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An Investigation of the Effects of Aerobic Exercise on Serum Brain Natriuretic Peptide and C-Reactive Protein in women with Cardiovascular Diseases

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ABSTRACT

Introduction: The aim of this study was to evaluate the effects of aerobic exercise on brain natriuretic peptide (BNP) and C-reactive protein (CRP) levels in women with cardiovascular diseases.

Materials and Methods: In this semi experimental study, thirty female patients with at least one coronary artery stenosis (more than70%) were chosen and divided into two groups of aerobic training (n=15) and control (n=15). Blood samples were obtained at the beginning and end of the study to measure brain natriuretic peptide (BNP) and C-reactive protein (CRP) levels. The aerobic group cycled on a stationary ergometer for three sessions per week (period of eight weeks). The control group did not receive any exercise. Each exercise session included a10-minute warm-up, a 15-minute or more aerobic training program and a 5-minute cool-down. In the warm-up and cool-down stages, running, walking and stretching activities were used. During the first week of training, subjects exercised for 15 minutes at 55-60% of their target heart rates. Each week, exercise duration extended by five minutes, while the intensity was unchanged.

Results: Results indicated that 8 weeks of aerobic training had a significant effect on decreasing the BNP and CRP levels in females with Cardiovascular Diseases (*P*=0.005 and P=0.017 , respectively). Moreover, a significant Difference was seen between the control and experimental groups in mean BNP and CRP values (P=0.0001 and *P*=0.001 respectively), while no significant difference were seen between the pre and post tests in the Control group for BNP (*P*=0.21) and CRP (P= 0.28). There were significant reduction in BNP (p<0. 05) and CRP levels (p<0.01) after 8 weeks aerobic exercise in experimental group, But no change was seen in the control group in both BNP and CRP levels.

Conclusion: Aerobic exercise can attenuate BNP and CRP levels in females with cardiovascular diseases; hence it can be used as a part of treatment.

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Introduction

Coronary artery disease (CAD) is known as a major cause of mortality worldwide. In the past, blood levels of lipids were considered as CAD markers. Although these markers are still used by some, recent studies on cardiovascular risk factors have focused on new markers of

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inflammatory diseases such as C-reactive protein (CRP) and brain natriuretic peptide (BNP) (1, 2).

CRP is a protein made by the liver and released into the blood within a few hours after tissue injury, start of an infection or other causes of inflammation (3). Studies have shown that physical activity reduces these markers (4-9). In contrast, some studies have reported that CRP increased after aerobic training (10-12). Olson et al. (2007) examined the effects of one year of resistance training, with moderate intensity, on biomarkers of inflammation and adhesion in healthy, overweight women. The results demonstrated significant reduction in CRP levels (13). Some researchers have suggested that aerobic exercise has no effects on CRP level (14-16).

BNP is a 32-amino acid polypeptide secreted by the cardiac ventricles in response to excessive stretching of cardio myocytes or pressure overload. Therefore, BNP is considered as one of the important biomarkers of cardiovascular failure. Muntner et al. (2008) studied NT-pro BNP in 78 patients after 6-minute walk and bicycle ergometer tests, but they did not observe any significant changes after the exercise sessions (17).

In another study, Maria Sarullo et al. (2006) showed that three months of physical activity with moderate intensity in patients with chronic heart failure, reduced the amount of NT-proBNP (18). In addition, a study by Passino et al. (2006) showed reduced BNP levels in patients with heart failure after nine months of physical activity (19). Moreover, elevated BNP levels were detected in marathon runners, in almost one third of whom increased levels did not fall into normal ranges within three hours after running (20).

There is a scarcity of studies, especially in Iran, on the effects of aerobic exercise on CRP and BNP levels of females with cardiovascular diseases. Given the importance of BNP and CRP in diagnosis of cardiovascular diseases, we aimed to study the effect of eight weeks of aerobic exercise on CRP and BNP levels in females with cardiovascular diseases.

Materials and Methods

Subjects and experimental design

In this semi-experimental study, 30 inactive females with cardiovascular diseases and the mean age of 57.3±2.5 years, who had referred to Shiraz hospitals, volunteered to enroll in the study. Those patients who had not engaged in any systematic exercise programs at least six months before the study, were included. Based on the level of coronary artery disease, the participants were divided into two groups of aerobic training (as the experimental group) (n=15) and control (n=15).

They all had at least one coronary artery stenosis (>70%), which was shown by angiography and electrocardiogram (ejection fraction<40%), and didn't have any acute signs of ischemia or heart failure. Pharmacotherapy was done based on the 2013 Guidelines for management of heart failure and chronic stable angina. They used atorvastatin, b-blocker, Ca-blocker, nitro, angiotensin I-converting enzyme and angiotensin receptor blocker (21).

Written informed consent was obtained from each subject prior to participating in the study. The subjects were informed of the protocol and possible risks or difficulties of the study. The study was approved by the Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran.

The exercise protocol

In each session, patients were warmed-up for ten minutes, and then performed the main exercise three times per week, for eight weeks, using bicycle ergometer. During the first week, the subjects practiced for 15 minutes with 60-55% of their target heart rate, followed by a five-minute cool-down. Exercise duration was extended five minutes each week, while its intensity was fixed. Warm-up and cool-down were done by running, walking and stretching. During the entire exercise sessions, a specialist was present and monitored the participants' heart rate using the heart rate monitor sensors connected to them.

Blood sampling

Blood samples were drawn from 8-12-hour fasting subjects prior to and at the end of the study. Subjects were asked not to do any physical activities 48 hours before blood sampling at the baseline. CRP was measured by ELISA Plate Reader (Dynex Opsys MR, USA) kit. Kit sensitivity was 10 ng/ml, and BNP was measured by ELISA Reader (Dynex Opsys MR, USA). Kit sensitivity was 2.56 ng/ l.

Statistical analysis methods

The obtained data were analyzed by both descriptive and inferential statistics. In the descriptive statistics, central tendency measures (mean), dispersion parameters such as standard deviation, variance, range and their corresponding graphs were used. Statistical methods were used to test the hypotheses. To show central tendency and variability, descriptive statistics were applied. To study the significance of differences within and between the groups, at pre-test and post-test stages, independent t-test were used, respectively. All the statistical analyses were performed using SPSS version 16, at the significance level of *P*-value≤ 0.05.

Results

Table 1 shows basic anthropometric and physical characteristics of the subjects in terms of the mean, standard deviation, minimum, and maximum values. Table 2 and 3 show Descriptive statistics of BNP and CRP levels (ng/lit) in the study groups and table 4 and 5 demonstrate changing BNP and CRP levels after 8 weeks of aerobic exercise respectively (p<0.005 and p<0.017).

Discussion

The present study examined the effects of eight weeks of aerobic exercise on serum levels of BNP and CRP in females with CAD. We found that BNP and CRP levels diminished after eight weeks of aerobic exercise in females with CAD. The results were in agreement with studies of Viviane et al. (2004) and Bordbar et al. (2012) (22, 23). Viviane et al. observed reduced levels of BNP after 4 months of combined endurance and resistance training in patients with high baseline levels of BNP as a result of cardiovascular diseases. The noticeable points in Viviane et al. study were type (combination of resistance and endurance training), duration and intensity of training (22).

Table 1. Baseline characteristics and parameters in the subjects

Characteristics	Experimental Mean±SD	Control Mean±SD	P-v=0.05
NO	15	15	-
Age (years)	54.86±8.22	62.86±7.98	0.489
Height (cm)	159.8±5.01	157.8±5.01	0.284
Weight (kg)	70.7±9.3	69.7±9.3	0.770
Body mass index (kg/m^2)	27.5±3.47	28.02±3.47	0.711
Brain natriuretic peptide (ng/lit)	189.1±47.03	172.4±25.58	0.239
C-reactive protein (ng/ml)	1556.9±939.32	1473.8±942.93	0.876

Note: NS, not significant

Table 2. Descriptive statistics of BNP levels (ng/lit) in the study group

Groups	Pre and post test	Standard deviation	Average	Maximum	Minimum
Control 15p	Pre	25.58	172.4	200	115
	Post	25.56	171.67	199.2	114.1
Experimental 15p	Pre	47.03	189.1	299.5	153
	Post	47.56	129.00	256	84.1

Table 3. Descriptive statistics of C-reactive protein levels (ng/ml) in the study group

Groups	Pre and post test	average	SD	Maximum	Minimum
Control 15p	Pre	1473.8	942.93	3199	315.9
	Post	1469.8	942.9	3196	312
Experimental 15p	Pre	1556.9	939.32	3004	382.8
	Post	687.03	733.7	2462	27.4

Table 4. Changing brain natriuretic peptide levels after 8 weeks of aerobic exercise

NO	group	average	SD	Value of t	df	Sig level
15	Control	171.67	25.56	- 3.061	28	0.005**
15	experimental	129.00	47.56			

**Significant (P<0. 05)

Table 5. Changing C-reactive protein levels after 8 weeks of aerobic exercise

NO	group	average	SD	Value of t	df	Sig level
15	Control	1469.8	942.93	-2.537	28	0.017*
15	experimental	687.03	733.73			

*Significant (P<0.05)

Bordbar et al. observed decreasing and increasing levels of BNP after eight weeks of aerobic training and resistance exercise, respectively. The reason for this reduction might be the fact that physical activity may reduce end-systolic diameter and left ventricular end-diastolic dimension, which lead to lowered wall pressure during diastole and reduction in BNP level (22).

Discrepancy in the findings of Bordbar and Viviane regarding resistance training may be due to differences in duration and intensity of training and the initial readiness of subjects. However, some studies have shown increasing levels of BNP after physical activity (24-26). Neilan et al. (2006) studied myocardial damage and ventricular impairment associated with training levels among non-professional participants in the Boston Marathon. The participants included 41 men and 19 women with an average age of 41 years. At baseline, overall median NT-proBNP concentrations were 106 pg/ml, after the marathon, NT-proBNP levels were significantly higher (182 pg/mL). Overall, 54% of participants had NT-proBNP levels above the upper limit of normal for exclusion of heart failure. Females were more likely than males to show post-race increase in NT-proBNP concentrations (63% versus 17%), and the increase in NT-proBNP was independently associated with the attenuation in left ventricular early diastolic filling (24).

Another finding of this study was reduction of CRP levels after eight weeks of exercise. Probably reductions in low-density lipoprotein (LDL) and increases in high-density lipoprotein (HDL) levels following regular physical activity can undermine the inflammatory markers.

Cross-sectional studies have shown that every mg/dl increase in HDL-C causes 2% and 4% reduction in the risk of CAD in men and women, respectively (27). Also, regular aerobic exercise increases endothelial nitric oxide synthase, improves endothelial function and raises the level of antioxidant agents, resulting in attenuation of inflammation levels in systemic and local cytokine production.

CRP concentration is lower in physically active people than in those not physically active (28, 29). In contrast, study of Rawson et al. (2003) has not confirmed the association between physical activity and reduction of CRP (30). This inconsistency may be pertinent to basic values of the CRP, type, intensity and duration of physical activity, inflammatory and infectious diseases and other factors.

It seems that this discrepancy in results depends on the baseline levels of BNP and CRP and the type of activity. For instance, subjects with cardiovascular diseases have high baseline levels of BNP and CRP and healthy subjects have normal levels of these two markers. In addition, the type (endurance or resistance), intensity and duration of physical activity may influence the results.

Considering the strong association between the inflammatory indices and the prevalence of cardiovascular diseases, any factor undermining these indices can reduce the risk of cardiovascular complications. To sum up, this study indicates that aerobic exercise can significantly reduce CRP and BNP levels. Thus, we can consider physical activity as a complementary therapy.

However, further studies are required to examine the effects of physical activity on CRP and BNP levels in females with CAD. The limitations of our study were small sample size and short duration. Conducting further studies with larger sample sizes and longer durations is recommended to elucidate the effects of aerobic exercise on serum concentration of CRP and BNP.

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Conflict of Interest

The authors declare no conflict of interest.

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