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ORIGINAL RESEARCH

Assessment of neurohormonal changes in chronic heart failure

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Abstract
Background: Chronic heart failure (CHF) in adults is characterized by high circulating levels of several chemical messengers of cardiac and extracardiac origin, collectively referred to as neurohormones. The present study was conducted to assess neurohormonal changes in chronic heart failure.
Materials & Methods: 42 patients of congenital heart disease of both genders were put into group I. Group II comprised sex and age matched control. The level of atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), epinephrine, norepinephrine and active renin were determined using immunoradiometric assays,
Results: The level of ANP (pmol/L) was 56.3 and 3.2, BNP (pmol/L) was 35.9 and 5.2, ET-1 (pmol/L) was 2.43 and 0.71, norepinephrine (nmol/L) was 2.16 and 1.52, epinephrine (nmol/L) was 0.50 and 0.41, renin (pmol/L) was 143.2 and 16.5 and aldosterone (pmol/L) was 540.2 and 332.6 in group I and II respectively. The difference was significant ($P< 0.05$).
Conclusion: Neurohormonal activation in adult congenital heart disease bears the hallmarks of chronic heart failure, relating to symptom severity and ventricular dysfunction.
Key words: congenital heart disease, Neurohormonal activation, ventricular dysfunction

Introduction

Chronic heart failure (CHF) in adults is characterized by high circulating levels of several chemical messengers of cardiac and extracardiac origin, collectively referred to as neurohormones. It is well established that the degree of neurohormonal activation in CHF relates to functional capacity, the degree of left ventricular dysfunction, and mortality.

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Contemporary evidence-based therapy for CHF involves pharmacological manipulation of neurohormonal pathways and has resulted in substantial improvements in morbidity and prognosis for patients with this condition.[1]

Neurohormonal activation has been observed in some manifestations of congenital heart disease, although reports have, in the main, been confined to small numbers of pediatric patients, have focused on specific types of cardiac lesions, and have been limited to the assessment of a single neurohormone system. After major advances in diagnosis and treatment in children, however, there are now as many as 1 million adults with congenital heart disease in the United States.[2]

Increased chemosensitivity correlates with increased neurohormonal activation, worsened functional capacity, and decreased survival. Augmented ergoreceptor reflexes are associated with worsened symptoms and reduced exercise tolerance (peak VO2). All of these neurogenic systems are likely to have a role in sustained neurohormonal activation, although the relative contribution of each system is unclear.[3,4] Although the activation of these 'neurohomonal' systems evolved to maintain cardiovascular homeostasis in the shortterm, the extant literature suggests that these compensatory mechanisms can cause additional damage to the heartand circulation when they are sustained. Further, the degree of neurohormonal activation correlates with disease severity and clinical prognosis in heart failure.[5]The present study was conducted to assess neurohormonal changes in chronic heart failure.

Materials & Methods

The present study comprised of 42 patients of congenital heart disease of both genders. The consent was obtained from all patients.

Data such as name, age, gender etc. was recorded. They were put into group I. Group II comprised sex and age matched control. Peripheral venous blood samples were obtained. Blood was collected into tubes containing EDTA, EDTA and aprotinin. The samples were centrifuged at 3000 rpm for 15 minutes at 4°C. Plasma and serum aliquots were stored at −75°C until analysis. Atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), and active renin were determined using immunoradiometric assays, ANP and BNP from EDTA/aprotinin plasma and active renin from EDTA plasma. Aldosterone was determined in serum by radioimmunoassay (EuroDPC). Endothelin-1 (ET-1) was determined in EDTA/aprotinin plasma by enzyme-linked immunosorbent assay (Bachem). Norepinephrine and epinephrine levels were measured in EDTA plasma using high-performance liquid chromatography with electrochemical detection, as previously described. For all subjects, the full blood count, renal function, and liver function were determined using routine laboratory method. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I Distribution of patients

Groups	Group I	Group II
Status	Congenital heart disease	Healthy
M:F	24:18	24:18

Table I shows that there were 24 males and 18 females in group I and in group II. Group I had patients with CHD and group II had healthy control.

Table II Neurohormone levels in both groups

Parameters	Group I	Group II	P value
ANP (pmol/L)	56.3	3.2	0.01
BNP (pmol/L)	35.9	5.2	0.02

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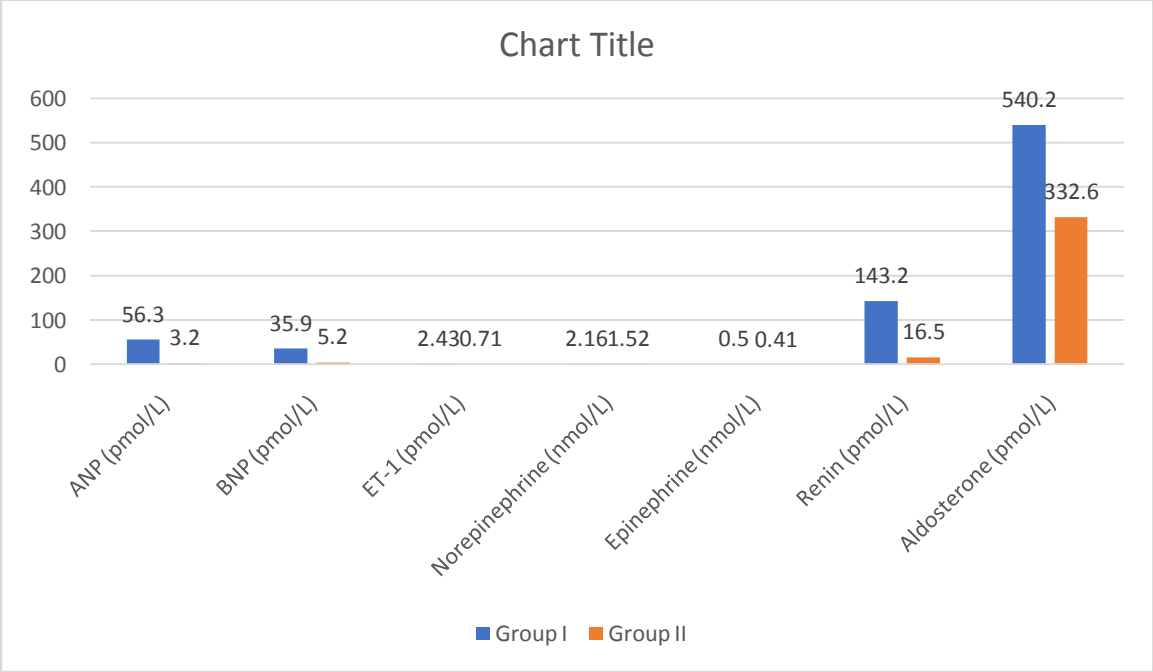
ET-1 (pmol/L)	2.43	0.71	0.05
Norepinephrine (nmol/L)	2.16	1.52	0.04
Epinephrine (nmol/L)	0.50	0.41	0.91
Renin (pmol/L)	143.2	16.5	0.02
Aldosterone (pmol/L)	540.2	332.6	0.01

Table II, graph II shows that the level of ANP (pmol/L) was 56.3 and 3.2, BNP (pmol/L) was 35.9 and 5.2, ET-1 (pmol/L) was 2.43 and 0.71, norepinephrine (nmol/L) was 2.16 and 1.52, epinephrine (nmol/L) was 0.50 and 0.41, renin (pmol/L) was 143.2 and 16.5 and aldosterone (pmol/L) was 540.2 and 332.6 in group I and II respectively. The difference was significant (P< 0.05).

Graph II Neurohormone levels in both groups



Discussion

Heart failure with reduced ejection fraction (HFrEF) classically develops after an 'index event' that reduces cardiac pump function.[6] The index event could be an acute injury to the heart, such as a myocardial infarction; or might develop slowly, as with long-standing haemodynamic overload; or occur in response to genetic variations that disrupt contractile function or lead to sarcolemmal fragility and myocyte death.[7] The circulatory changes that arise from impaired myocardial pump function are sensed by peripheral arterial baroreceptors as 'underfilling' of the circulation. More recent studies have suggested an important role for peripheral chemoreceptors and ergoreceptors.[8] These sensory receptors activate a series of compensatory mechanisms that lead to changes in heart rate and cardiac contractility, salt and water retention, and constriction of the peripheral blood vessels. These alterations work collectively to maintain cardiovascular homeostasis.[9] The compensatory mechanisms that have been described thus far include: activation of the sympathetic (adrenergic) nervous system (SNS) and renin–angiotensin–aldosterone system (RAAS), which maintain cardiac output through increased retention of salt and water, peripheral arterial vasoconstriction and increased contractility; and inflammatory mediatorsthat are involved in cardiac repair and remodelling.[10]The present study was conducted to assess neurohormonal changes in chronic heart failure.

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In present study, there were 24 males and 18 females in group I and in group II. Group I had patients with CHD and group II had healthy control. Bolger et al[11] in their study concentrations of atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), endothelin-1 (ET-1), renin, aldosterone, norepinephrine, and epinephrine were determined in 53 adults with congenital heart disease, comprising 4 distinct anatomic subgroups and 15 healthy control subjects (8 female; 32.3±1.3 years of age). Systemic ventricular function was graded by a blinded echocardiographer as normal or mildly, moderately, or severely impaired. Adults with congenital heart disease had elevated levels of ANP (56.6 versus 3.1 pmol/L), BNP (35.8 versus 5.7 pmol/L), ET-1 (2.5 versus 0.7 pmol/L, all $P<0.0001$), renin (147 versus 16.3 pmol/L), norepinephrine (2.2 versus 1.6 pmol/L, both $P<0.01$) and aldosterone (546 versus 337 pmol/L, $P<0.05$). There was a highly significant stepwise increase in ANP, BNP, ET-1, and norepinephrine according to New York Heart Association class and systemic ventricular function, with even asymptomatic patients having evidence of significant neurohormonal activation. In contrast, there was no direct relationship between the 4 anatomic subgroups and any of the neurohormones studied.

We found that the level of ANP (pmol/L) was 56.3 and 3.2, BNP (pmol/L) was 35.9 and 5.2, ET-1 (pmol/L) was 2.43 and 0.71, norepinephrine (nmol/L) was 2.16 and 1.52, epinephrine (nmol/L) was 0.50 and 0.41, renin (pmol/L) was 143.2 and 16.5 and aldosterone (pmol/L) was 540.2 and 332.6 in group I and II respectively. Ross et al[12] reported that infants and children (mean age, 3.3 years) with congenital heart disease and severe congestive heart failure had elevated plasma norepinephrine levels regardless of etiology. Systemic ventricular function, although not relating to neurohormonal activation when impairment was mild, seems to be an extremely sensitive discriminant in this regard when severely impaired. Although accounting for only 3 patients, mean levels of ANP (434 pmol/L), BNP (235 pmol/L), ET-1 (5.66 pmol/L), and norepinephrine (2.86±0.32 nmol/L) were higher in this group than in any other group by systemic ventricular function or NYHA class.

Conclusion

Authors found that neurohormonal activation in adult congenital heart disease bears the hallmarks of chronic heart failure, relating to symptom severity and ventricular dysfunction.

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