysfunction of only 53% in men and 26% in women. For moderate to severe left ventricular systolic dysfunction these values are 65% and 80%, well below those found in the other studies. This suggests that although BNP shows good test performance in acutely sick hospital patients it is less accurate in the detection of ventricular dysfunction in asymptomatic individuals.

Only two of the studies (involving 232 patients) investigated the use of BNP as a diagnostic tool for suspected congestive heart failure in general practice. Further research is needed to validate the test in the milder spectrum of disease seen in general practice. One such study is currently under way in Newcastle, New South Wales.

Congestive heart failure can be due to either systolic or diastolic ventricular dysfunction. While there are guidelines[10] and a wealth of good evidence from randomised controlled trials on the management of systolic dysfunction, there is scant evidence on how to manage diastolic failure. BNP is increased in both systolic and diastolic dysfunction so many patients will still need echocardiography in order to plan therapy. The value of the test may eventually be in its capacity to rule out heart failure as a cause of a patient's illness.

BNP has been shown to be a powerful predictor of prognosis in patients with heart failure. A high concentration is associated with a poor prognosis. Some centres are therefore using BNP concentrations to guide therapy, however this usage is still experimental.

E-mail: ben.ewald@newcastle.edu.au

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* Details of studies of BNP are available in the electronic version of this article.
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Self-test questions

The following statements are either true or false (answers on page 71)

7. Changes in end diastolic pressure stimulate the secretion of B-type natriuretic peptide from the brain.
8. In congestive heart failure concentrations of B-type natriuretic peptide increase.

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