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Chronic Aerobic Exercise Associated with Reduced Body Weight Decreases Serum Ghrelin in Adult Obese Individuals

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ABSTRACT
In the past decade, Ghrelin has gained considerable attention for its unique role in regulating appetite and short or long-term energy homeostasis. This study aims to clarify the effects t a chronic aerobic exercise program on serum ghrelin in obese males.
Subjects included in the study were thirty four adult obese males Aged 38 to 50 years and were divided into experimental (exercise intervention) or control (without exercise) groups. Anthropometrical measurements, fasting serum ghrelin and lipid profile performed before and after aerobic exercise and detraining interventions (3 days/wk for 3 months) in experimental and control groups respectively. Statistical analysis was used by independent - paired samples t-tests in SPSS software version 15.0.
Serum ghrelin concentration decreased significantly after exercise intervention in experimental group ($p \leq 0.05$). In addition, all anthropometrical indexes, resting heart rate and systolic blood pressure decreased in exercise group ($p \leq 0.05$). Triglyceride concentration was decreased significantly whereas total cholesterol, low and high lipoprotein cholesterol did not change after exercise training in experimental group ($p \geq 0.05$). All variable remind without changes in control group ($p \geq 0.05$).
Our finding demonstrated that chronic aerobic exercise associated with reduced body weight leads to decreased serum ghrelin in obese individuals and support of the role of exercise as a non-pharmacologic treatment in regulating and balancing this peptide hormone in these subjects.
***Keywords**: Obesity, Exercise, Ghrelin, Body mass index*

INTRODUCTION

In most people, body weight remains in a stable condition or energy balance and this can take years. The requirement for a stable weight is an energy balance; in a way that energy intake has to be equal to energy expenditure. Disorder in energy balance in humans is associated with sustained weight problems [1]. Hence, identification of environmental or genetic factors influencing the imbalance between energy intake and expenditure is always being investigated and several studies in the field are in progress. The role of hormonal factors is also the focus of on science and health professionals. Ghrelin is one of the circulation peptides, which is involved in regulating food intake and body weight by sending signals to the hypothalamus [2]. This 28 amino acid peptide hormone is secreted primarily by the stomach and to some extent by other tissues such as the gastrointestinal tract, pancreas and saliva [3, 4]. Ghrelin level increases pre-prandial and rapidly decreases postprandial as one hour after meals it reaches its lowest levels [5, 6]. But in obese people, in a short time after eating, ghrelin level increases again and increased ghrelin concentration is associated with renewed hunger [7]. On the other hand, regardless of ghrelin role in short-term regulating of food intake, its role in long-term regulation of energy balance has also been reported [8]. It has also been established that a daily intake of peripheral ghrelin induces adiposity by inhibiting fat utilization [8]. Ghrelin role in glucose homeostasis as well as lipid and carbohydrate metabolism has also been reported in some studies [9, 10]. As ghrelin administration in humans has led to decreased levels of insulin and increased glucose concentrations [11, 12]. A recent study also showed that ghrelin consumption by mice with abnormalities in lipid metabolism in adipose tissue, liver and skeletal muscle is associated with increased body weight [13].

In this regard, some studies have also suggested that a change in systemic levels of ghrelin is dependent on factors such as gender, type of obesity and insulin resistance [14]. In addition, the role of exercise and exercise-induced weight loss on systemic levels of this peptide hormone is also constantly being investigated and there are conflicting findings in this regard; as the findings of a recent study showed that a single session of cycling exercise significantly reduces the ghrelin concentration [15]. In another study, 4 weeks of exercise brought about a significant reduction in circulation ghrelin [16]. But despite these findings, long-term exercise program on obese subjects in a recent study was associated with weight loss led to a significant increase in plasma ghrelin concentration [17]. But in another study, 60 minutes of exercise on the treadmill did not lead to changes in obestatin and ghrelin levels [18]. Review of the research findings are suggestive of contradictions between the findings on ghrelin response to exercise. Hence, considering the key role of this peptide hormone in the regulation of homeostasis and body weight, this study aims to look into the effect of a 12-week aerobic training program on serum levels in obese adult males.

METHODS

Subjects: This semi-experimental study was conducted in order to look into the impact of a long-term aerobic exercise training program on serum ghrelin levels in obese adults. For this purpose, 34 male obese adults were randomized in two groups; experimental group (12 weeks of aerobic training) and control group (no training). Subjects were in the age range of 38 to 50 years and BMI of 29 to 36 kg/m^2. This protocol was approved by the exercise physiology department of Saveh Azad University, Iran. Informed consent was obtained from each subject after full explanation of the purpose, nature and risk of all procedures used.

Inclusion and exclusion criteria: Subjects included individuals with no cardiovascular diseases, gastrointestinal diseases, kidney and liver disorders or diabetes. In addition, if any of the people had been participating in regular exercise or diet program during the past 6 months, they were barred from in the study. All subjects were non-smokers. In addition, exclusion criteria included inability to exercise and supplementations that alter carbohydrate-fat metabolism.

Anthropometric Measurements: After introduction and awareness of the subjects of the objectives of the study and once they had completed consent forms, the process of test implementation began. Anthropometric measurements of height, weight, percent body fat, and circumference measurements were taken pre- and post-exercise training in the physiology laboratory. Height was measured without shoes on standing while the shoulders were tangent with the wall. Body weight was measured in duplicate in the morning following a 12-h fast. Obesity was measured by body mass index (BMI). Body mass index was measured for each individual by division of body weight (kg) by height (m2). Waist and hip circumferences were measured at the level of umbilicus and of trochanter major, respectively. Waist to hip circumference ratio was measured by dividing the abdominal circumference into that of the hip. Blood pressure was measured using the left arm after the subject had been sitting comfortably for 5 min, using an oscillometric device (Alpikado, Japans).

Blood sampling and exercise program: After anthropometric measurements, the individuals in the experimental and control groups were asked to attend Hematology Lab following12 hours of overnight fasting, between the hours of 8 to 9 am for blood sampling. The subjects were advised to avoid any physical activity or exercise 48 hours before the blood sampling. Resting heart rate (HR) was measured after a 15-min rest in a sitting position and in a quiet environment. Then, a 5 ml fasting blood samples were collected from brachial vein in sitting position. Serums were immediately separated and stored at -80° until the assays were performed. In fact, fasting blood samples were taken pre-training (pre-test) and 48 h after aerobic exercise training program(post-test). Exercise training program lasted 3 months (3 days/wk) 60 to 80 percent of maximum heart rate. Each session started by 15 min of warm up, 30-40 min of aerobic exercise and 5–10 min of cool down activity. Aerobic exercises in each session included walking on a treadmill and stationary cycling. Initially, subjects exercised at low intensity and the intensity of exercise was gradually increased to 80% of peak heart rate in next sessions. The intensity of the activity of any person was controlled using the Polar heart rate tester (made in the US). In this 12-week period, participants in the control group were barred from participating in any exercise training. Finally, all measurements consist of fasting blood sampling, anthropometric measurements and Blood pressure repeated 48 h after last exercise session. Serum ghrelin was measured by ELISA method using commercial kits made by Austrian Biovendor Company. Biochemical indicators of triglyceride (TG), total cholesterol (TC), and low-density lipoprotein (LDL) and high-density lipoprotein (HDL) were measured by enzymatic method by Kobas Auto-analyzer (German).

Statistical analysis: Data were expressed as individual values or the mean ± SD for groups. Data were analyzed using the program SPSS software version 15. Baseline characteristics were compared by using independent t-tests. Student's t-tests for paired samples were performed to determine whether there were significant within-group changes in the outcomes. Analysis of covariance was used to determine whether the changes in the outcomes were significantly different between groups while using the baseline values as the covariates. P value of <0.05 was accepted as significant.

RESULTS

In this study the effect of 12 weeks of aerobic exercise on serum levels ghrelin and anthropometric indices and lipid profile was assessed in adult obese males. Baseline and post training ghrelin levels, anthropometrical indexes and clinical characteristics of two groups are shown in Table 1. Findings from independent t-test showed that baseline levels of serum ghrelin and a biochemical indicator of lipid profile (HDL, LDL, TC, and TG) and anthropometrical indexes groups did not differ between the control and experimental groups ($p \geq 0.05$). Student's t-tests for paired samples indicate significant reduction of serum ghrelin levels in the experimental group ($p = 0.002$). In other words, a 12-week aerobic training of three sessions per week led to a significant reduction in Ghrelin serum whereas its concentration did not change in control group (Fig 1). With aerobic exercise training, subjects in experimental group lost fat mass seen as a decrease in percent body fat ($p=0.000$), body weight ($p=0.000$), waist circumference, and BMI ($p=0.000$). Although the reduction of total cholesterol levels in experimental groups was not significant ($p = 0.699$), but a significant decrease in triglyceride serum ($p = 0.002$, Fig 2) was observed. In other words, Triglyceride concentration was decreased 28% whereas concentrations of TC, HDL cholesterol, and LDL cholesterol did not change after exercise training in experimental group ($p \geq 0.05$). Also, despite the lack of significant increase in HDL, the TG / HDL ratio which is one of the determining factors for cardiovascular diseases significantly decreased ($p = 0.007$). Systolic blood pressure were significantly decreased in experimental group ($p = 0.000$). The resting heart rate of obese individuals in experimental group significantly decreased in response to exercise training ($p = 0.000$). None of the studied variables changed in the control group as a result of three months of detraining ($p <0.05$).

DISCUSSION

Our study shows that serum ghrelin levels were significantly decreased by exercise training in obese subjects. Although the mechanisms by which acute or chronic exercise leads to a short-term reduction or control in appetite have remained unknown, probably the effect of peptides secreted from adipose tissue or other endocrine tissues on this phenomenon cannot be ignored [19]. Recent studies have shown that some peptide hormones with different physiological concentrations, can affect the appetite in animals and humans [20, 21, 22]; as their physiological role in satiety after a meal reflects their role and influence as a pharmacokinetic factor for anti-obesity purposes. In humans, ghrelin injection leads to increased appetite but whether intravenous injection of ghrelin affects feeding behaviors in humans is not yet fully characterized [23]. Current evidence suggests that ghrelin stimulates appetite and regulates energy balance, and thus is one of the candidate genes for obesity and some chronic diseases [24]. Since blood ghrelin level is disrupted in presence of obesity, understanding the mechanisms contributing to development of this disorder and providing appropriate solutions for maintaining its balance is the focus of many studies today. Statistical findings of this study showed that 12 weeks of aerobic exercise in obese adult men resulted in a significant reduction in ghrelin serum levels. Over the years, both basic studies and correlation studies have reported ghrelin gene connection with obesity, metabolic syndrome and type-II diabetes [24]. After the discovery of ghrelin in 1999, its role in stimulating hunger and appetite has been repeatedly reported [8, 20, 25], so its peripheral consumption, effectively stimulates food intake in animals and its long-term consumption leads to increase in body weight and fat tissue in mice [26].

The results of a recent study, corroborating the finding of this study, showed that plasma levels of ghrelin significantly would reduce following aerobic exercise training in moderate intensity [15]. But the findings of another study reported no change in blood ghrelin levels by aerobic exercise [18]. In another study, the combination of long-term diet and exercise was associated with increased Obestatin and a significant reduction in leptin with unchanged ghrelin concentration in obese individuals [27]. On the other hand, a recent study reported a significant reduction in serum ghrelin after 4 weeks of exercise [16]. In this regard, some studies have suggested that if exercise program or long-term diet is not accompanied with a significant reduction in body weight it will result in no change in insulin resistance, insulin, ghrelin and other peptide hormones [27].

Table 1; Anthropometrical and biochemical characteristics before and after interventions in studied groups

Group / variables	Experimental group		Control group	
	Pre-test	**post-test**	**Pre-test**	**post-test**
Age (year)	44 ± 0.88	----	45 ± 1.02	----
Height (cm)	177 ± 1.2	----	176 ± 1.08	----
Body Weight (kg)	103 ± 4.12 *	96 ± 4.47	102 ± 3.68	103 ± 4.11
WC (cm)	110 ± 3 *	104 ± 3.08	109 ± 4	110 ± 5
HC (cm)	109 ± 2.62 *	106 ± 2.80	108 ± 1.63	110 ± 2.14
WHR	1.01 ± 0.01 *	0.98 ± 0.01	1.01 ± 0.02	1 ± 0.97
BMI (kg/m2)	33.25 ± 0.99 *	30.99 ± 0.95	32.55 ± 1.08	32.88 ± 1.14
BF (%)	33.33 ± 1.09 *	27.59 ± 0.63	32.98 ± 1.14	33.21 ± 0.98
Systolic BP (mm/hg)	129 ± 26 *	116 ± 16	131 ± 21	128 ± 19
Diastolic BP (mm/hg)	89 ± 26	87 ± 17	91 ± 19	89 ± 21
TG (mg/dl)	167 ± 14 *	120 ± 10	173 ± 11	178 ± 9
TC (mg/dl)	185 ± 7	190 ± 12	189 ± 9	185 ± 11
LDL (mg/dl)	110 ± 8	114 ± 9	113 ± 11	110 ± 9
HDL (mg/dl)	43 ± 0.92	45 ± 1.56	44 ± 1.02	43 ± 0.96
TH / HDL	3.88 ± 0.33 *	2.67 ± 0.21	3.93 ± 0.19	4.13 ± 0.28
HR (bpm)	77 ± 2 *	66 ± 2	79 ± 3	81 ± 2
Ghrelin (Pg/ml)	57 ± 2.16 *	46 ± 1.61	55 ± 3.11	57 ± 2.14

Values are expressed as mean ± SE.
* represent significant changes by intervention.
Definition of abbreviations. WC indicates waist circumference, HC= Hip circumference, WHR= Waist-hip ratio, BMI= Body mass index, BF = Body fat percentage, BP= Blood pressure, TG= Triglyceride, TC= Total cholesterol, LDL= low-density lipoprotein, HDL= High-density lipoprotein, TH/HDL= Triglyceride to High-density lipoprotein, HR= Heart rate

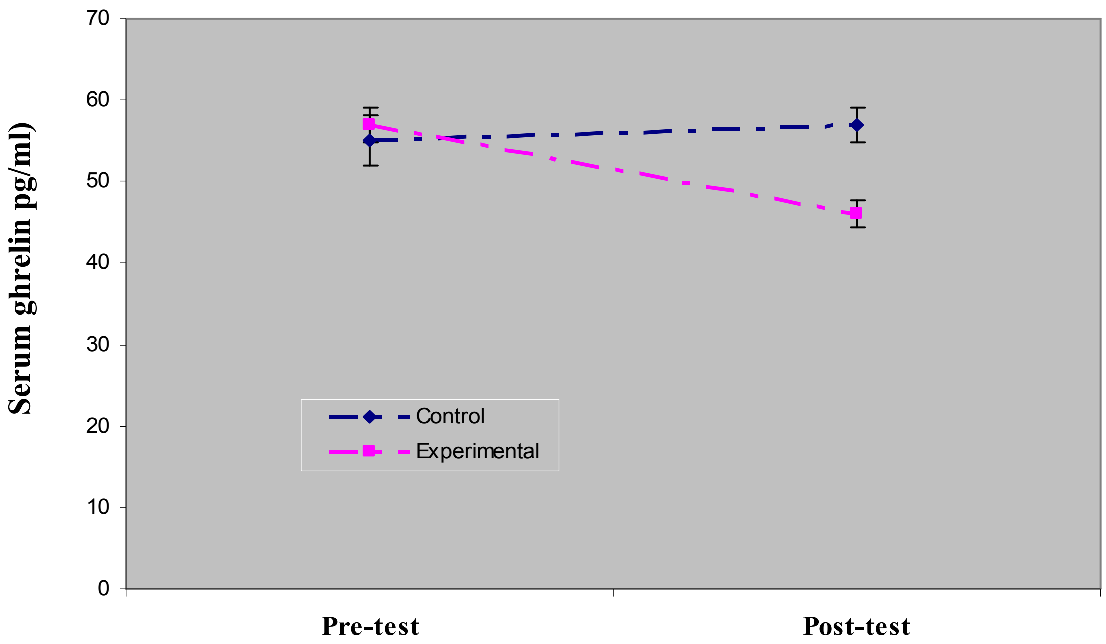

Figure 1: The changes pattern of serum ghrelin concentration in control and experimental groups. Aerobic exercise leads to a significant reduction in serum ghrelin (p = 0.002) experimental group whereas its concentration did not change in control group

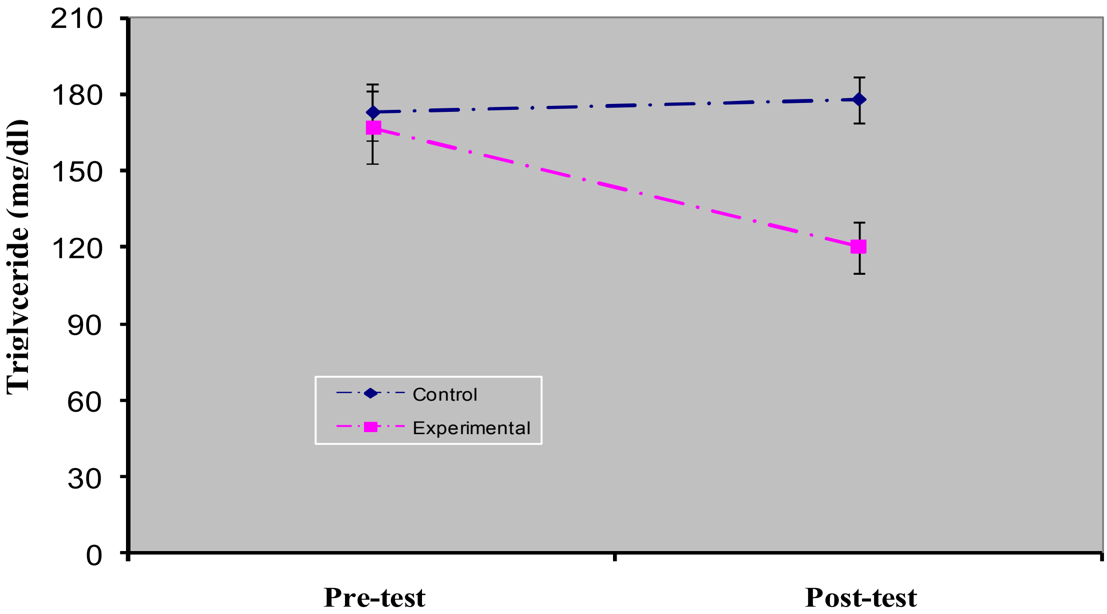

Figure 2: The changes pattern of triglyceride concentration by intervention in control and experimental groups. Aerobic exercise leads to significant decrease in triglyceride concentration in experimental group, while this variable remained without change in control group

Our study showed that 19% reduction in serum ghrelin is associated decreased body weight and anthropometric indices in the studied subjects. In this regard, Wang et al based their findings suggest that reduced ghrelin levels in the hypothalamus due to long-term exercise training leads to decreased appetite and body weight [18]. But a recent study has emphasized the independence of blood ghrelin of factors such as age and BMI and the fact states that that levels of blood ghrelin is independent of BMI and age [28]. In this study, a significant reduction in serum ghrelin was associated with significant reduction in triglyceride concentration and the Triglyceride to High-density lipoprotein ratio (TG / HDL). These findings point out that the decrease or increase in serum ghrelin is associated with similar changes in circulation triglyceride. In confirmation of these findings, some recent studies have revealed that ghrelin has an important role in the process of adipogenesis and energy reserves in fat tissue [8, 29, 30] and long-term consumption of ghrelin leads to increase in body fat reserves in humans and animals [8]. In this regards, some recent evidence has shown that ghrelin increase body fat, also independently of changes in food intake [8]. A specific effect of ghrelin on lipid metabolism was suggested by the observation that rodents treated with ghrelin showed enhanced fat content independently of feeding behavior, as assessed by magnetic resonance imaging (MRI), increased respiratory quotient (suggesting enhanced carbohydrates utilization and decreased fat utilization), dual energy x-ray absorptiometry (DEXA) and weight of omental and retroperitoneal fat pads [8,31,32]. In visceral adiposity, ghrelin increases Fat accumulation by increasing expression of adipogenic genes as acetyl-coA carboxylase [29]. Ghrelin injection, independently affects adipose tissue metabolism by inhibiting lipolysis enzymes [33], regulating adipogenesis [34, 35] and suppressing the release of noradrenaline in adipose tissue [36].

CONCLUSION

In summary, based on this data, it was concluded that chronic aerobic exercise training associated with reduced body weight leads to decreased serum ghrelin in obese individuals and supports the role of exercise as a non-pharmacologic treatment in regulating and balancing peptide hormones effective in prevalence of obesity. Despite the findings of this and other previous studies, identifying the specific mechanisms responsible for interaction of ghrelin and obesity and the role of physical activity on them necessitates conducting further studies in this field.

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Conflict of interest

The authors declare that they have no Conflict of Interests.

