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The effect of an exhaustive aerobic exercise on NT-proBNP levels in healthy males

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Abstract

Introduction: Many studies documented the relationship between elevated plasma concentrations of brain natriuretic peptide (BNP) and its aminoterminal propeptide (NT-proBNP) and cardiovascular diseases, especially heart failure (HF). However, it is still uncertain whether physical exercise leads to a significant release of NT-proBNP in healthy subjects. The aim of this study was to determine the effect of an exhaustive aerobic exercise on NT-proBNP levels in healthy males.

Material & Methods: In this study, Fifteen healthy male (aged: 22.2 ± 2.3 years; ± SD) volunteered to participate in this study. The subjects were performed Bruce protocol as the exhaustive aerobic exercise. NT-proBNP plasma concentrations were measured before and immediately after

the exhaustive aerobic exercise. Paired-sample t- test was used to analyze the data.

Results: The results demonstrated that NT-proBNP levels were increased significantly after the exhaustive aerobic exercise ($P<0.05$). We did not find any correlation between the post-exercise increase of NT-proBNP levels and body mass index (BMI), body fat percentage (%BF) or VO_{2max}.

Conclusions: In conclusion, the exhaustive aerobic exercise in healthy individuals led to a fast rise of plasma NT-proBNP concentrations.

Keywords: Exhaustive aerobic exercise, NT-proBNP, Heart failure, Cardiac damage

1. Introduction

Natriuretic peptides are synthesized and secreted by myocardium in response to increased wall stress during volume and/or pressure overload (1,2). With regard to this fact, brain natriuretic peptide (BNP) and its aminoterminal propeptide (NT-proBNP) became valuable biomarkers for heart failure diagnosis and prognosis in clinical practice (3). Increased plasma concentrations of natriuretic peptides were also found in patients with acute coronary syndromes, even in those without myocardial necrosis or accompanying heart failure (4). Previous studies indicated that regular and continuous aerobic exercise, strength exercise and combined endurance/resistance exercise reduces NT-proBNP levels in healthy and heart failure (HF) patients (5-7).

Several studies have documented that transient ischemia induced by exercise stress testing triggers the release of BNP and NT-proBNP (8,9). Moreover, elevated natriuretic peptide levels were detected in marathon runners. In almost one third of them increased levels did not fall into normal range within 3 hours after running (10). The response of natriuretic peptides to short-term and exhaustive exercise in healthy individuals is not well known. We hypothesized that sympathetic activation leading to increased blood pressure, heart rate and left ventricular filling pressures during the exercise test will cause NT-

proBNP secretion. To test this hypothesis we examined plasma NT-proBNP levels before and immediately after exhaustive exercise.

2. Material & Methods

Subjects

Thirty sedentary male enrolled and volunteered to participate in this study. All the people were asked to complete a personal health and medical history questionnaire, which served as a screening tool. Fifteen healthy and sedentary male with a mean (±SD) age of 22.2 ± 2.3 years selected as the subject after screening by inclusion criteria. All the subjects were completely inactive at least 6 months before the study and they were nonsmokers and free from unstable chronic condition including dementia, retinal hemorrhage, and detachment; and they had no history of myocardial infarction, stroke, cancer, dialysis, restraining orthopedic or neuromuscular diseases. The Islamic Azad University, Marvdasht branch Ethics Committee approved the study and written informed consent was obtained from all subjects.

Measurements

Anthropometric and body composition measurements

Height and body mass were measured, and body mass index (BMI) was calculated by dividing body mass (kg) by height (m^2). Waist circumference was determined by obtaining the minimum circumference (narrowest part of the torso, above the umbilicus) and the maximum hip circumference while standing with their heels together. The waist to hip ratio (WHR) was calculated by dividing waist (cm) by hip circumference (cm). Body fat percentage was assessed by skinfold thickness protocol. Skinfold thickness was measured sequentially, in chest, abdominal, and thigh by the same investigator using a skinfold caliper (Harpenden, HSK-BI, British Indicators, West Sussex, UK) and a standard technique.

Exhaustive exercise and VO_{2max} measurement

The Bruce test protocol was used as the exhaustive exercise. This test includes 7 phases. This test is done on the treadmill and started with low intensity; every 3 minutes. The speed and the gradient (slope) of the

device increased up to the level in which the subject could not perform the test anymore and became totally exhausted. The length of time on the treadmill were scored and used to estimate the VO_{2max} value. During the test, heart rate, blood pressure and ratings of perceived exertion were also collected. VO_{2max} value was estimated by following formula:

$$VO_{2max} = 14.8 - (1.379 \times t) + (0.451 \times t^2) - (0.012 \times t^3)$$

Biochemical measurement

Blood samples were collected before and immediately after the exhaustive exercise. Plasma NT-proBNP levels were determined in duplicate via an enzyme-linked immunosorbent assay (ELISA) kits (Biomedica Immunoassay China, Inc). The intra and inter-assay coefficients of variation for NT-proBNP were $< 4\%$ and $< 7\%$ respectively.

Statistical analysis:

Data were analyzed using SPSS software for windows (version 17, SPSS, Inc., Chicago, IL). Paired sample t-test was used to evaluate the changes of Plasma NT-proBNP levels before and after the intervention. Pearson correlation test was used to evaluate the relationship between the variables. The significance level of this study was set at $P < 0.05$.

3. Results

Personal characteristics of the subjects are presented in the Table 1.

Table 1. Anthropometric, body composition and physiological characteristics of the subjects

Variables	Mean	SD
Age (y)	22.2	2.3
Height (cm)	176.4	7.2
Weight (Kg)	70.9	14.4
BMI ($Kg.m^{-2}$)	22.5	3.3
WHR	0.84	0.05
Body fat (%)	17.8	7.1
VO_{2max} ($ml.kg^{-1}.min^{-1}$)	38.3	6.04

Changes on NT-proBNP levels are presented in the Figure 1. The results demonstrated that NT-proBNP levels were increased significantly after the exhaustive aerobic exercise ($P<0.05$).

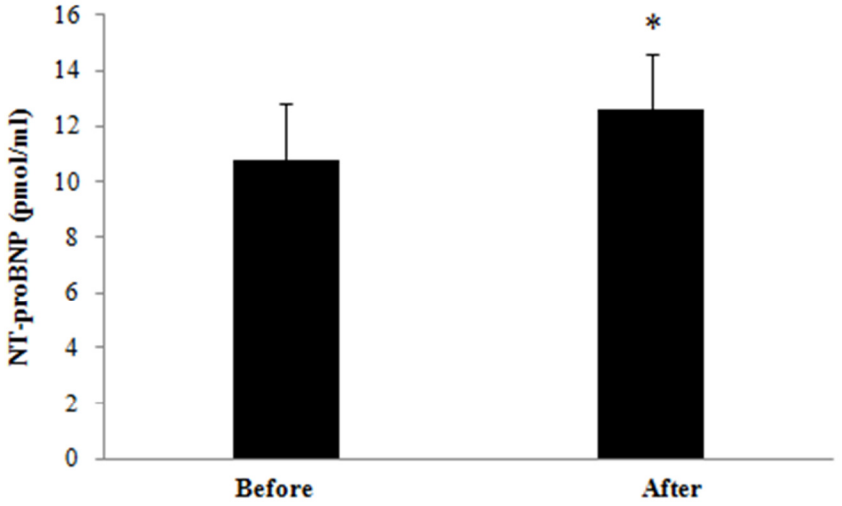

Figure 1. Change on NT-proBNP levels before and after the exhaustive exercise
* Significant differences $P<0.05$

There were no significant relationships between the post-exercise increase of NT-proBNP levels and BMI, body fat percentage or VO_{2max} (Table 2).

Table 2. Relationships between NT-proBNP and body composition and physiological characteristics of the subjects

Variables	NT-proBNP (pmol/ml)	
	r	P
BMI ($Kg.m^{-2}$)	0.07	0.7
Body fat (%)	0.08	0.7
VO_{2max} ($ml.kg^{-1}.min^{-1}$)	– 0.06	0.8

4. Discussion

It is well known from animal experiments that increased myocardium wall stress rapidly triggers synthesis and release of natriuretic peptides (11). Magga et al. (1994) measured BNP mRNA and plasma BNP

during pressure overload in rats. Natriuretic peptide gene expression followed by increased plasma BNP levels started within 1 hour and peak BNP values were detected at 4 hours after the intervention (11). Therefore, it could be possible that BNP plasma concentrations will increase after short-term exercise also in healthy subjects. To test this hypothesis we examined plasma NT-proBNP levels before and immediately after exhaustive exercise. We found that NT-proBNP levels were increased significantly after the exhaustive aerobic exercise.

Several studies documented the relationship between natriuretic peptides rise and the severity of ischemia during exercise stress testing in patients with coronary artery disease or healthy subjects (2,7-9,12,13). Another study described the exercise induced elevation of plasma BNP levels in patients with chronic heart failure (14).

Wozakovska-Kapłon et al. (2009) observed increase of BNP plasma levels after treadmill ergometry in patients with atrial fibrillation (15). This was in contrast with controls, where BNP remained almost unchanged (15). Nevertheless, the reports on natriuretic peptide response to exercise in healthy individuals are controversial. Sabatine et al. (2004) reported that plasma levels of BNP and NT-proBNP in subjects without ischemia during exercise did not change significantly within 4 hours after stress testing (9). On the other hand, Kato et al. (2000) reported small but significant increase of BNP values in healthy volunteers immediately after exercise (14). Bordbar et al. (2012) noted that NT-proBNP was significantly increased after a session of endurance training; however plasma NT-proBNP showed no significant changes immediately after a session of resistance training (7). Middelton et al. (2006) showed that both cardiac Troponin-T and NT-proBNP levels were significantly elevated after exercise, indicative of increase in either left ventricular wall stress or left ventricular end-diastolic pressure (12). Leers et al. (2006) proposed that post-exercise transient increases in Troponin-T and NT-proBNP may reflect myocardial stunning (13). In line with our findings, Krupicka et al. (2010) indicated that BNP was significantly increased after short-term exercise and there were no significant relationships between the post-exercise increase of NT-proBNP levels and BMI, body fat percentage or VO_{2max} (2).

To explain these discrepancies is not easy. The reason can be in different study design, subjects characteristics, exercise test protocol, etc. For example, our subjects were healthy similarly to the control subjects in the study of Kato et al. (2000). Sabatine et al. (2004) studied individuals with suspected coronary artery disease (9). Their mean workload was substantially lower than that in our study. The feasible mechanism explaining the observed transient BNP rise could be a release of BNP from cardiomyocyte storage granules caused by increase in left ventricular wall stress during short-term maximal physical exercise. On the other hand, long-lasting intensive physical activity, such as long-range athletic races, could trigger cardiomyocytes BNP gene expression and synthesis *de novo* (2). To confirm this hypothesis, additional studies need to be performed.

5. Conclusion

Our results indicated that NT-proBNP levels were significantly increased after the exhaustive aerobic exercise in healthy individuals in response to left ventricular wall stress during short-term maximal physical exercise, left ventricular end-diastolic pressure or/and myocardial stunning.

Conflict of interests: There was no conflict of interest among authors.

Reference

1. Levin ER, Gardner DG, Samson WK. Natriuretic peptides. N Engl J Med 1998; 339: 321-328.

2. Krupicka J, Janota T, Kasalová Z, Hradec J. Natriuretic peptides-physiology, pathophysiology and clinical use in heart failure. Physiol Res 2009; 58: 171-177.

3. Emdin M, Passino C, Prontera C, Iervasi A, Ripoli A, Masini S, et al. Cardiac natriuretic hormones, neuro-hormones, thyroid hormones and cytokines in normal subjects and patients with heart failure. Clin Chem Lab Med 2004; 42: 627-636.

4. de Lemos JA, Morrow DA, Bentley JH, Omland T, Sabatine MS, McCabe CH, et al. The prognostic value of B-type natriuretic peptide in patients with acute coronary syndromes. N Engl J Med 2001; 345: 1014-1021.

5. Passino C, Severino S, Poletti R, Piepoli MF, Mammini C, Clerico A, et al. Aerobic training decreases B-type natriuretic peptide expression and adrenergic activation in patients with heart failure. J Am Coll Cardiol 2006; 47: 1835-1839.

6. Conraads VM1, Beckers P, Vaes J, Martin M, Van Hoof V, De Maeyer C, et al. Combined endurance/resistance training reduces NT-proBNP levels in patients with chronic heart failure. Eur Heart J 2004; 25: 1797-1805.

7. Bordbar S, Bigi MA, Aslani A, Rahimi E, Ahmadi N. Effect of endurance and strength exercise on release of brain natriuretic peptide. J Cardiovasc Dis Res 2012; 3: 22-25.

8. Foote RS, Pearlman JD, Siegel AH, Yeo KT. Detection of exercise-induced ischemia by changes in B-type natriuretic peptides. J Am Coll Cardiol 2004; 44: 1980-1987.

9. Sabatine MS, Morrow DA, de Lemos JA, Omland T, Desai MY, Tanasijevic M, et al. Acute changes in circulating natriuretic peptide levels in relation to myocardial ischemia. J Am Coll Cardiol 2004; 44: 1988-1995.

10. Herrmann M, Scharhag J, Miclea M, Urhausen A, Herrmann W, Kindermann W. Post-race kinetics of cardiac troponin T and I and N-terminal pro-brain natriuretic peptide in marathon runners. Clin Chem 2003; 49: 831-834.

11. Magga J, Marttila M, Mäntymaa P, Vuolteenaho O, Ruskoaho H. Brain natriuretic peptide in plasma, atria, and ventricles of vasopressin- and phenylephrine-infused conscious rats. Endocrinology 1994; 134: 2505-2515.

12. Middleton N, Shave R, George K, Whyte G, Forster J, Oxborough D, et al. Novel application of flow propagation velocity and ischaemia-modified albumin in analysis of postexercise cardiac function in man. Exp Physiol 2006; 91: 511-519

13. Leers MP, Schepers R, Baumgarten R. Effects of a long-distance run on cardiac markers in healthy athletes. Clin Chem Lab Med 2006; 44: 999-1003.

14. Kato M, Kinugawa T, Ogino K, Endo A, Osaki S, Igawa O, et al. Augmented response in plasma brain natriuretic peptide to dynamic exercise in patients with left ventricular dysfunction and congestive heart failure. J Intern Med 2000; 248: 309-315.

15. Wozakowska-Kapłon B, Opolski G. Effects of exercise testing on natriuretic peptide secretion in patients with atrial fibrillation. Kardiol Pol 2009; 67: 254-261.