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ORGINAL ARTICLE

# The Effect of Eight Weeks Moderate Intensity Aerobic Training on Obestatin and Ghrelin of Obese Male Rats

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**Abstract**
Aim of present research was to review the probability changes in ghrelin and obestatin hormones following eight weeks aerobic training with moderate intensity in Sprague–Dawley male rats. For this purpose randomly selected 47 two month age rats from animal lab. All rats made fat by stimulate the appetite with lettuce and vegetables and reached from mean weight 240±15 to 320±20 kg and after that randomly divided to two groups (control=23 and training=24). The training program of training group included eight weeks running on rodent specific treadmill; in parallel control group in this period of the time had no training. At the end for review the research variables, blood samples collected directly from the heart. For statistic analysis of data used independent t test. Findings showed that eight weeks moderate intensity aerobic training made significant reduction in obestatin (p=000); also this training had no significant effect on ghrelin (p=0/99). Regard to findings of research it conclude that eight weeks moderate intensity aerobic training can induces reduction in obestatin nevertheless does not affect ghrelin.

**Key words:** Obestatin, Ghrelin, Aerobic Training

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## Introduction

Overweight and obesity have known as important factor of mortality in world (Aydin et al., 2008). In order to intensity of obesity in both men and women, the risk of disease such as arthritis, lung disease, type 2 diabetes, hypertension, hyperlipidemia, coronary artery disease, heart abnormality and cancer would rise and so, fat or overweight people may lose their life expectancy (Zhao et al., 2008; Fontenot et al., 2007). Overweight and obesity are the symbols of chronic imbalance between input and output energy. In past the central nerve system specifically hypothalamus with complex functional process, were single center of energy balance; but with improve human knowledge, the effect of Superahypothalamus factors and their consistent relationship in balance and regulation of energy more appeared (Gourcerol et al., 2007). In recent years regard to different research and importance of weight controlling, appetite and improve knowledge in this filed, new information reported. As example researchers found that fat tissue, skeletal muscle and liver act like endocrine organs and contribute in energy homeostasis with secretion of some hormones (Fontenot et al., 2007). Although role of central factors in regulation of energy balance has more importance, but different studies have shown that peripheral massages (such as intake and consumption of energy) from different body tissues have significant effects on homeostatic control (Zhao et al., 2008; Green et al., 2007). With explore of peptides which secrete from digestive system, made role of this organ in energy balance important and stomach like fat tissue, muscle and liver has known as an effective endocrine organ on energy balance. From hormones secreted from stomach can point to obestatin and ghrelin. Obestatin is a factor that secrete from fundus of stomach. It seems that obestatin has important role in regulation of food intake and body weight (Zhang et al., 2005). This hormone is a 23 amino acid peptide that produces with common gene of ghrelin. Some researchers believe that this hormone prohibits appetite and raises body weight and also by interaction with receptor of $GPR_{39}$ obstructs movement of small intestine (Tang et al., 2008). Probability intra intestinal injection of obestatin (regard to dose) reduces or stops the absorption of food (Ghanbari-Niaki et l., 2008; Ivy et al 1928) regard to this issue in some researches (in rats) have reviewed the role and biological activity of obestatin in energy balance (Ghanbari-Niaki et al., 2008). Other hormone that has role in energy balance is ghrelin that main source of this appetite peptide is stomach and more than 70 percentage of circulating ghrelin is due to stomach. By explore of ghrelin it observed that this substance affects appetite, body weight and body composition that all of these items help regulation of energy balance (Ghanbari-Niaki et al., 2006). Studies have shown that ghrelin reduces in obesity, rises in Anorexia nervosa patients and also modifies by rise and reduction in body weight (Fathi et al., 2010). Regard to this issue that energy balance has specific importance in exercise and regard to role of these two hormones in body energy balance, metabolism and wellness of people, it seems that study the effect of exercise on obestatin and ghrelin in obese subject is helpful. In a research examined the effect of six weeks running on total intestinal and fundus obestatin that findings of this research showed that total intestinal and fundus obestatin reduce significantly in trained rats (Ghanbari-Niaki et l., 2008). In contrast, in a study that reviewed the effect of eight weeks running on treadmill, plasma obestatin levels in obese rats did not change significantly (Wang et al., 2008). In the other hand Reinehr et al reviewed the effect of one year controlling regimen and physical activity on serum obestatin of obese children with mean age 11/2 year. Before start of research obestatin in experimental group was higher than control group but at the end of research and follow weight loss in experimental group, obestatin levels raised (Reinehr et al., 2008). Furthermore can point to research of Ghanbari-Niaki et al, these researchers examined the effects of a single bout of circuit resistance exercise on plasma glucose, ghrelin ,GH, and c-peptide, and cortisol in male college students. Plasma ghrelin showed a significant decrease immediately after the exercise and increased significantly 24-hfollowing the exercise (Ghanbari-Niaki et al., 2006). Also Ebal et al reviewed the effect of five weeks resistance training on serum ghrelin levels of rats and saw resistance training induces 4/6 percent weight loss and significant reduction in serum ghrelin levels (Ebal et al., 2007). Regard to noted issues and different responses of these hormones (obestatin and ghrelin) to exercise and their importance in energy homeostasis, in present study researchers want to examined dose moderate intensity aerobic training affect obestatin and ghrelin of obese male rats?

**Methods**

In this experimental study 47 Sprague–Dawley male rats randomly selected from animal lab. Objects in all period of study had free access to water and food. All rats made fat by stimulate the appetite with lettuce and vegetables and reached from mean weight 240±15 to 320±20 kg and after that randomly divided to two groups (control=23 and training=24). The training group for familiarity with treadmill ran on treadmill tree sessions in one week by speed of 10 mph for 10 minutes. Program of training group included eight weeks running on rodent specific treadmill (table 1); in parallel control group in this period of the time had no training. 24 hours after latest training session, all rats had fainted by mixed of ketamine and xylozin and for review obestatin and ghrelin, blood samples collected directly from the heart. For measure obestatin and ghrelin used CBS-E13642r, Eliza Rat Kit, produce by U.S.A and Mitsubishi Kagaku Iatron, Eliza Rat Kit, produced by Japan respectively. For statistical analysis of finding used independent t test ($p \leq 0/05$).

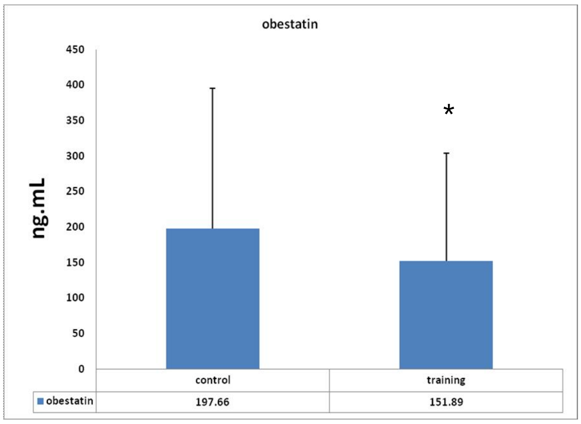
**Results**

Results of independent t test showed that eight weeks aerobic training has significant effect on reduction of obestatin ($t(45) = -5/29$, $p \leq 0/000$) (fig 1) and eight weeks aerobic training has no significant effect on ghrelin ($t(45) = -0/005$, $p \leq 0/99$) (fig2).



**Tab 1. moderate intensity aerobic training program**

| | Speed (meter per minute) | Time (minute) | Slop (grade) |
|---|---|---|---|
| First week | 10-12 | 10 | 0 |
| Second week | 10-12 | 20 | 0 |
| Third week | 18-20 | 20 | 0 |
| Fourth week | 18-20 | 30 | 0 |
| Fifth week | 18-20 | 50 | 0 |
| Sixth week | 18-20 | 50 | 0 |
| Seventh week | 18-20 | 50 | 0 |
| Eighth week | 18-20 | 50 | 0 |




* Significant reduction, p≤0/05
Fig1. Obestatin in training and control groups

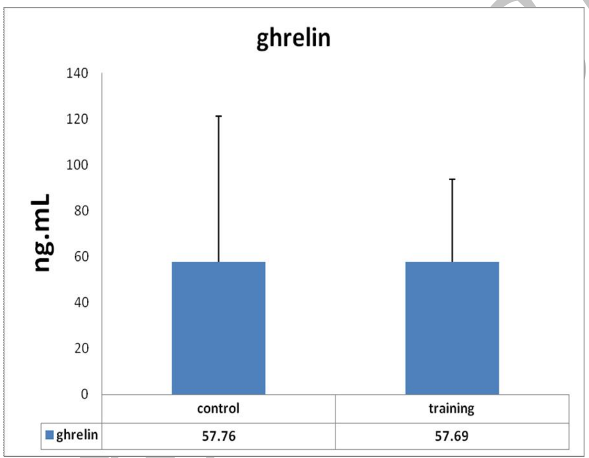



Fig2. Ghrelin in training and control groups

**Discussion and Conclusion**

Findings of this study showed that eight weeks moderate intensity aerobic training makes significant reduction in obestatin. In this research it clears that obestatin in training group reduced 20 percent than control group. Also changes in weight of rats during research were another important issue in present study. Weight of rats at beginning of training program raised approximately 33 percent (one month overweight period) but at the end of training program weight of rats reduced approximately 30 percent. When this process of changes in weight compare with changes of obestatin hormone, can observe significant and direct relationship. Although energy balance and regulation seem simple but they have complex processes. Weight loss or weight gain that are due to imbalance of energy, are simple indexes for recognizing of energy imbalance (Woods et al., 2004). Obestatin has essential role in energy homeostasis so that reduces appetite and as a result weight loss. Noted hormone by inhibit activity of geogenum of digestive system, sends a message via vagus nerve to center of food intake and makes full sense in central nerve system (Ivy et al., 1928). In current research reduction in obestatin in obese rats is a portion of negative feedback for inhibit of appetite and body weight. Researches show that obestatin levels change due to reduction of daily energy intake via food restriction or via raise in energy expenditure following exercise but these processes are different. Findings of researches indicate that obestatin hormone raises follow food restriction and have reported that reason of this issue is exercise. Exercise induces reduction in hungry and rises in full sense; because break down of storage food sources during exercise happens faster than food restriction and postpone hungry sense (Reinehr et al., 2008, Woods et al., 2004; Ziou et al., 2009; Borer et al., 2007; Saghebjoo et al., 2009). Also researches show that intense and long duration trainings induce rise in glycogen breakdown and make oxygen deficit and also after such these trainings protein production postpones and glycogen remakes and this issue changes energy homeostasis (change in levels of energy homeostasis related hormones) (Ghanbari-Niaki et al., 2008; Ivy et al., 1928; Wang et al., 2008; Reinehr et al., 2008; Woods et al., 2004; Ziou et al., 2009; Borer et al., 2007; Saghebjoo et al., 2009). Some researchers have reported that when training program is concluding heavy and resistance training, this reduction is more significant. As example Saghebjoo et al (training includes five weeks resistance training, four days per week and one session per day) have found that resistance training with intensity of 80 percent of 1 RM induces significant reduction in plasma obestatin (Saghebjoo et al., 2009). Heavy activity induces muscular damage and disorder in glycogen remake after exercise. Reviews have shown that insulin induced rise in uptake and transport of glucose by muscle has positive correlation with content of glucose transporter protein (GLUT4) and it has been clear that muscle content of GLUT4 has direct relationship with muscular glycogen levels. So disorder in muscular glycogen remake after intense contractions maybe due to muscular damage induced reduction of GLUT4 content (Ziou et al., 2009; Borer et al., 2007; Saghebjoo et al., 2009). It seems that in present research because of damage in muscular fiber and delay in glycogen storage remake, training may have induced negative energy balance and in response to it, obestatin have more reduced so that body can compensates its lost energy storage. Here should attention to this issue that would we get these findings after acute training or no? Findings of researches that use acute training programs show that the answer of this question is negative. Manshouri et al reviewed plasma obestatin level in response to anaerobic acute training and saw plasma obestatin levels after 24 hours, 48 hours and follow seven days recovery period did not change (Manshouri et al., 2008). In another study, Wang et al after 40 minutes running on treadmill by incline of five degrees and speed of 20 meter per minute measured obestatin levels of obese rats and did not find significant changes in noted hormone (Wang et al., 2008). Ziou et al showed that 2 hours intestinal/stomach electrical stimulation of rats has no effect on obestatin and they said this process is not suitable method for stimulation of obestatin (Ziou et al., 2009). Also findings of Ghanbari-Niaki., study showed that a single circuit-resistance exercise has no effect on plasma obestatin levels (Ghanbari-Niaki et al., 2008). For interpretation of these findings, noted researchers have expressed that acute exercise does not induce reduction in serum glucose and triglyceride immediately after exercise and there is this probability that obese subjects awhile after exercise can stimulate their extra body energy (nevertheless in log duration training program situation is different). Furthermore by compare the results of present study with other researches it clears that changes of obestatin hormone are depend on duration of training in per session. In present research duration of per training session were 50 minutes that induces significant reduction in obestatin but in some researches that duration of training were less than our research (less than 40 minutes) levels of obestatin hormone did not significant change. As example in a study, researchers expressed that when obese rats run 40 minutes per session for eight weeks, plasma obestatin levels do not change significantly. These researchers expressed that cause of this result can be due to less duration of training per session (Wang et al., 2008). Finally can say follow weight reduction during training program, energy balance fluctuates and maybe body reduces levels of obestatin hormone for manage this negative energy balance. On the other hand findings of present research showed that eight weeks moderate intensity aerobic training has no significant effect on ghrelin. Ghrelin is an appetite peptide that has important and key role in regulation of energy balance. About this hormone and exercise have done some studies. These studies have conflict findings about ghrelin responses to exercise. For example Foster et al reviewed effect of 12 months aerobic exercise in 173 overweight women and reported that serum ghrelin levels raised 18 percent in people who had more than 3 kg weight loss (Foster et al., 2004). Also Ebal et al examined effect of 5 weeks resistance training on serum ghrelin levels in rats and reported that this training program can induces 4/6 percent weight loss and significant reduction in serum ghrelin levels (Ebal et al., 2007). On study of Fathi et al serum ghrelin of rats raised follow fasting (Fathi et al., 2010). Some researchers reported that high volume low intensity training protocols affect appetite, energy balance and body weight via change in key hormones which regulate energy balance (Karamouzis et al., 2002). Another mechanism can point about serum ghrelin is energy metabolism regulation. Reviews show that long duration exercises are along with depletion of liver and muscle ATP and glycogen (Li et al 2003). Training and exercise change intracellular energy balance and homeostasis of muscle and also raise energy needs of cell. It reported that long duration exercise with intensity of 60-90 $VO_{2max}$ especially if repeated for one or some weeks, induces reduction and depletion in cell energy storages (included ATP and glycogen). Ghanbari-Niaki et al reported that six weeks low to moderate intensity exercise induces reduction in total levels of plasma and soleus muscle ghrelin in rats (Ghanbari-Niaki et al., 2006). Nevertheless there are information that certainly indicate that exercise stops the ghrelin circulation so that this issue induces reduction in food intake (Kraemer et al., 2007). It has been reported that ghrelin in overweight and obese subjects raises during long duration exercises (Foster et al., 2004). Study of Fathi et al showed that endurance running on treadmill induces raise in ghrelin gene expression in skeletal muscle and raise of serum ghrelin levels in rats (Fathi et al., 2010). Indeed regard to training intensity and also sequences of training days in one hand and shortening of time of latest training session and rats killing in another hand, that probability postpones complete recovery of muscle energy storages, it expected that if training would have less volume or intensity or time between latest training session and rats killing would be high, would see different responses of ghrelin. For example one session running on treadmill with intensity of 50 and 75 percent of $VO_{2max}$ for 3 minutes and one minute running with intensity of 90 percent of $VO_{2max}$ did not change plasma ghrelin levels (Dietz et al., 2004). Furthermore it has been cleared that submaximal aerobic training has no relationship with changes of circulating ghrelin concentration (Kraemer et al., 2007). In reverse, continued energy restriction in obese people or athletes who use high portion of their body muscles and in athletes who have less body fat mass, induces rise in ghrelin concentration, nevertheless its mechanism is not clear.

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