

The relation of plasma level of atrial and brain natriuretic peptides to left ventricular function in hypertensive patients

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ABSTRACT

Objective: To examine the plasma level of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) in patients with hypertension and to evaluate the importance of plasma level of these hormones in predicting the left ventricular function in these patients.

Design: A case-series study.

Setting: Echocardiography Unit of Ibn-Sena teaching hospital and Medical college, Mosul. During the period from August 2004 to March 2005.

Participants: Sixty patients with essential hypertension, were divided into 3 groups depending on severity of the disease. Group I, included 17 patients, group II, included 24 patients and group III, included 19 patients. The study also included 30 apparently healthy volunteers as a control group.

Methods: Plasma ANP, BNP and left ventricular ejection fraction (LVEF%) were measured in hypertensive patients as well as in the control group. The ANOVA test was used to examine the difference in the mean of the studied parameters within patient groups themselves and between patient groups and control. Pearson correlation coefficient was used to study the correlation of the studied parameters within each group. All values are expressed as mean \pm SD.

Results: The mean of plasma ANP was significantly higher in group III than that in control group ($p < 0.001$) and group I ($p < 0.05$). The mean of plasma BNP was significantly higher in group III than that in control group ($p < 0.0001$), group I ($p < 0.0001$) and group II ($p < 0.0001$). Furthermore, the plasma BNP was significantly higher ($p < 0.01$) in group II than that in control group. The mean of LVEF% was significantly lower in group III than that in control group ($p < 0.0001$), group I ($p < 0.0001$) and group II ($p < 0.001$). There was a significant negative correlation between plasma BNP level and LVEF% in group III ($r = -0.62$, $p < 0.005$).

Conclusion: The results of this study showed that plasma ANP and BNP levels are significantly increased in patients with severe hypertension. The results also indicate that BNP may be an excellent screening test for left ventricular dysfunction in hypertensive patients.

الخلاصة

الهدف: دراسة مستوى هورمون البيبتيد الاذيني المدر للصوديوم وهورمون البيبتيد الدماغى المدر للصوديوم فى البلازما لدى المرضى المصابين بفرط ضغط الدم الشريانى ولمعرفة أهمية هذا الهورمون فى تحديد كفاءة وظيفة البطين الأيسر.

التصميم: دراسة حالات متسلسلة.

المكان: وحدة الايكو فى مستشفى ابن سينا التعليمى وكلية طب الموصل - الموصل/العراق.

الزمان: آب ٢٠٠٤ إلى آذار ٢٠٠٥.

المشاركون: أجريت الدراسة على ٦٠ مريضاً مصاباً بفرط ضغط الدم الشريانى، تم تقسيمهم إلى ثلاث مجاميع بالاعتماد على شدة ارتفاع ضغط الدم الشريانى. المجموعة الأولى ضمت ١٧ مريضاً، المجموعة الثانية وضمت ٢٤ مريضاً والمجموعة الثالثة وضمت ١٩ مريضاً. وعينة ضابطة مكونة من ٣٠ شخصاً من الأصحاء.

الطريقة: تم قياس مستوى هورمون البيبتيد الاذيني المدر للصوديوم وهورمون البيبتيد الدماغى المدر للصوديوم فى البلازما ومعدل القذف التجزيئى للبطين الأيسر لجميع المرضى ولأفراد العينة الضابطة. تمت مقارنة لتغيرات الحاصلة فى القياسات المذكورة أعلاه باستعمال اختبار انوفا كما تمت دراسة العلاقة بين هذه المتغيرات باستخدام معامل ارتباط بيرسون.

النتائج: أظهرت الدراسة وجود زيادة إحصائية معنوية في قيم مستوى هورمون البيبتيد الاذني المدر للصوديوم في البلازما لدى مرضى المجموعة الثالثة بالمقارنة مع العينة الضابطة ($P < 0.001$) والمجموعة الأولى ($P < 0.05$). كما أظهرت الدراسة وجود زيادة إحصائية معنوية في قيم مستوى هورمون البيبتيد الدماغي المدر للصوديوم في البلازما لدى مرضى المجموعة الثالثة بالمقارنة مع العينة الضابطة ($P < 0.0001$) والمجموعة الأولى ($P < 0.0001$). إضافة إلى ذلك لوحظ أن مستوى هذا الهرمون لدى مرضى المجموعة الثانية أعلى مما هو عليه لدى أفراد العينة الضابطة وقيمة إحصائية مقدارها ($P < 0.01$). وأظهرت وجود نقصان معنوي في قيم القذف التجزيئي للبطين الأيسر لدى مرضى المجموعة الثالثة بالمقارنة مع العينة الضابطة ($P < 0.0001$) والمجموعة الأولى ($P < 0.0001$) والمجموعة الثانية ($P < 0.001$). وتشير نتائج الدراسة إلى وجود علاقة معنوية سالبة بين مستوى هورمون البيبتيد الدماغي المدر للصوديوم في البلازما وقيم القذف لتجزئي للبطين الأيسر لدى مرضى المجموعة الثالثة ($r = -0.62, p < 0.005$).

الاستنتاج: يستدل من نتائج الدراسة أن ارتفاع مستوى هورمون البيبتيد الاذني المدر للصوديوم وهورمون البيبتيد الدماغي المدر للصوديوم في البلازما هي حالة مألوفة لدى المرضى المصابين بفرط ضغط الدم الشرياني الشديد واعتمادا على نتائج هذه الدراسة يمكن القول أن قياس المستوى المصلي لهورمون البيبتيد الدماغي المدر للصوديوم لدى هؤلاء المرضى يعتبر ذا أهمية كبيرة في تحديد مدى اعتلال وظيفة القلب لديهم.

predicting left ventricular performance in these patients.

PATIENTS AND METHODS

Sixty patients with hypertension (33 males and 27 females) who were attending the Echocardiography Unit at Ibn-Sena teaching hospital during the period from August 2004 to March 2005 were included in this study. The patients were divided into three groups depending on recommendations of Fifth Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure⁽¹²⁾. Group I (patients with mild hypertension, systolic blood pressure 140-159 mmHg and diastolic blood pressure 90-99 mmHg) included 17 patients (8 males and 9 females), their age ranged from 34 to 69 years with a mean \pm SD of (47.3 ± 14.5); group II (patients with moderate hypertension, systolic blood pressure 160-179 mmHg and diastolic blood pressure 100-109 mmHg) included 24 patients (14 males and 10 females), their age ranged from 36 to 73 years (49.6 ± 14.0), and group III (patients with severe hypertension, systolic blood pressure 180-209 mmHg and diastolic blood pressure 110-119 mmHg) included 19 patients (11 males and 8 females), their age ranged from 34 to 67 years (47.3 ± 14.5). The study also included 30 apparently healthy volunteers (16 males and 14 females), their age ranged from 38 to 70 years (46.9 ± 16.2) as a control group.

Five ml of venous blood was obtained from a suitable forearm vein into heparinized tube, and immediately placed in ice and centrifuged within 30 minutes, the plasma then separated and kept in capped plastic tubes in deep freeze (-20°C) until analysis (3-6 months). Plasma ANP and BNP concentrations were determined by Enzyme Linked Immunosorbent Method

Atrial natriuretic peptide (ANP) and BNP are the predominant members of a family of at least three structurally and functionally related hormones that exert a wide array of effects on body fluids and electrolytes homeostasis and cardiovascular function⁽¹⁾. The natriuretic and diuretic effect of natriuretic peptides are due to hemodynamic alteration in glomerular filtration⁽²⁾, inhibition of sodium reabsorption in the inner medullary collecting ducts⁽³⁾, and antagonism of the major neural and hormonal salt and fluid conserving mechanisms⁽⁴⁾. The hypotensive effect of these peptide hormones, on the other hand, is mediated primarily by a decrease in cardiac output brought about by a reduction in intravascular volume⁽⁵⁾, and by inhibition of compensatory autonomic reflex increase in heart rate⁽⁶⁾ and vascular resistance⁽⁷⁾. The earliest indication that natriuretic peptides may play a role in blood pressure regulation originated with the observation that abnormalities in natriuretic peptide secretion are sometimes manifested in hypertensive patients⁽⁸⁾. The most definitive evidence for a role of natriuretic peptide in regulation of blood pressure is derived from studies in genetic mouse model⁽⁹⁾. Left ventricular dysfunction is a common finding in patients with fixed or borderline hypertension⁽¹⁰⁾. Heart failure is the end stage of progressive deterioration of left ventricular dysfunction. Because the overall survival of patients with heart failure is bleak, intervention at the pre-clinical stages of these sequences of events would seem to be the strategy of choice to decrease the morbidity and mortality associated with heart failure⁽¹¹⁾. This study is an attempt to assess the plasma level of both ANP and BNP in patients with hypertension and to evaluate the validity of these hormones in

(ELISA)⁽¹³⁾ utilising kits provided by DRG International Inc., USA. Echocardiograph is performed for every participant in the study to determine the value of LVEF%.

Statistical analysis was performed using the ANOVA test (one way analysis of variance) to examine the difference in the mean of the studied parameters in between patient groups themselves and between patient groups and control group. Pearson correlation coefficient was used to study the correlation of the studied parameters within each patient group. All values are expressed as mean \pm SD.

RESULTS

The plasma levels of ANP, BNP and LVEF% of group I, group II, group III and control group are shown in (Table 1). The

mean of plasma ANP was significantly higher in group III than that in control group ($p < 0.001$) and group I ($p < 0.05$), (Figure 1). The mean of plasma BNP was significantly higher in group III than that in control group ($p < 0.0001$), group I ($p < 0.0001$) and group II ($p < 0.0001$). Furthermore, the plasma BNP was significantly higher ($p < 0.01$) in group II than that in control group (Figure 2). The mean of LVEF % was significantly lower in group III than that in control group ($p < 0.0001$), group I ($p < 0.0001$) and group II ($p < 0.001$). There was a significant negative correlation between the mean of plasma BNP level and the mean LVEF% in group III ($r = -0.62$, $p < 0.005$). Two patients in group II and 9 patients in group III had left ventricular dysfunction (LVEF% $< 33\%$).

Table (1): The mean \pm SD of plasma ANP, BNP and LVEF% in group I, group II, group III and control group.

	Mean \pm SD		
	Plasma ANP pg/m	Plasma BNP pg/ml	LVEF%
Control group (n=30)	36.2 \pm 6.9	9.4 \pm 3.2	52.5 \pm 7.4
group I (n= 17)	38.3 \pm 10.8	10.6 \pm 2.0	51.3 \pm 8.1
group II (n= 24)	39.4 \pm 6.5	12.5 \pm 1.8 ^c	49.2 \pm 7.9
group III (n= 19)	43.8 \pm 6.6 ^a	32.6 \pm 9.1 ^b	40.5 \pm 10.6 ^b

a: significantly higher in group III from respective values in group I and control.

b: significantly higher in group III from respective values in group I, group II and control group.

c: significantly higher in group II from respective values in control group.

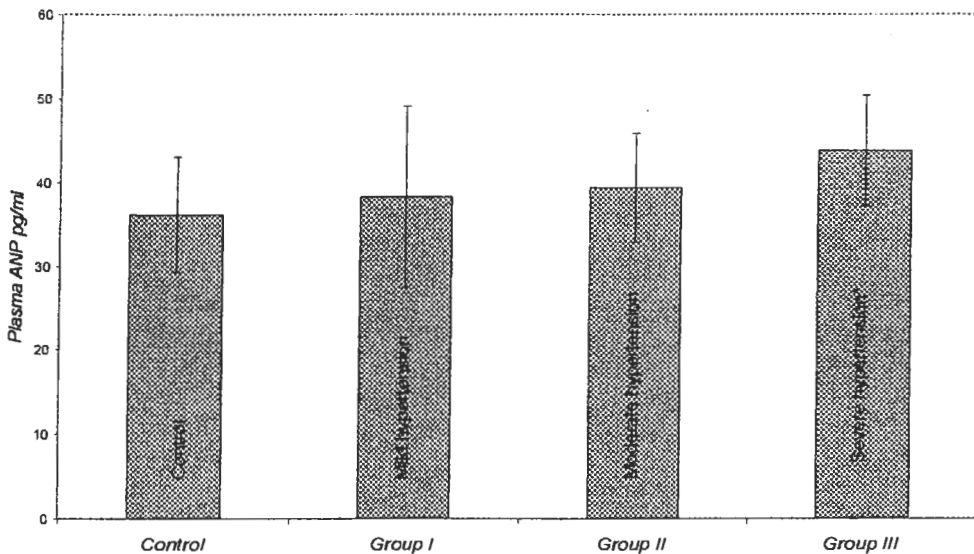


Figure (1): Mean \pm S.D. of plasma level of atrial natriuretic peptide (ANP) in group I, II, III and control group. (*: significantly differ in group III than respective values in group I and control group).

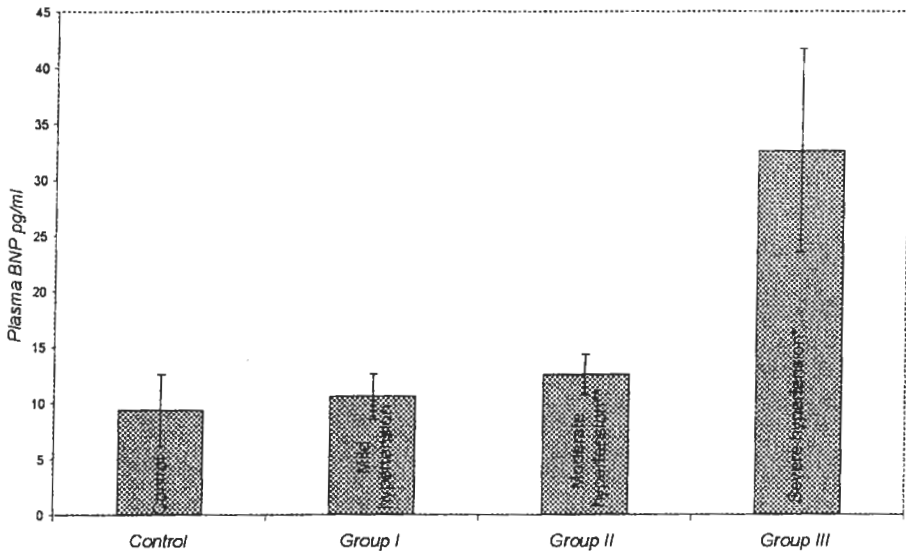


Figure (2): Mean \pm S.D. of plasma level of brain natriuretic peptide (BNP) in group I, II, III and control group. (*: significantly differ in group III than respective values in group I, II and control group, **:significantly differ in group II than respective values in control group).

DISCUSSION

Early detection of left ventricular dysfunction among hypertensive patients enables administration of proper treatment that can improve survival and well-being of these patients⁽¹⁴⁾. Echocardiography is the most commonly used method to diagnose left ventricular dysfunction⁽¹⁵⁾. However, the limited availability of Echocardiography in community setting and its expense may not make it the best screening test for patients with probable left ventricular dysfunction. Recently cardiac natriuretic peptides have received close attention as cardiovascular markers. Plasma levels of ANP and BNP may be useful as a marker for left ventricular dysfunction in patients with heart disease⁽¹⁶⁾. The increase in cardiac filling pressure in this setting is the stimulus for the release of these natriuretic hormones. The result of this study revealed a statistically significant increase in plasma level of both ANP ($p < 0.001$) and BNP ($p < 0.0001$) in patients with severe hypertension (group III) in comparison with control group. Furthermore, the plasma BNP in moderate hypertension (group II) was significantly higher ($p < 0.01$) than that in control group. There was also a significant negative correlation between plasma BNP level and LVEF% ($r = -0.62$, $p < 0.005$) in patients with severe hypertension (group III). The sensitivity of plasma BNP value of 20 pg/ml or more in

detecting left ventricular dysfunction (LVEF% $< 33\%$) was 77% and specificity was 90% in group III. Although both peptides are released from the cardiac myocyte in response to increased stretching of the wall of cardiac chambers⁽¹⁷⁾, the increase in BNP plasma level appears to be more predictive of ventricular performance because it is solely secreted by ventricular myocyte⁽¹⁸⁾.

The prevalence of heart failure tends to increase as the proportion of elderly within the population increases. Despite recent advances in medical and surgical intervention, the prognosis for this disorder has not improved significantly. To make a major impact on the prognosis for heart failure, it would be important to be able to recognize various forms of heart disease before severe heart failure has developed. Chest X-radiography, ECG and echocardiography may not be adequate screening tools for heart failure in large populations. Natriuretic peptides, specifically B-type natriuretic peptide, are practically stable and can be measured without an extraction procedure. Accordingly the measurement of the plasma level of BNP can provide a simple and cost effective diagnostic tool for early detection of left ventricular dysfunction among hypertensive patients.

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