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Effects of Different Exercise Intensities on Serum Levels of Apelin and Chemerin in Male Wistar Rats

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Abstract
Background: Adipose tissue is a large source of fat that has the task of storing fat in the body, and is also extremely important in energy homeostasis. The purpose of this study was to compare the effects of different exercise intensities (12 weeks) on serum levels of Apelin and Chemerin which are produced by adipose tissue in male Wistar rats.
Method: In this study, 30 male Wistar rats randomly divided into three groups (n=10); 1. Control group, 2. High intensity group and 3. Low intensity group. Rats in exercise training groups ran on a treadmill with low and high intensity for 12 weeks (5 sessions per week). The serum levels of Aplin and Chemerin were measured using the ELISA technique, and the inter group comparison was done using one-way analysis of variance (One-Way ANOVA) with the Tukey test.
Results: The findings suggest that both low and high intensity exercise training can increase the serum levels of Apelin ($P<0.05$); but there was no significant difference between the serum levels of Apelin in different exercise training groups. There were no significant changes in serum levels of Chemerin after two different exercise intensities.
Conclusion: To summarize, the intensity of exercise training can be a criterion for Apelin secretion in adipose tissue, whereas Chemerin, according to our observations, is not a trainable factor.
Keywords: Apelin, Chemerin, High intensity, Low intensity

Introduction:

Adipose tissue is a type of connective tissue made up of brown and white fat tissues that contain multi-cylinder stem cells capable of transforming into muscle, cartilage, bone, and fat cells. Adipose tissue also contains macrophages, endothelial cells, vessels, and adipocytes (productive adipokines) [1]. This tissue contains 80% lipids and its primary function is to store energy as fat; thus, it contributes to obesity and overweight. Adipose tissue's metabolic activities include producing cytokines, regulating hormones, producing hormone to regulate energy at the tissue level, and regulating energy at the central nervous system level [2]. Furthermore, this tissue's non-metabolic activities include thermal insulation, electrical insulation and storing. Understanding the biology of adipocytes (fat cells) and processes occurring in the context of adipocytes in the body has become possible as a result of the global obesity and diabetes

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epidemic [3]. Adipose tissue (adipocytes) is a hormonal system that is important in controlling the body's metabolism as well as energy storage.

Adipokines also known as adipocytokines are cytokines that are secreted from adipocyte tissue and play this important role. Researchers recognized the importance of adipose tissue when they discovered leptin as the first hormone secreted by adipose tissue and its impact on food consumption and energy homeostasis [4]. Adipokines secrete several hormones, including IL-6 (Interlukine-6), Resistin, necrosis factor alpha, RBP4 (Retinol Binding Protein 4), vaspin, adiponectin, apelin, and Chemerin [5]. Apelin is an adipokine that is important role in the cardiovascular system and the regulation of lipid metabolism [6]. Apelin inhibits AMPK release by adipocytes by activating adenosine monophosphate-activated protein [7]. Shaibani et al (2012) found that in obese women, exercise can reduce plasma apelin, insulin, and TNF levels. If both body mass index and body fat mass are reduced, regular physical activity causes a decrease in apelin plasma levels [8]. Jing Zhang et al. (2006) discovered that swimming exercise improves hypoxic pulmonary hypertension in rats by regulating the pulmonary Apelin/APJ system [9]. Drake et al. (2008) investigated the effect of Apelin on glucose uptake in healthy and obese rats resistant against insulin, and they concluded that Apelin can be a promising target in the management of insulin resistance [10].

Chemrin hormone has the ability to regulate adipokines, autocrine, paracrine, and angiogenic functions. It is thought of as a chemokine in the immune system and as an adipokine in fat cells. The association of this factor with inflammation and its role as a Chemokine is perfectly clear. In addition, Chemerin can regulate lipid metabolism, and growth of adipose tissue [11]. So far, only one report has shown that Chemerin reduces the glucose uptake [12], while the results of other studies indicate the supportive role of Chemerin in normal glucose uptake [13].

Given the importance of Chemerin and Apelin hormones and lack of research on the impact of the type of different exercise intensities on the secretion of those hormones and also the inconsistency in the results of research and insufficiency of studies, this study considered the necessity of research on this area for the first time to respond the following question. How is the effect of aerobic and anaerobic exercise protocols (12 weeks) on serum levels of apelin and Chemerin of adult male rats?

Methods:

Animals

Male Wistar rats (6 weeks old) were purchased from Kerman Physiology Research Center and were maintained at 22 ± 2 ºC with a 12 h light/dark cycle. All rats were fed with chow diet and water during the 2-week acclimation period. At the age of 8 weeks, the rats were randomly assigned to three groups (n=10) including healthy control (CTL), High intensity training (HIT), Low intensity training (LIT). The protocol of this experimental study was approved by the Ethical Committees on Animal Care at the Physiology Research Center of Kerman University of Medical Sciences.

Training Intervention

This practice was performed in compliance with progressive principle and overload. Speed and time were adjusted according to a specific program and each practice session was held

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at a certain time in the morning (Table 1 and 2) [14]. After using the independent variable (12 weeks of aerobic and anaerobic activities), two groups were anesthetized with sodium thiopental at the very same and base conditions (at least 24 hours after the last exercise session for exercise group) and then 2^{cc} of blood was extracted from their eye sinus. This extracted blood was centrifuged at 3500 rpm for 10 minutes and then the plasma was separated. Obtained plasma was kept in 1.5cc tubes and at the temperature of -20°C; it was then transferred to the laboratory so that Chemerin and apelin hormones could be measured. To start the experiment, plasma was left at ambient temperature so that it could reach ambient temperature. Then serum size of apelin and Chemerin hormones was measured using ELISA kits made in China and ELISA laboratory method.

Table 1. High intensity exercise training (speed and time)

Week	3	4	5	6	7	8	9	10	11	12	13	14
Speed (m/min)	32.8	34	35	35.5	36	37	37	37.5	37.5	38	38	38
Time (min)	5	5	5	5	5	5.5	6	6	6.5	7	7	7.5

Table 2. Low intensity of exercise training (speed and time)

Week	3	4	5	6	7	8	9	10	11	12	13	14
Speed (m/min)	18	18.7	20	21.4	22	22.5	23	23.5	23.5	24	24	24
Time (min)	9	9	8.75	8.1	8.1	9	9.6	9.5	10.3	11	11	11.8

Tissue Samples

At the end of the experimental period, the animals were fasted overnight. The animals were anesthetized (ketamine and xylazin 90/10 mg/kg).

Statistical Analysis

All the data are expressed as Mean±SD. Comparisons of variables between studied groups were carried out by One-Way analysis of variance (One -Way ANOVA) test. When a significant effect was found, tukey test was performed between groups. The $p<0.05$ was considered significant. All analysis was carried out using SPSS version 22.

Results:

Both low and high intensity exercises increase the serum levels of apelin protein; however, there are no significant differences between the apelin levels of exercise groups statistically. Levels of Chemerin did not show any significant changes after aerobic and anaerobic activities. These results indicate that serum levels of apelin had a significant increase in control group compared with high and low intensity exercise groups.

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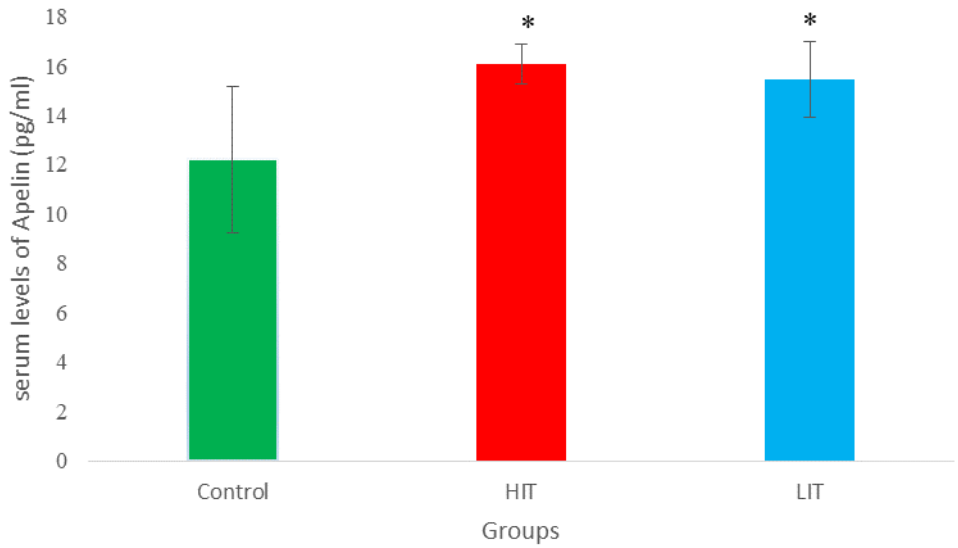

Figure 1. Serum levels of Apelin (pg/ml). * statistically significant compared to Control group.

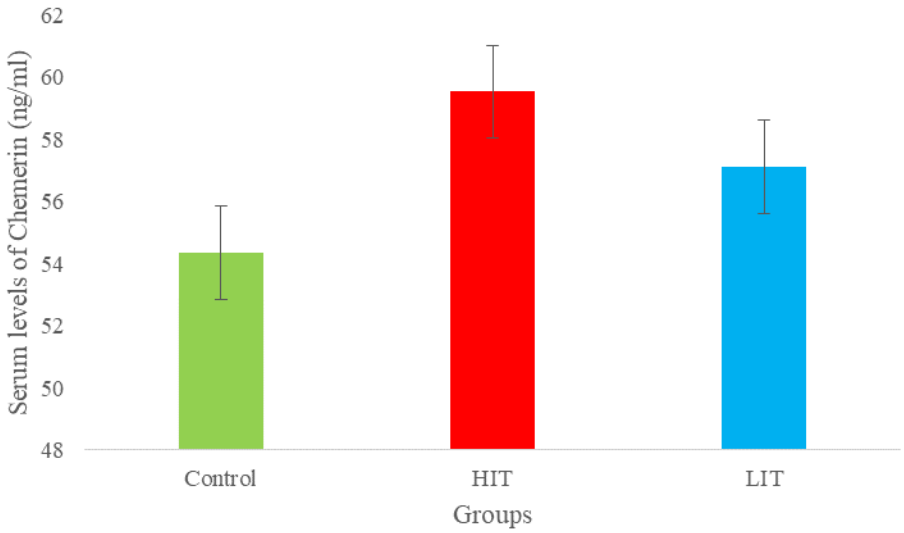

Figure 2. Serum levels of Chemerin (ng/ml)

Discussion:

The present study was performed to investigate the long-term effects of different exercise intensities on serum levels of Apelin and Chemerin. The most important results were that the Chemerin is not a trainable factor, and does not change in response to long period training, but Apelin is a trainable factor and increases in response to exercise training.

Our result showed that Chemerin levels increased non-significantly in the training groups. Chemerin is an adipokine that has recently been identified as a regulator of adipose tissue differentiation and metabolism [15, 16]. Chemrin is believed to cause insulin resistance and reduced glucose uptake in skeletal muscle (in vitro and in vivo) [17]. There is little research on the effect of Chemerin on cellular metabolic reactions, and clarification of this relationship

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requires further study; a study of adipose tissue in women with polycystic ovary syndrome also showed (Polycystic ovary syndrome), Chemrin production is significantly increased by insulin, which is decreased by metformin and is not altered by the gonads and adrenals [18].

In recent years, adipose tissue has been reported to secrete adipocyte (Apelin), which is involved in carbohydrate metabolism and insulin function [19] and is a potent vasodilator [20]. Preliminary laboratory studies on animal species indicate that Apelin and its receptor are involved in cardiovascular homeostasis, so that its vascular tone may play a role in regulating vascular tonnage, cardiac contractile function, and fluid balance [21]. Apelin acts as a mediator in the control of the cardiovascular system, including blood pressure and blood flow, and is known to be one of the strongest factors in the contraction of the heart [22, 23]. Our findings show that serum levels of Apelin can rise in response to prolonged exercise training, and that the rise is not dependent on intensity. The results of our research were consistent with the results obtained by Shaibani et al. (2012) and Kadogholu et al. (2012) [8, 24].

Eventually, the present study showed that 12 weeks of high and low exercise intensities would not lead to significant changes in plasma levels of Chemerin. The results of this research showed that the secretion of Chemerin hormone is not influenced by exercise programs with low to high intensities. But the duration of an exercise program in a study should be taken into consideration to affect the hormone levels of Apelin and it seems that if the duration of exercise sessions increases, improvements are observed in cardiovascular factors and these improvements are the main task of this hormone. Inflammation plays an important role in processes of insulin resistance and it seems that chemical intermediates such as Chemerin and Apelin play a pivotal role in insulin resistance. Chemerin and apelin have a significant impact on important systems of body, especially the metabolic syndrome, type 2 diabetes and inflammatory factors.

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