EFFECT OF ENDURANCE EXERCISE ON BRAIN NATRIURETIC PEPTIDE (BNP)

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ABSTRACT

OBJECTIVE: To evaluate the effect of maximal exercise on the level of brain natriuretic peptide (BNP) and cardiac adaptive changes in endurance trained elite athletes and sedentary healthy subjects.

METHODOLOGY: This Cross-sectional comparative study was conducted at Army Medical College in collaboration with Armed Forces Institute of Cardiology (AFIC) Rawalpindi. Twenty two elite endurance athletes (Long Distance Runners) and 22 matching sedentary (from same unit having no sports activity) controls were selected by convenience (non-probability) sampling technique. Height, body weight, blood pressure, pulse rate and ECG were recorded. The blood was drawn from antecubital vein for measuring BNP and aldosterone before exercise and again after exercise. The echocardiography of left ventricle was done to measure the end-diastolic internal diameter (LVIDd), diastolic interventricular septal thickness (IVSTd), and diastolic posterior wall thickness (PWTd). The left ventricular mass (LVM) was calculated by Devereux formula. The data were recorded in a proforma and analyzed by SPSS version 10.

RESULTS: It was observed that the heart rate and blood pressure of athletes were significantly less than the controls ($p<0.001$); while LVIDd, IVST, PWTd, and LVM was greater in athletes than controls ($p<0.001$). Pre-exercise BNP level was 45.29+18.69 pmol/l & 34.16+13.74 pmol/l while post-exercise BNP level was 58.32+19.65 pmol/l & 43.638+11.82 pmol/l in athletes and controls respectively ($p<0.01$). Pre-exercise Aldosterone level was 15.34+2.77 ng/dl & 13.05+2.134 ng/dl while post-exercise BNP level was 16.01+2.14 ng/dl & 14.65+2.30 ng/dl in athletes and controls respectively ($p<0.01$).

CONCLUSION: The maximal exercise increases the level of BNP in elite athletes significantly.

KEY WORDS: Athlete's heart, cardiac natriuretic peptide, endurance exercise, left ventricular mass and dimensions.

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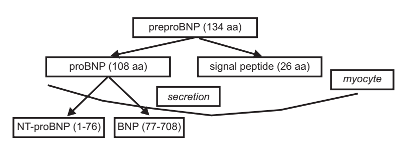
INTRODUCTION

Top-level training is often associated with morphological changes in heart including increased left ventricular (LV) cavity dimension, wall thickness and mass.[1] It is assumed that the dimensional changes affect all cardiac cavities to the same extent and result in a balanced cardiac hypertrophy[2] which is known as the "athlete's heart".[3] The enlarged heart is a beneficial adaptation enabling the athlete to perform more work.[4] The mammalian heart synthesizes and secretes a family of related peptide hormones called cardiac natriuretic hormones, (CNHs).[5] In 1981, de Bold et al found that atrial extracts contained a substance, which caused natriuresis and vasodilatation[6]. In 1988, as the initial flush of research activity was wearing off, a second related compound was identified. This peptide was called brain natriuretic peptide (BNP) because it was first identified in porcine brain[7]. BNP is produc NP), before it is secreted by cardiomyocytes.[8] BNP, is composed of 32 amino acid residues and is predominantly synthesized and secreted from the ventricles.[9] The main source of this peptide is the cardiac ventricle rather than the brain, and therefore BNP (having more profound dilating effects on ventricles) is now sometimes called B type natriuretic peptide.[10] BNP promotes diuresis, natriuresis, hypotension and smooth muscle relaxation through an unsettled mechanism. However, it has



been suggested that CNHs exert their action by inhibiting renin and aldosterone secretion and by increasing the rhythm of diuresis.[11]

The present study was planned to evaluate cardiac adaptive changes and the effect of maximal exercise on the levels of brain natriuretic peptide and aldosterone in endurance trained elite athletes and sedentary healthy subjects. As it was reported from developed world that BNP play an active role in left ventricular remodeling in endurance athletes, so to see the level of BNP increase in south Asian athletes this study was planned.

METHODOLOGY

The present study was carried out at the Department of Physiology, Army Medical College, Rawalpindi with collaboration of Armed Forces Institute of Cardiology (AFIC) Rawalpindi. A total number of 44 subjects were included in this study. These comprised of 22 elite endurance athletes (long Distance runners) and 22 healthy sedentary volunteers (selected from same Unit) as controls.

SAMPLING TECHNIQUE: The subjects were taken by non-probability purposive sampling technique.

INCLUSION CRITERIA: The subjects were inducted in the study as two groups:

GROUP-I: The male Elite endurance athletes (n=22): were recruited from Pakistan Army. Their age ranged between 18 -35 years and BMI 19-22 kg/m^2.

GROUP-II: Included the age, sex and BMI matched healthy sedentary controls (n=22). The controls were recruited from same unit from where the athletes were recruited.

EXCLUSION CRITERIA:

All subjects were examined clinically to rule out the cardiovascular and pulmonary diseases on the basis of medical history, physical examination (blood pressure ≥140/90 mm Hg), and echocardiography. The family history was considered positive if there was a history of coronary artery disease, cardiomyopathy, severe arrhythmias, or any other disabling cardiovascular disease. Such subjects were not included in the study

STUDY DESIGN: Cross-sectional comparative study.

DATA COLLECTION PROCEDURE:

1. **Medical history:** was recorded on a structured Proforma.

2. **General physical examination:** was recorded as follows.

   a) Height (cm)

   b) Weight (kg)

   c) BMI: Weight in Kg/ Height in meters2 (Kg/m2)

   d) **Heart Rate:**

Heart rate was measured by auscultatory method at mid clavicular line in left fourth intercostal space before and within 3 minutes after exercise.

e) **Blood Pressure:** Arterial blood pressure (mm Hg) was recorded before and after 5 minutes after stoppage of exercise in a seated position by mercury sphygmomanometer.

3. **Bicycle Exercise Test:** An electrically braked bicycle ergometer was used for maximal exercise test until exhaustion. The sedentary controls exhausted much earlier than the athletes depending upon their level of exercise.

a. **Echocardiography:** Was done by using the M-mode echocardiography methods.

b. **Blood Sampling:** Subjects remained in a relaxed supine position for 20 minutes prior to the blood sampling. A sample of 5 ml of peripheral venous blood was drawn into plastic syringe by observing antiseptic measures from an antecubital vein in each subject. The blood was centrifuged at 1600g for 20 minutes and plasma was separated which was kept frozen below -70°C until the estimation of BNP. The Aldosterone was measured to see the the correlation of increased cardiac overload, if it increases with the increased cardiac output proportionately or otherwise?

4. **STATISTICAL ANALYSES:** The data were entered and analyzed on SPSS Version-10 Computer Software.

RESULTS

Present study was designed to work-out the effect of maximal exercise on the levels of plasma BNP and aldosterone in elite endurance athletes. Mean age of athletes (n=22) and controls (n=22) was 22.73±3.89 years and 22.5±2.48 years respectively (Table 1).

Pre-exercise, heart rate, systolic BP, diastolic BP & mean arterial BP were 55.86±3.47 107.05±7.01mm Hg, 58.09±2.43 mm Hg & 83.29±24.86 mm Hg in athletes and 74.09±2.86 per minute, 115±5.12 mm Hg, 74.55±5.1 mm Hg & 95.00±21.05 mm Hg in controls respectively. It was observed that pre and post exercise heart rate and blood pressure of athletes were significantly less than the controls (Table II & III); while the plasma levels of BNP and aldosterone were significantly higher in athletes than controls (Table IV). However no significant change was observed in plasma levels of aldosterone when pre-exercise levels were compared to that on completion of exercise. The paired sample t-test was applied on pre and post exercise levels of two groups. Comparison of left ventricular dimensions on echocardiography between athletes and controls are presented in Table V, showing significantly higher levels in athletes than controls.

DISCUSSION

This study was carried out to determine the levels of BNP with aldosterone along with cardiac adaptive changes in endurance trained elite athletes. We also evaluated the effects of maximal exercise on the level of BNP and aldosterone in elite athletes and sedentary healthy subjects. Most studies on highly trained athletes have been conducted on Caucasian populations; therefore, the effect of racial variation on heart has not yet been established. No such type of work has been documented before in this part of the world. The cardiac remodeling during endurance training is regarded as the central regulator of BNP secretion.[12] Exertion puts extra strain on heart by increasing the cardiac work load in order to supply more blood to match the increased metabolic needs.[13] It is well known fact that left ventricular end-diastolic internal diameter (LVIDd) in athletes heart is increased as compared to sedentary persons. Therefore, it was not surprising that in present study the LVIDd, (54.63 ±1.79 mm) in elite athletes was found to be significantly higher

TABLE I: DEMOGRAPHIC VARIABLES OF ELITE ATHLETES AND CONTROLS

(The values of age and BMI are given as mean ±SD)

Variables	Elite Athletes (N=22)	Controls (N=22)
Age (years)	22.73±3.89	22.5±2.48
BMI	20.36±1.56	20.89±0.96
Height (m)	1.74±0.05	1.76±0.07
Weight (kg)	61.48±2.40	63.58±4.47

TABLE II: HEART RATE, SYSTOLIC BLOOD PRESSURE, DIASTOLIC BLOOD PRESSURE BEFORE AND AFTER EXERCISE IN ATHLETES AND CONTROLS

(The values are given as mean ± SD)

	Variables	Athletes (n=22)	Controls (n=22)
Pre-exercise	Heart rate (per minute)	55.86±3.47**	74.09±2.86
	Systolic Blood Pressure (mmHg)	107.05±7.01**	115±5.12
	Diastolic Blood Pressure (mmHg)	58.09±2.43**	74.55±5.1
	Mean Arterial blood pressure (mmHg)	83.29±24.86**	95.00±21.05
Post-exercise	Heart rate	120.82±8.27**	136.00±6.87
	Systolic Blood Pressure (mmHg)	131.36±5.16*	139.32±9.04
	Diastolic Blood Pressure (mmHg)	56.14±3.76**	70.68±5.19
	Mean Arterial blood pressure (mmHg)	93.75±37.86**	105±35.06

*The difference is statistically significant at $p<0.008$

**The difference is statistically significant at $p<0.001$

TABLE III: COMPARISON OF DIFFERENCES BETWEEN PRE AND POST-EXERCISE HEART RATE AND ARTERIAL BLOOD PRESSURE, DIASTOLIC BLOOD PRESSURE IN ATHLETES AND CONTROLS

Variables	Athletes	Control
Heart rate	46.96	61.91*
Systolic Blood Pressure (mmHg)	24.31	24.32
Diastolic Blood Pressure (mmHg)	-1.95	-3.87*
MAP (mean arterial blood pressure) (mmHg)	10.46	10.00

*: The difference is statistically significant at $p<0.001$

TABLE IV: PLASMA LEVELS OF BRAIN NATRIURETIC PEPTIDE (BNP) AND ALDOSTERONE BEFORE AND AFTER EXERCISE IN ELITE ATHLETES AND CONTROLS

(The values are given as mean ± SD)

	Variables	Athletes (n=22)	Controls (n=22)
Pre-exercise	Brain Natriuretic Peptide (pmol/L)	45.29±18.69*	34.16±13.74
	Aldosterone (ng/dl)	15.34±2.77*	13.05±2.134
Post- exercise	Brain Natriuretic Peptide (pmol/L)	58.32±19.65*	43.638±11.82
	Aldosterone (ng/dl)	16.01±2.14*	14.65±2.30

** The difference is statistically significant at $p<0.008$*

than sedentary controls (40.63±2.08 mm). D'Andrea A et al found that LV end-diastolic diameter was greater ($P<0.01$) in endurance trained athletes.[14] Abernethy WB et al reported that the mean LVIDd was 53±0.5 mm in elite football players.[1] Which was comparable to our findings. In addition, Pela G et al documented the similar finding that is; LVIDd = 56±5.6 mm.[15] These values are also close to our data. Date H et al[16] documented that left ventricular mass (LVM) and left ventricular wall thickness (LVWT) in marathon runners and judo practitioners were significantly greater than those of sedentary controls. Although the LVIDd was significantly greater in the marathon runners, while it was smaller in the judo players.[16] Sundstedt M et al suggested that a large increase in stroke volume in endurance

TABLE V: COMPARISON OF LEFT VENTRICULAR DIMENSIONS ON ECHOCARDIOGRAPHY BETWEEN ELITE ATHLETES AND CONTROLS

(The values are given as mean ± SD)

Parameter	Elite Athletes (n=22)	Controls (n=22)
LV end-diastolic internal diameter (LVIDd) (mm)	54.63±1.79**	40.6364±2.08
Diastolic interventricular septal thickness (mm)	9.86±0.89**	8.52±0.37
Diastolic posterior wall thickness (PWTd) (mm)	8.63±0.73*	8.04±0.32
Left Ventricular Mass (LVM) (gm)	196.36±22.86**	102.5±11.01

** The difference is statistically significant at p<0.008*

*** The difference is statistically significant at p<0.001*

athletes could be explained by the linear increase in end-diastolic volume[17] due to the increase in LVIDd and LVM.

The data of diastolic posterior wall thickness (PWTd) of present study is close to that of Sharma S et al[18] In their study mean PWTd of elite athletes was 9.5±1.7 mm and PWTd of sedentary controls was 8.4 ± 1.4 mm (p < 0.001), while Abernethy et al reported the maximal wall thickness as 11.2 ± 0.2 mm which is comparable to our study (PWTd = 11.0 ± ±0.73).[1] Nagashima J et al studied 291 male100-km ultramarathon participants and documented that IVSTd was 10.2 ± 1.9 mm, PWTd = 10.0 ± 1.4 mm.19 In 2002 Pellicia A et al in their latest study in 40 elite male athletes measured the PWTd as 9.3±1.4mm, which is close to what we found in present study.[20] The high values of echocardiographic findings may be due to the racial difference as Caucasian populations have more body surface area as compared to Asians. In 2004 Palazzuoli A et al concluded that LV septum thickness, LV posterior wall thickness, were significantly higher in runners as compared to controls (p < 0.001).[21]

Scharhag J et al calculated the LVM in endurance trained athletes as 200±20 g 3 which is close to our calculated value. Kasikcioglu et al stated that Left ventricular mass and mass index were higher in the athletes than in control subjects.[22] Vinereanu D et al calculated the left ventricular mass in endurance-trained and strength-trained athletes as 172±27 and 188±39 g respectively.[23]

Tanabe K et al[24] examined the changes in BNP levels on exercise testing. In their study levels of BNP tended to increase but the rise was not significant. No study before ours has examined the response of plasma BNP to prolonged strenuous exercise in healthy individuals. Scharhag J et al has concluded that release of BNP during and after exercise may not be the result of myocardial damage but may have cytoprotective and growth-regulating effects.[3] Ohba H et al studied the athletes of marathon racing and found that mean plasma level of BNP in athletes was significantly increased not only in response to short-term exercise but also following the endurance exercise.[25] Cardiac strain during long-distance running may explain the pronounced increase in BNP. Other explanations for the observed rise in plasma levels of these markers may be associated to the change in the permeability of myocardial cells and an impaired clearance. It has been documented that BNP plasma levels respond differently to the type of exercise as evidenced from the study of Planer et al which reported the intimate link between plasma concentrations of natriuretic peptides and cardiac morphology in different types of athletes.[26]

Sahlén A et al in a study on recreational cyclists (n = 29) during the Otztal Radmarathon 2004, reported a significant increase in NT-pro-BNP levels from 28 ±21 to 278 ±52 (278±52) ng/L (p <0.001).27 In addition, Herrmann M et al documented that the Pre-race NT-proBNP level as 44ng/L. while NT-proBNP levels at 15 minutes and 3 hours after the race was significantly increased upto 137ng/L and 123ng/L respectively. NT-proBNP levels can frequently increase in recreational runners after a marathon race.[28] Engelmann MD et al found that BNP levels increased significantly during exercise in the healthy subjects.[29] Konig et al has documented that BNP levels increased significantly from 47.5±37.5 to 75.3 ±55.3 pg./ml (P < 0.01).[30] Mottram PM et al have stated that BNP levels increase with exercise (from 48 ± 5.7 to 74 ± 9.7 pg/mL,), which was associated to the maximal workload (P <.01 for all).[31] While Kruger S et al disagreed to this finding and proposed that BNP levels did not change significantly during exercise in the control group.[32]

CONCLUSIONS

The arterial blood pressure (systolic and diastolic) and heart rate are lower in endurance elite athletes than the matched sedentary controls. In addition maximal exercise lead to significant increase in the levels of brain natriuretic peptide in elite athletes in contrary to the non-significant rise in sedentary healthy controls which explains the adaptive response of athletes heart to the enhanced work load during exercise. We recommend that the more extensive work may be started to see the rising levels of BNP in endurance athletes and the cause of sudden cardiac deaths in athletes may be worked out.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

HWA: Conception and design, Acquisition of data, final approval of the version to be published

MA & MZH: Analysis and interpretation of data, drafting the manuscript, final approval of the version to be published

SA: Analysis and interpretation of data, final approval of the version to be published

FW: Critical revision, drafting the manuscript & final approval of the version to be published