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Effects of 8 Weeks of Combined Rehabilitation Training on Plasma Levels of Leptin, Adiponectin, and Resistin in Middle-Aged Men after CABG

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ABSTRACT

Background and objectives: Coronary artery bypass graft (CABG) is a surgical procedure used to treat coronary heart disease. The present study aimed to investigate effects of 8 weeks of combined rehabilitation training on plasma levels of leptin, adiponectin, and resistin in middle-aged men who have undergone CABG.

Methods: The present research was a quasi-experimental study with a pretest-posttest design. The statistical population included all patients who have undergone CABG in Mashhad, Iran. Overall, 26 middle-aged men who have undergone CABG were enrolled in the study. The subjects were divided into a training group (n=14) and a control group (n=12). Data were analyzed in SPSS software (version 21) using analysis of covariance and paired t-test at significance level of 0.05.

Results: Plasma levels of leptin did not change significantly (p=0.709), adiponectin increased significantly (p=0.001), and resistin decreased significantly (p=0.005) after the training intervention.

Conclusion: As a non-pharmacological intervention, the rehabilitation training has cardioprotective effects on patients who undergone CABG.

Keywords: Rehabilitation, Leptin, Adiponectin, Resistin.

INTRODUCTION

With a prevalence of 5.8 million per year in the United States and over 23 million worldwide, as well as a 5-year mortality rate of over 75% after the first admission, heart failure is a major health problem worldwide (1). Coronary artery bypass graft (CABG) is a surgical procedure used to treat coronary heart disease. Every year, more than 2 million operations are performed on heart patients, and in Iran, more than 25,000 heart surgeries are performed annually, of which, 50-60% are CABG (2). In CABG, a secondary pathway is created through a vein graft to increase blood flow in the coronary artery (3).

Leptin is a protein hormone with a molecular weight of 16 kDa, which is mainly produced by adipose tissue. This hormone acts as a physiological regulator of cardiovascular function and a pathophysiological activator of cardiovascular disease (4). Some factors such as body mass index (BMI), gender, inflammation, and a high-fat diet increase leptin, while exercise and a decrease in body fat mass can lower this hormone. Plasma levels of leptin are associated with increased thickness of the myocardial wall and left ventricular mass, indicating that this hormone is involved in left ventricular hypertrophy. Leptin also causes the elongation of cardiac myocytes through the Janus kinase-signal transducer and activator of transcription pathways. Leptin receptor is expressed in atherosclerotic coronary arteries, mainly in vascular endothelial cells, macrophages, and foam cells (5, 6).

Adipose tissue secretes several important adipokines such as adiponectin and resistin. Studies have shown that reducing adiponectin increases the risk of coronary heart disease, hypertension, left ventricular hypertrophy, and myocardial infarction. Adiponectin protects the heart against the development of systolic dysfunction after myocardial infarction. It also protects cardiomyocytes and capillaries through suppression of cardiac hypertrophy and interstitial fibrosis. Resistin affects vascular endothelial cells, causes proliferation of vascular smooth muscle cells, and accelerates the migration of these cells, which in turn causes pathological enlargement of blood vessels (7-9).

Considering the important effects of these adipokines on the cardiovascular system (10-15) and the contradictory results of previous studies, this study aimed at evaluating effects of 8 weeks of combined rehabilitation training on leptin, resistin, and adiponectin levels in middle-aged men who have undergone CABG.

MATERIALS AND METHODS

This quasi-experimental research was performed on patients aged 45-60 years old who were admitted to Javad Al Aemeh Hospital in Mashhad, Iran. Sample size was determined according to the Cochran's method. Accordingly, 26 men who have undergone CABG were selected via convenience sampling and then divided into a training group (n=14) and a control group (n=12) according to the following inclusion criteria: no cognition, vision, or hearing disorder, systolic blood pressure of less than 160 mmHg, diastolic blood pressure of less than 100 mmHg, and lack of need for assistive walking devices such as walkers. Exclusion criteria included the occurrence of ventricular arrhythmias, rising or falling ST-segment in the patient's electrocardiogram during training sessions, the occurrence of respiratory disorders during rehabilitation and training, unstable angina, and personal reluctance to participate in the study.

Height of the subjects was measured by using a SEKA digital device (Germany), with an accuracy of 0.1 cm. Body fat percentage and BMI were determined using an Inbody 720 digital device (South Korea). Heart rate was recorded by an F1tm pulse meter (Finland). Resting blood pressure was measured by an ALPK-2 sphygmomanometer. Training times were monitored by a digital timer, with an accuracy of 0.01 seconds (Table 1).

After matching the diet and holding two psychology sessions at the hospital, a combined training was performed 3 sessions a week, for 8 weeks. During this time, the control group was asked to follow their normal course of life and did not engage in any regular physical activity. Blood samples (5 ml) were taken from the brachial vein of the subjects 24 hours before the start of the training session and 48 hours after the last training session by an expert. After transferring the samples to laboratory for examination, leptin, resistin, and adiponectin levels were measured using commercial enzyme-linked immunosorbent assay kits (East Biophanrm, China).

Table 1- Mean weight, height, age, fat percentage, body mass index, disease history, and plasma levels of leptin, adiponectin, and resistin in CABG patients before and after the training intervention

Variables	Combined training (n=14)		Control group (n=12)	
	Pretest	Posttest	Pretest	Posttest
Height (m)	1.65±0.09	1.73±0.77	.....	.....
Weight (kg)	74.26±12.49	80.53±12.71	70.20±11.35	81.33±12.72
Age (year)	52.16±5.80	51.60±5	.....	.....
BMI (kg/m^2)	26.02±4.41	26.74±2.49	25.56±3.44	27±2.48
fat percentage	35.53±1.56	35.53±1.64	31.60±1.50	37.40±1.63
Disease history (months)	18±6.19	25.20±8.57	.....	.....
Leptin (ng/ml)	5.58 ± 1.77	6.46 ± 1.44	5.60 ± 1.85	6.41 ± 1.18
Adiponectin (mg/l)	1.13 ±0.33	0.99 ±0.23^{ab}	3.09 ±0.54	0.96 ±0.19
Resistin (ng/l)	230.78 ± 71.43	276.91 ±1337.4	208 ± 59.17	278.33 ±133.54

a Significant difference between the pretest and posttest value (dependent t-test)
b Significant difference between the two groups (independent t-test)

One-repetition maximum (1RM) was measured in the first and fourth weeks according to the Brzycki equation: 1RM = (repetition × 2.78 – 102.78) / workload × 100.

The combined rehabilitation training program was performed 3 sessions a week, for 8 weeks. Each session lasted 60-90 minutes, depending on the evaluations (cardiopulmonary status, exercise tolerance test, etc.). The training program included walking on a treadmill fore 20-30 minutes, pedaling a stationary bike for 10-12 minutes, and using a manual ergometer for 10 minutes. The duration and intensity of trainings were adjusted considering 60% of the patients' maximum heart rate as the target heart rate. The intensity and duration of the trainings increased gradually and reached 80% of patients' maximum heart rate in the last 7-10 sessions. The reserve heart rate was calculated by the Karvonen method:

Reserve heart rate= [resting heart rate + (55, 75%) × resting heart rate - maximum heart rate)].

Each week, as the intensity of exercise increased, the target heart rate also increased by approximately 5%. The resistance training program was performed with 8 repetitions in the initial sessions and 15 repetitions in three sets in subsequent sessions. The exercises included squat with physioball, shoulder flexion, hip flexion, shoulder abduction, hip abduction, elbow flexion, ankle plantar flexion, and wrist dorsiflexion. The exercises were initially performed with 8 repetitions using a lighter TheraBand (yellow). Then, the intensity was increased by using a pink TheraBand and gradually increasing the number of repetitions to 15 in the next sessions. There was no specific order for aerobic and resistance trainings, and patients performed the resistance training in the interval between aerobic training or separately after the aerobic training. The control group did not participate in any regular physical activity. At the end of each session, cooling exercises were performed for 5-10 minutes, and relaxation exercises were performed for 5-10 minutes. Fluctuations in the patient's heart rate at all stages of the trainings were controlled by a medical monitoring team supervised by a cardiologist who was with the research team at all stages of the research. Blood pressure was measured and recorded by rehabilitation nurses after using each training device.

Data were expressed as mean ± standard deviation. Statistical analysis of data was done in SPSS software (version 21) using analysis of covariance and paired t-test at significance level of 0.05.

RESULTS

Table 1 shows the mean values of height, weight, age, fat mass, BMI, disease duration, and plasma levels of leptin, adiponectin, and resistin before and after the training intervention.

Leptin levels showed did not change significantly after the intervention, and there was no significant difference between the two groups in terms of plasma leptin levels (p=0.504). Plasma levels of adiponectin increased significantly after the training intervention (p=0.001). The posttest value of plasma adiponectin was significantly higher in the training group compared with the control group (p=0.005). In addition, plasma levels of resistin decreased significantly after the training intervention (p=0.006), and the posttest value of plasma resistin was significantly lower in the training group compared with the control group (p=0.005).

DISCUSSION

The results of the present study showed that 8 weeks of combined training decreased the plasma levels of resistin and increased the plasma levels of adiponectin but had no effect on plasma levels of leptin. Little research has been done on leptin levels in patients with cardiovascular disease. Consistent with our findings, Saremi et al. (2011) showed that 12 weeks of aerobic training did cause a significant change in plasma levels of leptin (13). Irandoost et al. (2008) reported that after 8 weeks of running with an intensity of 55-75% of maximum heart rate, no significant change in leptin levels was observed in women of normal weight (16). In a study by Bijeh et al. (2011), no change in leptin levels was observed in middle-aged lean women after 6 months of aerobic exercise with an intensity of 60-70% of maximum heart rate (15). Similarly, Ara et al. (2006) reported no change in serum levels of leptin after 6 weeks of resistance training (17). Khalili et al. (2013) reported that resistance training with an intensity of 60-70% of 1RM caused a significant decrease in leptin levels of obese female students (18). The reason for the inconsistency of the results of previous studies and the present study may be related to the difference in the characteristics of subjects and the training protocol or intensity (19). Nutritional, immune, and neuroendocrine statuses, as well as levels of sex hormones, catecholamines, and thyroid hormones affect the regulation of leptin levels in the body. These hormones affect the production of leptin by regulating the gene responsible for obesity. In addition, growth hormones and cortisol are among the most important hormones that increase leptin secretion (20). In the present study, due to the condition of the subjects and the low intensity of exercise, the amount of fat reduction was not significant enough to cause changes in plasma levels of leptin. In addition, Bagheri et al. (2005) concluded that the average plasma level of leptin in women is higher than in men (21). Therefore, the gender of the subjects in the present study could be another reason for the lack of significant change in the plasma level of leptin. Numerous studies have shown that aerobic exercise reduces serum level of leptin. However, in the present study, combined training (aerobic and resistance) was used as a rehabilitation intervention. The mechanism of the effect of resistance training on leptin levels is different from that of aerobic exercise. Resistance training is a stronger, non-oxidative stimulus compared with aerobic exercise, which produces different neurological, metabolic, and neuroendocrine responses. Resistance training reduces serum leptin by glycogen depletion, inhibiting glycolysis, increasing glucose uptake in the presence of lactate, acidosis, and catecholamines. However, different responses have been observed to resistance training protocols.

In our study, 8 weeks of combined training increased plasma levels of adiponectin. Consistent with this finding, Kazemi et al. (2014) also reported a significant increase in adiponectin levels in overweight children following 8 weeks of rapid intermittent exercise (22). Balagopal et al. (2005) showed that 3 months of aerobic exercise significantly increased adiponectin levels (23). Ilkhani et al. (2017) stated that 8 weeks of aerobic exercise in elderly men with diabetes caused a significant increase in adiponectin levels (24). Inconsistent with these findings, Hulver et al. (2002) reported that exercise did not affect the plasma levels of adiponectin (25). Jeon et al. (2013) reported that 12 weeks of resistance training did not affect adiponectin levels (26). It has been demonstrated that adiponectin has a protective effect on coronary artery disease. Researchers believe that repetition and intensity of exercise are important parameters that increase adiponectin levels. In this regard, Martinez et al. (2011) showed that exercise, 2 days a week, with an intensity of 30 meter/minute for 60 minutes increased adiponectin by 150% compared to the same exercise, 2 and 5 days a week, with an intensity of 25 meters/minute for 30 minutes (11). Interleukin 6 (IL-6) is secreted by white blood cells and has an important role in inflammatory and immune responses. Tumor necrosis factor (TNF)-alpha plays a major role in regulating the body's immune cells and is one of the most important mediators of inflammation. These cytokines reduce the secretion of adiponectin and its expression by adipocytes. Exercise can increase the release of IL-6 from active muscles, which can stop the activity of the pro-inflammatory marker TNF-α and thus increase adiponectin levels (27). Recent studies have shown that endothelial nitric oxide synthase (eNOS),

the catalytic enzyme required for NO production, plays a key role in the synthesis of adiponectin in adipocytes. As the intensity of exercise increases, NO production increases. It seems that with increasing NO, eNOS also increases following exercise (28). In addition, studies have shown that mitochondrial biogenesis increases following exercise. In this regard, Koh et al. (2010) demonstrated that mitochondrial biogenesis increases adiponectin synthesis (29). Therefore, it seems that the mentioned factors could be involved in the increased level of adiponectin in our subjects.

The combined training intervention reduced resistin in the subjects. In agreement with this finding, Balducci et al. (2010) reported that 12 months of high-intensity aerobic exercise and combined training (aerobic and resistance) decreased leptin and resistin and increased adiponectin levels (28). Davoodi et al. (2014) reported that moderate-intensity aerobic exercise significantly reduced resistin levels (30). Fathi et al. (2015) reported that 8 weeks of aerobic exercise reduced resistin by 50-70% (31). Inconsistent with these findings, a previous study showed that 2 months of aerobic exercise with an intensity of 60-80% of the maximum heart rate increased the resistin levels. The most important mechanism explaining the increase in resistin after aerobic exercise in this study is the role of this hormone in the body's antioxidant defense (32). Resistin acts as an antioxidant in response to an inflammatory stimulus (33). Generally, the results of studies on the response of resistin levels to exercise have been contradictory. Some of these studies have reported no change (34), decrease (35), and increase (36) in resistin levels following an exercise program. Different mechanisms have been proposed for changes in resistin levels. Some studies have stated that weight loss and fat mass are important for reducing resistin levels. However, Tawfiqi et al. (2013) reported that 12 weeks of combined training had no significant effect on resistin levels in obese postmenopausal women with type 2 diabetes (35). The reason for this inconsistency could be the gender of the subjects. Therefore, it seems that duration, intensity, and type of exercise as well as gender could affect the production of resistin following physical activity. Other mechanisms of resistin reduction include changes in pro-inflammatory cytokines, including IL-1, IL-6, and TNF-alpha (37).

CONCLUSION

The combined rehabilitation training could increase cardioprotective factors and reduce inflammatory factors that could damage the cardiovascular system.

DECLARATIONS

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Ethics approvals and consent to participate

The study received approval from the Ethics Committee of Islamic Azad University, Neishabour Branch (ethical code: IR.IAU.NEYSHABUR.REC.1399.012).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding publication of this article.

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