ESTIMATION OF PLASMA BNP
(BRAIN NATRIURETIC PEPTIDE)
IN PATIENTS WITH CONGESTIVE HEART FAILURE:
A DIAGNOSTIC AID

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ABSTRACT:
To evaluate the levels of plasma BNP (Brain natriuretic peptide) in patients suffering from transmural myocardial infarction of anterior wall (AMI) with and without congestive heart failure. The present study was carried out at Hamdard College of Medicine and Dentistry in collaboration with National Institute of Cardiovascular Diseases Karachi from Jan 2004 to Aug 2004. Seventy subjects were selected in a case control study. Thirty-five patients suffering from transmural myocardial infarction of anterior wall without congestive heart failure (mean age 45.77 ± 1.76) and thirty-five patients suffering from transmural myocardial infarction of anterior wall with congestive heart failure (mean age 46.86 ± 1.15). Their histories were taken and they were physically examined. Two fasting venous blood samples were collected; one is additive free blood while other containing EDTA. Baseline characters of the two groups were similar. Mean plasma BNP levels was [86.92 ± 6.60pg/ml, 510.16 ± 50.51 pg/ml] respectively in MI patients without failure and MI patients with failure, the levels are significantly high in patients with failure as compared to non failure.

CONCLUSION: Significantly high levels of plasma BNP in transmural MI patients with failure suggests a diagnostic importance to be use as a marker for early identification of CHF.

INTRODUCTION
Congestive heart failure (CHF) is a common and profound problem faced by all practicing family physicians. Roughly 2 million Americans have this condition, and 400,000 new cases are diagnosed each year (Grauer, 2000). CHF is accountable for significant morbidity and mortality in America's elderly, and is the leading cause of hospitalization nationwide (Davies, 2000).

CHF can be divided into two distinct subtypes: systolic dysfunction and diastolic dysfunction. Approximately 70% of patients with CHF have the systolic variety, characterized by left ventricular dilatation, wall thinning, and decreased ejection fraction.

With the use of echocardiography, this form of heart failure is recognized by globally reduced contractility. Diffuse dilatation of at least 3 cardiac chambers is frequently seen, but in the early stages, dilatation may be absent (Pfeffer et al., 1992 and Gavras, 1991).

Diastolic heart failure, commonly caused by hypertension, is characterized by hypertrophic myocardium with normal ejection fraction (Gavras, 1991).

Despite significant advances in medical therapy, patients with heart failure remain at increased risk of overall mortality, progressive ventricular dysfunction, and sudden cardiac death. Although a number of individual clinical and laboratory variables have been
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identified as being associated with increased mortality risk in heart failure, there remains a clear need for an integrated method of diagnosis and prognosis. Elevated plasma B-type natriuretic peptide (BNP) has been demonstrated to be a powerful marker for diagnosis, severity, prognosis and risk stratification in the setting of heart failure. Patients with elevated BNP levels have been shown to be at significantly higher risk (Kramer, 1999 and Coodley, 1999). B-type natriuretic peptide (BNP) also called Brain Natriuretic Peptide is a small cardiac hormone comprises of 32 amino acid polypeptide, containing a 17 amino acid ring structure released from the heart in direct proportion to ventricular volume expansion and pressure overload. (Peter, 2003).

In this study we have estimated the levels of plasma BNP in two groups of patients suffering from same type of ischemic heart disease but with and without heart failure.

SUBJECT AND METHOD

The proposed study was carried out at Hamdard College of Medicine and Dentistry in collaboration with National Institute of Cardiovascular Diseases Karachi. From Jan 2004 to Aug 2004. Subjects were divided into two groups, Group A and Group B.

Group A:
Thirty-five subjects suffering form transmural myocardial infarction with out failure. They were age and sex matched with subjects in-group B.

Group B:
Thirty-five subjects suffering form transmural myocardial infarction with failure.

The data collection for various groups was standardized through the use of similar methodology, protocol and procedure using a standard questionnaire.

The questionnaire provided information about type of work, medical history of cardiovascular disease and hypertension. Weight was measured on a balance scale while participants were with out shoes and heavy outer garments, height was measured in the standing position following weight measurement. Blood pressure of subject was measured twice in the right arm after 5 minute of rest, using a standard mercury sphygmomanometer. Values from the second measurement were used in this study. Diagnosed Transmural myocardial infarction patients with and without failure were selected from National Institute of cardiovascular disease Karachi. The subjects were asked to fast for 10-12 hours, 6 ml of blood was collected from the antecubital vein, (after all aseptic measures) while the subjects were sitting up right. Sampling was done between 0700 and 0900 hours.

Specimen Handling and Storage

Strictly predefined protocol was used for specimen preparation. Blood was collected in neotube from Nipro Japan two different samples were made one was additive free, and other was containing EDTA, blood-tubes were put on ice in the icebox immediately after collection. Whole blood tubes were kept at room temperature until clotting was complete. Those samples that showed sign of haemolysis were discarded. Samples were centrifuged at 1000 rpm for 10 minutes with in one hour after collection; serum was separated and stored in aliquots in deep freezer at minus 20°C until assayed (with in one month). Samples were analyzed in one run at the end of the study, to omit between run analytical variations except plasma glucose and BNP that were analyzed within four hours of sample collection. Serum total cholesterol, HDL-C, triglycerides and glucose were analyzed enzymatically, using the kits supplied by SPINREACT, Spain. LDL-C was calculated by the Friedwald formula. Plasma BNP was analyzed by MEIA (Microparticle Enzyme Immunoassay) using the AxSYM system of Abbot Laboratories Pakistan.

Statistical analysis: Categorical data are presented as number (percent),and continuous
The values are expressed as mean ± s.e.m. The number of observation and units are given in parentheses.
BMI: Body mass index

Table-2
Comparison of history of hypertension, systolic blood pressure, diastolic blood pressure, heart rate among Group A and Group B subjects

<table>
<thead>
<tr>
<th>Groups</th>
<th>Hypertension</th>
<th>SBP (mm/Hg)</th>
<th>DBP (mm/Hg)</th>
<th>Heart Rate (b/min)</th>
<th>Previous MI %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-A (MI patients without failure) (35)</td>
<td>16.45 (47%)</td>
<td>127.14 ± 1.71</td>
<td>80.48 ± 0.76</td>
<td>78.29 ± 0.97</td>
<td>3.5 (10%)</td>
</tr>
<tr>
<td>Group-B (MI patients with failure) (35)</td>
<td>17.85 (51%)</td>
<td>126.19 ± 3.35</td>
<td>77.62 ± 2.92</td>
<td>74.48 ± 2.25</td>
<td>15.40 * (44%)</td>
</tr>
</tbody>
</table>

The values are expressed as mean ± s.e.m. The number of observation and units are given in parentheses
*P< 0.01, significant as compared to control
SBP : Systolic Blood Pressure   DBP : Diastolic Blood Pressure

data as mean ± SEM. The student t was used as indicated.

RESULTS

A total of seventy subjects were studied. Table-1 shows the mean values and comparison of age, weight, height and body mass index of group A and group B subjects. When age, weight, height and BMI of control subjects were compared with group B patients. No significant difference of age, weight height and BMI was observed, Table 2 shows mean values of hypertension, systolic blood pressure, diastolic blood pressure, heart rate and history of previous MI of group A and group B. When history of hypertension, systolic blood pressure (SBP), diastolic blood pressure (DBP), was compared a nonsignificant difference was found. History of previous MI was significantly high in-patients with failure as compared to non-failure patients.

Table 3 shows the mean values of plasma glucose, triacyl glycerol, total cholesterol of group A and group B. The value of plasma glucose, serum Triaclyglycerol and Total cholesterol of group B were non-significant when they were compared to group A.
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Table 3
Comparison of fasting plasma glucose, serum triacylglycerol, total cholesterol among Group A and Group B subjects

<table>
<thead>
<tr>
<th>Groups</th>
<th>Glucose (mg/dl)</th>
<th>Triacylglycerol (mg/dl)</th>
<th>Total Cholesterol (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-A (MI patients without failure) (35)</td>
<td>84.29 ± 0.88</td>
<td>121.40 ± 3.73</td>
<td>173.00 ± 5.13</td>
</tr>
<tr>
<td>Group-B (MI patients with failure) (35)</td>
<td>84.17 ± 0.80</td>
<td>119.86 ± 3.74</td>
<td>169.71 ± 4.23</td>
</tr>
</tbody>
</table>

The values are expressed as mean ± s.e.m. The number of observation and units are given in parentheses.

Table 4
Comparison of fasting high density lipoprotein cholesterol, low density lipoprotein cholesterol, and plasma BNP among Group A and Group B subjects

<table>
<thead>
<tr>
<th>Groups</th>
<th>HDL-C (mg/dl)</th>
<th>LDL-C (mg/dl)</th>
<th>BNP (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-A (MI patients without failure) (35)</td>
<td>24.63 ± 1.39</td>
<td>124.09 ± 4.60</td>
<td>86.92 ± 6.60</td>
</tr>
<tr>
<td>Group-B (MI patients with failure) (35)</td>
<td>25.32 ± 1.48</td>
<td>120.42 ± 3.68</td>
<td>*** 510.16 ± 50.51</td>
</tr>
</tbody>
</table>

The values are expressed as mean ± s.e.m. The number of observation and units are given in parentheses.

***P< 0.001 significant as compared to control group
HDL-C: High density lipoprotein cholesterol
LDL-C: Low-density lipoprotein cholesterol, BNP: Brain Natriuretic Peptide

Table 4 shows comparison of mean value of high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and plasma BNP. A non-significant difference was seen in HDL-C, LDL-C whereas significantly high levels of plasma BNP was observed in group B as compared to group A.

DISCUSSION

Congestive heart failure (CHF) is a syndrome of progressive cardiac decompensation caused by increasing ventricular dysfunction, most often resulted by coronary artery disease (Grauer, 2000). About 70% of patients with congestive heart failure (CHF) have the systolic dysfunction, characterized by left ventricular dilatation, wall thinning and decrease ejection function. On average the 5-year mortality rate for CHF is 50% with 90% dead at 10 years (Davies, 2000). However the modern advances in the medical therapy have been shown to decrease both its mortality and progression but still its detection needs access to cardiac imaging, which requires highly specialized personnel and technology. B-Type natriuretic peptide (BNP) is a neurohormone synthesized in the
cardiac ventricle and is release upon ventricular myocyte stretch. Blood measurement of BNP is an important and reliable marker to identify patients with CHF. The level that shows the possibility of CHF is in between 100-500pg/ml while probability at the level greater than 500pg/ml. Level less than 100pg/ml shows absent CHF (Peter, 2003). In our study we have observed a significantly high levels of plasma BNP in patients with transmural myocardial infarction with congestive heart failure and this is in agreement with Damien Lorgeart et al (2002) and Brain et al (2003). While lipid parameters and plasma glucose levels are not different significantly. We there fore conclude that Elevated levels of plasma BNP are significant in the diagnosis of congestive heart failure.

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REFERENCES