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ORIGINAL ARTICLE

Usefulness of plasma B type natriuretic peptide as a predictor to identify responders following CRT

Amr Nawar *, **Wael Samy, Hisham Elaasar, Amal Rizk, Sherif Mokhtar**

Critical Care Department, Faculty of Medicine, Cairo University, Egypt

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KEYWORDS

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Abstract It has been shown that patients with heart failure have high levels of brain or type B natriuretic peptide (BNP), and that there is a correlation between these and the severity of their condition. Many studies report that monitoring BNP levels could be a sensitive method for diagnosing heart failure and performing risk stratification, and that they could act as an independent predictor of adverse events helping clinicians arrive at a prognosis.

To achieve this purpose we studied 30 patients with CHF (27 males, mean age 57 years) undergoing CRT implantation.

The main finding of our study was that CRT exerted a substantial reduction in plasma BNP levels among responders, but no significant change in nonresponders after 3 months follow-up, only responders showed a significant decrease in plasma BNP levels (229.64 pg/ml ± 111) as compared to non-responders (468 pg/ml ± 96) P value <0.01. Response could be predicted with a cut-off value of 360 pg/ml, with a sensitivity and specificity of 90.9% and 87.5%, respectively.

In conclusion, BNP monitoring is potentially a good prognostic indicator of LV functional recovery and reverse remodeling after CRT can accurately identify echocardiographic responders after CRT. Percentage change in plasma BNP levels from baseline to 3 months was the strongest predictor of long-term response to CRT and may have potential to predict outcome.

1. Introduction

Cardiac resynchronization therapy (CRT) is an established therapy for patients with moderate-to-severe heart failure (HF) and ventricular dyssynchrony. CRT improves Cardiac function, quality of life (QoL), and life expectancy in patients with HF [1–4]. Biventricular pacing improves symptoms (New York Heart Association [NYHA] class), exercise tolerance (6-min walk distance), and quality-of-life scores by decreasing dyssynchrony in patients with advanced chronic HF [5–7]. Cardiac resynchronization therapy (CRT) optimizes ventricular loading conditions, improves systolic function,

* Corresponding author.

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and reduces mitral regurgitation, thereby leading to reverse remodeling [5,6,8].

However, lack of response to CRT has been reported in up to 30% of patients [6,8,9]. On the basis of these considerations, a variety of parameters, including echocardiographic ventricular dyssynchrony [10], QRS reduction after implantation [11], and the location and extent of myocardial scarring [12], have been reported to be predictors of the response to CRT, but disappointing results from PROSPECT study indicated the limitation of these parameters [13].

There has been growing interest in identifying new markers for dyssynchrony and the techniques to optimize device settings to increase the true-responder rate, in addition to optimal medical management [14–17]. CRT-induced reverse remodeling could reduce neurohormonal activity in addition to improving anatomic and functional parameters.

Brain natriuretic peptides (BNP) and its inactive amino terminal portion (NT-pro BNP), are neurohormones released by the ventricle in response to increase LV wall stress. Hence, BNP level may play a valuable role for the assessment of cardiac dysfunction, particularly LV dysfunction, and for monitoring of the response to cardiac therapy [18,19]. Decrease in BNP associated with drug treatment in patients with CHF correlates with improvement in hemodynamic parameters [20–22], clinical status and prognosis, including number of hospitalizations for deterioration of CHF [23,24]. Fruhwald et al. [25] showed that CRT leads to an early and sustained decrease in NT-pro BNP potentially reflecting improvement in LV function. In responders, left lateral wall pacing increases systolic function, reduces mitral regurgitation (MR) and thus decrease the wall motion stress. In this favorable remodeling process, neurohumoral activity is reduced and the decrease in plasma B-type natriuretic peptide after initiation of CRT predicts clinical improvement during follow-up [26].

1.1. Aim of work

The aim of this study was to evaluate the effect of CRT on plasma concentrations of β-type natriuretic peptide (BNP) and the value of BNP in predicting the clinical response to CRT.

2. Patients and methods

Over a period of one year from September 2012 to November 2013, thirty patients who received a biventricular pacing system were studied. They included 27 males and 3 females, with a mean age of 57.5 ± 6 years.

The patients were studied at the (Critical care department) Cairo University.

2.1. Inclusion criteria

- Advanced CHF (NYHA class II-IV) despite optimized drug therapy including angiotensin converting enzyme inhibitors or Angiotensin receptor antagonists, diuretics, beta-receptor blockers and spironolactone when tolerated.
- Intraventricular conduction delay (QRS $\geqslant$ 120 ms) in the form of left bundle branch block.
- Left ventricular ejection fraction (LVEF) $\leqslant$35% as assessed by echocardiography.

2.2. Exclusion criteria

(1) Patients with uncontrolled HF requiring hospital admission or not on stable medical therapy for the last three months; (2) serum creatinine level $\geqslant$2 mg/dl; (3) myocardial infarction within previous 3 months; (4) previous valve replacement or reconstructions.

2.2.1. The studied patients were subjected to baseline assessment including

Informed written consent, Full history taking and clinical examination, twelve lead ECG, NYHA class, blood pressure, heart rate, CHF compensation status and QRS duration were assessed during each clinical follow-up visit, and their exercise capacity was assessed by a 6-min walk test.

2.3. All patients were subjected to

2.3.1. Biochemical assays

BNP level was assessed in the absence of uncontrolled HF one to 10 days before implantation. Blood samples were drawn from an antecubital vein in the morning before and 3 months after the implant. Blood for measurement of plasma BNP was transferred to a chilled tube containing *ethylenediaminetetraacetic acid* (EDTA) (1 mg/ml) and aprotinin (500 kallikrein inactivator U/mL). Test tubes were immediately centrifuged. Plasma samples were stored at −70 °C until assay. Plasma BNP concentrations were measured using a specific immunoradiometric assay (non-extracted) for human BNP. (RayBio®, USA) done at our unit Lab. The analysis was blind to the outcome.

2.3.2. Echocardiographic measurements

All patients were subjected to transthoracic echocardiographic examination using ATL.HDI 5000 colored echocardiographic machine using a 3.5 MHz transducer (PHILIPS).

Two-dimensional Doppler-flow echocardiography was performed at baseline and at follow up to assess left ventricular (LV) ejection fraction (EA), diastolic dimensions and the degree of mitral regurgitation quantification (from grade 1 to 4). LVEF was calculated using the single plane method. The analysis was blinded to the outcome.

2.4. Study protocol

Peripheral blood samples for analysis of BNP were drawn at baseline and 3 months after initiation of CRT. At baseline, history, clinical status, drug therapy, echocardiographic parameters and Exercise capacity testing were evaluated. Three months after implantation of the CRT system, clinical status, drug therapy and echocardiographic data were assessed.