ORIGINAL ARTICLE

Relation of Brain Natriuretic Peptide, Mean arterial and Pulse pressures among Normotensive, Pre-hypertensive and Hypertensive male cohort

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ABSTRACT

Background: Hypertension is an increasingly important medical and public health issue. Individuals prone to the development of hypertension often have a hyperdynamic circulation antedating the onset of hypertension by several years. Brain Natriuretic Peptide is a new promising cardiovascular risk marker due to its association with high blood pressure via its mechanisms of secretion and actions. Both pulse and mean arterial pressures are independent markers of cardiovascular diseases.

Objective: This study was designed to find out any relation between the rising values of pulse and mean arterial pressures among normotensives, pre-hypertensives and newly diagnosed hypertensives with the changes in plasma brain natriuretic peptide levels.

Methods: This was an observational, analytical cross-sectional study conducted in department of physiology at Basic Medical Sciences Institute, Jinnah Post Graduate Medical Center, Karachi. Study included 85 adult males, aged between 20-60 years, non- smokers, non- diabetic and having no other chronic illnesses. Pulse and mean arterial pressure values were found. Study participants were divided into three groups ranging from normotensive to hypertensive stages, as stated by Joint National Committee -7. Brain Natriuretic Peptide was assayed by AxSym technology.

Results: Brain Natriuretic Peptide developed a positive correlation with both pulse and mean arterial blood pressures and was also found out to be significantly raised in pre-hypertensive group.

Conclusions:This study concluded that Brain Natriuretic Peptide is positively related with increasing values of both variables i.e. pulse as well as mean arterial blood pressures. It also concluded that Brain Natriuretic Peptide is significantly elevated in pre-hypertensive stage and is not very different from the levels seen in sustained hypertension.

Key Words: Brain Natriuretic Peptide, Pre-hypertensive, Pulse pressure, Mean arterial blood pressure.

INTRODUCTION

The prevalence of increased blood pressure is increasing and there is no threshold of blood pressure that identifies cardiovascular risks. Hypertension experts have proposed a new definition of hypertension as "A progressive cardiovascular syndrome arising from complex and interrelated etiologies" which features early markers that are often present before blood pressure elevation is sustained. This revision of the definition of hypertension and the need to assess the blood pressure levels in the context of cardiovascular risks has

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guided for an earlier detection of patients at risk.[1]

Brain Natriuretic Peptide (BNP) is a new promising cardiovascular risk marker [2] that has been associated with high blood pressure.[3] Brain natriuretic peptide is found to be raised in hypertensives[4]and is related with increased incidence of cardiac events.[5]Volume overload increases mean arterial pressure (MAP)[6-7] and Pulse pressure (PP). Investigators have reported that individuals prone to the development of high blood pressure often have a hyperdynamic circulation antedating the onset of hypertension by several years.[8] BNP gene expression is one of the earliest responses to hemodynamic pressure overload and occurs before development of left ventricular hypertrophy.[9] BNP-dependent decrease in blood pressure results in part from a reduction in cardiac preload and partly after-load .BNP release is increased both in response to increased pre-load as well as after load.[10] So we speculated that increased plasma BNP levels may antedate or be closely related to subsequent increase in PP and MAP. However, the role of BNP in the clinical assessment of increasing blood pressure has not been fully investigated and actual meaning of a slight increase in BNP is still unclear. In view of above knowledge this study was designed to find out any existing relationship between plasma BNP levels, PP and MAP values.

MATERIAL AND METHODS

This study was carried out during February to October 2007 at Basic Medical Sciences Institute JPMC, Karachi. This study included a total of 85 apparently healthy males ranging between the ages of 20 to 60 years. The selected subjects had no history of diabetes, any hypertensive complication or any other chronic systemic illness. Exclusion was made on the basis of history and lab findings including TLC >10.9 x10^9/L or <3.9 x10^9/L, C-Reactive protein > 6 mg/L, Serum Creatnine >1.1 mg/dl, Fasting Blood Sugar>115 mg/dl .

According to JNC-7,[11] hypertensive subject was defined as a person having diastolic blood pressure or systolic blood pressure 140/90 mm Hg. All selected hypertensives were the newly diagnosed ones and had not yet started the treatment. Mercury sphygmomanometer was used for blood pressure measurements between 8-10 AM to avoid diurnal variations. Average of three readings was considered to be the needed observation. Blood samples were collected between 8 to10 AM after a fast of 12 to14 hours. Samples were preserved at –20C.BNP was determined by AxSYM technology based on microparticle enzyme immunoassay (MEIA) provided by Abbot Diagnostic Laboratories having kit Ref.No.8G82-20ABBL001/R4.

Systolic and Diastolic blood pressure values were recorded.Pulse pressure value was calculated by subtracting DBP value from SBP value.Mean arterial pressure was found out by adding 2/3rd of DBP value to 1/3rd of SBP value.The study participants were divided into three groups on the basis of PP and MAP values as normotensive(<120/<80mmHg),pre-hypertensive(120-139/80-89mmHg)and hypertensive (140/90 mmHg) according to JNC-7.[11]

RESULTS

In this study BNP value increased from a value of 12.39 to 27.85 pg/ml with the increasing values of MAP in all the three groups ranging from < 90 to >110 mmHg respectively. It showed a positive and statistically significant correlation on linear regression between MAP and BNP (P<0.251 r=0.25*)as shown in Table-1 and Figure-1.

Table 1: Values of Plasma Brain Natriuretic Peptide (BNP) Levels In Mean Arterial Pressure Groups
(All the values are expressed in Mean±SEM)

Mean arterial pressure (mmHg)	n	BNP (pg/ml) Mean±SEM	P value
< 90	24	12.39±4.52	*0.251
90-110	53	24.66±4.92	
>110	08	27.85±9.38	

n= Number of subjects.

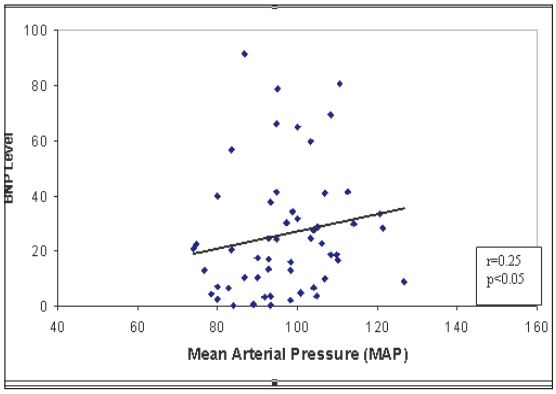

Figure – 1 : Correlation Between BNP And Mean Arterial Pressure (MAP)

We also found an increase in the BNP levels from 20.99 to 24.75 pg/ml with the increase in the PP values from ≤40 to ≥50 mmHg respectively. A positive but statistically non-significant correlation was found between PP and BNP (P<0.949 r=0.16)as shown in Table-2.

Table 2: Values of Plasma Brain Natriuretic Peptide (BNP) Levels In Pulse Pressure Groups
(All the values are expressed in Mean±SEM)

Pulse pressure (mmHg)	n	BNP (pg/ml) Mean±SEM	P value
≤40	52	20.99±5.08	0.949
41-49	24	21.37±5.15	
≥50	09	24.75±5.93	

n= Number of subjects.
r=0.16

Table 3: Descriptive Statistics of Study Population

Variables	n	Minimum	Maximum	Mean	S.D	SEM
Age (years)	85	22	60	41.06	9.629	1.04
BNP (pg/ml)	85	0.00	163.50	21.4938	31.94292	3.4647
Systolic BP (mmHg)	85	90	162	122.11	15.887	1.72
Diastolic BP (mmHg)	85	60	112	82.95	10.611	1.15
Pulse pressure (mmHg)	85	20	70	39.1529	9.94450	1.0786
Mean arterial pressure (mmHg)	85	73.33	126.67	96.0039	11.71379	1.2705

DISCUSSION

Hypertension is widely recognized as a major risk factor for cardiovascular disease.[12] Acknowledging the graded and continuous nature of the relations of blood pressure to vascular risk JNC-7 introduced "pre-hypertension" to describe people with SBP between 120-139 and DBP between 80-89mmHg.Framingham Heart Study indicated that BP values in the 130-139/85-89mmHg range are associated with a more than two fold increase in relative risk from cardiovascular disease compared with the BP levels below 120/80mmHg. A strategy of estimating cardiovascular risk and adjusting the intensity of blood pressure lowering to the absolute risk of cardiovascular disease is desirable in prehypertensive individuals.[13] With the knowledge of such discussion it is useful to have a bio-marker that can serve as a reliable indicator of the risks attributed to the progression of blood pressure above and beyond other clinical determinants. Plasma BNP was thought to be a candidate bio-marker based on cross-sectional associations with blood pressure measures.[14] Studies have extended the potential role of BNP measurements to risk stratification of the general population in which long term mortality increases in proportion to BNP concentration both in patients with or without evidence of cardiovascular

disease.[15-16]BNP has related itself positively with the pathophysiological conditions characterized by alterations of cardiac function and systemic hemodynamics as hypertension when compared with their controls.[17-10] A high BNP concentration may reflect the cardiac load based on the mechanism of its secretion[18] while Framinghm study demonstrated that an increase in BNP predicted the risk of death and cardiovascular events in community residents.[2] However there is little information about the role of BNP in subjects with the rising values of blood pressure and without any established overt cardiovascular disease.

Higher PP is associated with higher risk for cardiovascular mortality and adverse cardiovascular outcomes.[19] Zakopouls in 2001 found PP a marker of cardiovascular disease even in subjects without hypertension.[20] PP is mainly determined by stroke volume and arterial compliance.[21]A higher PP in patients with a normal cardiac function probably reflects more severe atherosclerosis as reduced compliance of the vessels leads to an increased systolic and decreased diastolic pressures and this scenario is thought to apply especially to hypertension.[22]

The rising values of both PP and MAP are independent markers of cardiovascular risks so we speculated that the increase in these pressures may correlate with the changes in plasma BNP levels. Shingo Seki et al[23] in 2008 found a positive relationship between PP and BNP but could not exclude the influence of aging on both variables.His study group had a mean age of 58 years and mean PP value of 65mmHg. Further, his study included untreated essential hypertensives only. Minora Yambe[24] in 2006 found the same results but in an older age group of mean 54 years with a mean PP value of 49mmHg.Our study also found a positive relationship between the two variables but in a graded manner with the rising values of PP(mean 39mmHg) among normotensive to hypertensive in a younger age group of mean 41 years.We could not find a statistically significant relation probably because of the limited number of study participants.

Cataliotti et al[25] in 2005 observed a decrease in MAP after oral administration of human BNP in normal conscious dogs. Kin vander zander et al[26] in 2003 also found a decrease in MAP after BNP infusion in his study group of advanced age(mean 60 years).Our study group comprising of younger age (mean 41 years) developed a positive relation between BNP and MAP in gradually increasing pattern among all the three groups and on linear regression a statistically significant relation was disclosed between the two variables as shown in Table-1and Figure-1.

CONCLUSION

Our study found that BNP is positively related with the increasing values of both variables i.e. pulse as well as mean arterial blood pressures. This study also found that BNP levels are significantly raised in the prehypertensive stage which may remain increased in the sustained hypertension. BNP may be valuable for risk stratification in primary care by general practitioners so it is suggested that BNP levels should not only be assayed in hypertensive but in prehypertensive preferably to decide all those measures which may prevent or delay the onset of hypertension.

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