International Journal of Biosciences | IJB |
ISSN: 2220-6655 (Print) 2222-5234 (Online)
http://www.innspub.net
Vol. 4, No. 4, p. 150-155, 2014

RESEARCH PAPER OPEN ACCESS

Polypeptide hormone ghrelin is decreased in response to long term aerobic training in those with type II diabetes

Masoud Moeini*, **Ali Jalalvand, Javad Almasi, Naser Farokhroo**

Department of Physical Education and Sport Sciences, Hamedan Branch, Islamic Azad University, Hamedan, Iran

Key words: Type II diabetes, ghrelin, exercise program.

http://dx.doi.org/10.12692/ijb/4.4.150-155 Article published on February 20, 2014

Abstract

Ghrelin is the most recently identified adipocytokine, but their role in tye II diabetes is not completely understood. In present study, we investigated effects of aerobic training program on plasma ghrelin in patients with type 2 diabetes mellitus (T2DM). For this purpose, anthropometrical markers and fasting plasma ghrelin were measured before and after an aerobic exercise program for three months in adult men with type II diabetes. Data were analyzed by computer using SPSS software version 15.0. Aerobic exercise program resulted significant decrease in plasma ghrelin when compared with baseline levels. All anthropometrical markers such as weight and body mass index were also decreased after exercise program. There was no significant relation between plasma ghrelin with anthropometrical markers after exercise program. Based on these data, we conclude that long term aerobic training is associated with decreased ghrelin in those with type II diabetes.

* **Corresponding Author:** Masoud Moeini ✉ masoud_moinysep@yahoo.com

Introduction

In 1997 the number of diabetics in the world was reported 125 million. However, as predicted by the World Health Organization the number will increase to 300 millions in 2025. Several studies have shown that obesity has a potential role in the pathogenesis of Type-2 diabetes, particularly in those who are genetically predisposed to the disease. Adipose tissue and other secreting tissues of the body secrete certain adipocytokines and peptide mediators the secretion disorder of which impairs such factors as controlling appetite, energy balance, insulin sensitivity, energy metabolism and homeostasis which all contribute to the incidence of obesity and its related diseases such as diabetes, hypertension, asthma, and inflammatory diseases (Boulet, 2008).

Among these peptide mediators, ghrelin is a hormone affecting hunger and long-term regulation of body weight (Rotsides *et al.*, 2009).The plasma levels of this 28-aminoacid peptide hormone increase shortly before meals and decrease after meals (Kriketos *et al.*, 2004). Although the effect of ghrelin on insulin secretion and changes in blood glucose concentration in humans is not yet fully understood, clinical studies support the role of this peptide hormone in regulating glucose metabolism and energy balance (Tong *et al.*, 2010). Some studies have also suggested that consumption of ghrelin in healthy humans leads to increased blood glucose and have pointed to a significant positive relationship between these two variables (Broglio *et al.*, 2004). Recent studies suggest that ghrelin plays an important role in glucose homeostasis, particularly in diabetic patients (Ariga *et al.*, 2008; Korbonits *et al.*, 2004).

The role of exercise as a non-therapeutic agent in the regulation of appetite, energy balance and weight control has been the focus of a large number of researches and clinical studies. The relationship between physical activity and fluctuations in plasma concentrations of this hormone in obese or overweighed as well as diabetics is not yet fully determined and the results are still contradictory. Some of these studies suggest decreased plasma ghrelin levels caused by exercise or exercise-induced weight loss (Malkova *et al.*, 2008; Broom *et al.*, 2007; Robert *et al.*, 2007) and some other studies report increased plasma concentrations of this hormone as a result of exercise (Kelishadi *et al.*, 2008). Also some other studies deny any effect of exercise on this peptide hormone (Schmidt *et al.*, 2004; Nitsche *et al.*, 2007). The probable reason could be the differences in the duration, intensity and frequency of physical activity in each study. This study aims to explore the effects of three months of aerobic exercise on plasma levels of this hormone in obese or overweighed diabetics (BMI ≥ 26).

Method and subjects

Participants

In this study, twenty four sedentary, non-trained adult obese men with type II diabetes aged 40-48 year and body mass index 30-36 kg/m2 were recruited through an accessible sampling in and randomly divided into exercise (three months aerobic training) and control (no training) groups. The aim on this study was investigation the effect of mentioned exercise program on plasma ghrelin. An informed consent was obtained from all participants before the studies were carried out.

Inclusion and exclusion criteria

Inclusion criteria to study were body mass index higher than 30 kg/m2 for two groups and existing type II diabetes for at least 3 years. Subjects of two groups were reported to be non-smokers and non-athletes. Neither the control nor exercise subjects had participated in regular exercise for the preceding 6 months, nor did all subjects have stable body weight. The exclusion criteria were as follows: Patients with known history of acute or chronic respiratory infections, neuromuscular disease, cardiopulmonary disease and those who orthopedic disorders. Those that were unable to avoid taking hypoglycemic drugs or insulin sensitivity-altering drugs for 12 hours before blood sampling were excluded.

Anthropometric and hormone measuring

Plasma ghrelin and anthropometric measurements of height, weight and circumference measurements were taken pre- and post-exercise training. Abdominal circumference and hip circumference were measured in the most condensed part using a non-elastic cloth meter. Body weight was measured in duplicate in the morning following a 12-h fast. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m). Height was measured on standing while the shoulders were tangent with the wall.

To compare of circulating levels ghrelin between pre and post training, blood samples were collected of all participant after a overnight fast at before and 48 hours after exercise program. Samples were centrifuged immediately for 10 minutes with 3500 rpm in +4°C in order to measure serum ghrelin levels. The intra-assay and inter-assay coefficient of variation of ghrelin (Biovendor, Austria) were 8.10% and 8.3% respectively.

Exercise program: all subjects of exercise group were completed an aerobic training for 3 months (3 days/wk) 60 to 80 percent of maximum heart rate. Each session started with 10-15 min flexibility exercises, 30-40 min of aerobic exercise involved running and pedaling on stationary cycle and 5–10 min of cool down activity.. 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.

Statistical analysis

The Kolmogorov-Smirnov test was applied to determine the variables with normal distribution. Statistical analysis was performed with the SPSS software version 15.0 using an independent paired t-test. Pair-wise correlations between plasma ghrelin with anthropometrical markers were assessed by Pearson's partial correlation coefficients.

Results

Baseline and post training ghrelin levels and anthropometrical markers of exercise and control groups are shown in Table 1. The data were reported as mean and standard deviation. At baseline, there were not differences in all anthropometrical characteristics between two groups. Plasma ghrelin levels were similar in two groups at baseline. Data of statistical analysis showed that aerobic training program is associated with decreased significantly in plasma ghrelin when compared with baseline ($p = 0.008$, Fig 1). Anthropometrical markers such as body weight (0.000), BMI (0.001), abdominal obesity (0.002) were decreased by exercise program in exercise group. No changes were observed in all variables in control group. We did not a significant correlation between the change in plasma ghrelin with BMI by exercise training in exercise groups ($p = 0.92$, $r = 0.032$, Fig 2).

Table 1. Mean and standard deviation of anthropometrical and spirometric markers and VO2max before and after intervention in studied groups.

Variables	Control diabetic		Exercise diabetic	
	Pretest	post-test	Pretest	post-test
Age (year)	44.08 ± 5.6	44.08 ± 5.6	45.3 ± 4.2	45.3 ± 4.2
Height (cm)	173.3 ± 5.14	173.3 ± 5.14	174.1 ± 4.3	174.1 ± 4.3
Weight (kg)	92.25 ± 7.77	88 ± 8.73	93.7 ± 6.11	92.4 ± 5.63
Waist circumference (cm)	104.7 ± 7.25	101.3 ± 7.4	103.8 ± 6.33	104.1 ± 5.3
BMI (kg/m2)	30.67 ± 2.64	29.33 ± 30.3	30.91 ± 3.3	30.48 ± 2.4
Plasma ghrelin (pg/ml)	60.3 ± 9.11	46.6 ± 12	58.3 ± 7.9	61.52 ± 6.8

Discussion

Although the incidence of type-1 and Type-2 diabetes worldwide is expected to increase, the rate of increase in Type-2 diabetes seems to be higher due to changed lifestyle and reduced physical activity resulting in increasing prevalence of obesity (Powers *et al.*, 2001; King *et al.*, 2005). Research findings on short or long-term effects of exercise on levels of peptide hormones, including serum ghrelin in healthy populations or patients, obese or lean, athletes or non-athletes, are more or less contradictory and so far there has been no overall consensus in this regard. However, in this study, a three-month aerobic exercise led to a significant decrease in ghrelin levels in Type-2 diabetic patients. A three-month aerobic exercise program three times a week with intensity of 60 to 85% Vo2Max led to a significant reduction in serum levels of this peptide hormone.

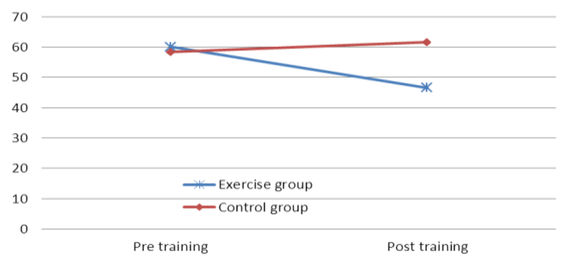

Fig. 1. Plasma ghrelin level at pre and post training in exercise and control groups of diabetic patients.

Obesity-related lifestyle changes, eating behavior and physical activity play a key role in the prevention and treatment of Type-2 diabetes. Research studies indicate the role of exercise-induced weight loss on regulating peptide hormones involved in obesity and the related chronic diseases such as diabetes. The positive role of exercise in energy balance through such other adipocytokines as leptin, adiponectin and resistin has been proven many times (Tajima *et al.*, 2005; Reinehr *et al.*, 2005).

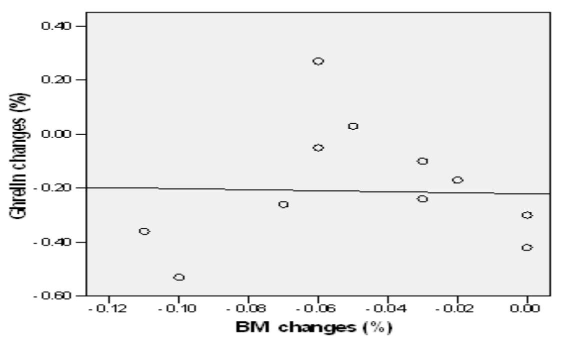

Fig. 2. correlation pattern between the changes in ghrelin and BMI by aerobic program in exercise group.

Although the three-month aerobic exercise in this study led to a significant reduction in ghrelin, another study has reported a significant increase of plasma ghrelin following a long-term exercise program which was associated with weight loss (Kelishadi *et al.*, 2008). In another study, a 12-week training program led to a significant increase in ghrelin levels (Kim *et al.*, 2008). Contrary to the findings of the said study and confirming those of this study, in another study, four weeks of exercise led to a significant reduction in ghrelin levels (Vestergaard *et al.*, 2007). In this context, some studies suggest that if a long-term exercise or diet programs are not accompanied by a significant reduction in body weight they lead to no change in insulin resistance, insulin, ghrelin and other peptide hormones (Reinehr *et al.*, 2008). In a recent study, however, a one-year weight-loss program associated with significant changes in such variables as insulin, insulin resistance and leptin and increased adiponectin levels did not result in significant changes in ghrelin levels (a 4% increase) (Reinehr *et al.*, 2005). Also, in another study, weight loss induced by the combination of diet and exercise was associated with increased obestatin and a significant reduction in leptin and unchanged ghrelin concentrations in obese subjects (Reinehr *et al.*, 2008).

In this study, the training program led to a significant reduction of each of the anthropometric indices in subject diabetics. Hence, decreased ghrelin levels may be attributed to the reduction of body fat in these patients. Furthermore, a linear relationship between changes in ghrelin and changes in the said anthropometric indices was observed but it was statistically insignificant. It is likely that the lack of a significant relationship between changes in ghrelin and changes in other variables due to a three-month exercise is due to small sample size of the study. It is also possible that changes in the levels of anthropometric indices affect secretion of ghrelin levels in the subjects not directly but indirectly by affecting other peptide mediators.

References

Ariga H, Imai K, Chen C, Mantyh C, Pappas TN, Takahashi T. 2008. Does ghrelin explain accelerated gastric emptying in the early stages of

diabetes mellitus? American Journal of Physiology - Regulatory, Integrative and Comparative Physiology **294(6),** 1807-12.
http://dx.doi.org/10.1152/ajpregu.00785.2007

Boulet LP. 2008. Influence of obesity on the prevalence and clinical features of asthma. Clinical & Investigative Medicine **31(6),** 386-90.

Broglio F, Gianotti L, Destefanis S, Fassino S, Abbate Daga G, Mondelli V. 2004. The endocrine response to acute ghrelin administration is blunted in patients with anorexia nervosa, a ghrelin hypersecretory state. Clinical endocrinology (Oxford) **60,** 592-599.
http://dx.doi.org/10.1111/j.1365-2265.2004.02011.x

Broom DR, Stensel Dj, Bishop NC, Burns SF, Miyashita M. 2007. Exercise-induced suppression of acylated ghrelin in humans. Journal of Applied Physiology **102,** 2165-2171.
http://dx.doi.org/10.1152/japplphysiol.00759.2006

Kelishadi R, Hashemipour M, Mohammadifard N, Alikhassy H, Adeli K. 2008. Short- and long-term relationships of serum ghrelin with changes in body composition and the metabolic syndrome in prepubescent obese children following two different weight loss programs. Clinical endocrinology (Oxford) [Epub ahead of print].

Kim HJ, Lee S, Kim TW, Kim HH, Jeon TY, Yoon YS. 2008. Effects of exercise-induced weight loss on acylated and unacylated ghrelin in overweight children. Clinical endocrinology (Oxford) **68(3),** 416-22.

King H, Aubert RE, Herman WH. 1998. Global burden of diabetes 1995-2005: prevalance numerical estimates and projections. Diabetes care **21,** 1414.
http://dx.doi.org/10.2337/diacare.21.9.1414

Korbonits M, Grossman AB. 2004. Ghrelin: update on a novel hormonal system. European Journal of Endocrinology **151(Suppl 1),** 67–70.
http://dx.doi.org/10.1530/eje.0.151S067

Kriketos AD, Gan SK, PoyntenAM, Furler SM, ChisholmDJ, Campbell LV. 2004. Exercise increases adiponectin levels and insulin sensitivity in humans. Diabetes Care **27,** 629–630.
http://dx.doi.org/10.2337/diacare.27.2.629

Malkova D, McLaughlin R, Manthou E, Wallace AM, Nimmo MA. 2008. Effect of Moderate-intensity Exercise Session on Preprandial and Postprandial Responses of Circulating Ghrelin and Appetite. Hormone Metabolic Research Journal [Epub ahead of print].

Nitsche H, Nitsche M, Sudi K, Tschop M, Zotter H, Weinhand G. 2007. Ghrelin--an indicator for fat oxidation in obese children and adolescents during a weight reduction program. Journal of Pediatric Endocrinology and Metabolism **20(6),** 719-23.
http://dx.doi.org/10.1515/JPEM.2007.20.6.719

Powers AC, Diabetes Mellitus, In:Braunwald E, Fauci AS,Kasper DL, Haunser SL, Longo DL, Jameson JL. 2001. Harrison's, Principles of Internal Medicin 15th ed. USA: McGraw Hill **2,** 2109-38.

Reinehr T, De Sousa G, Roth CL. 2008. Obestatin and ghrelin levels in obese children and adolescents before and after reduction of overweight. : Clinical endocrinology (Oxford) **68(2),** 304-10.

Reinehr T, Roth CL, Alexy U, Kersting M, Kiess W, Andler W. 2005. Ghrelin levels before and after reduction of overweight due to a low-fat high-carbohydrate diet in obese children and adolescents. International Journal of Obesity (London) **29(4),** 362-8.
http://dx.doi.org/10.1038/sj.ijo.0802913

Reinehr T, Roth CL, Alexy U, Kersting M, Kiess W, Andler W. 2005. Ghrelin levels before and after reduction of overweight due to a low-fat high-carbohydrate diet in obese children and adolescents. International Journal of Obesity (London) **29(4),** 362-8. http://dx.doi.org/10.1038/sj.ijo.0802913

Robert R, Daniel C. 2007. Exercise and Humoral Mediators of Peripheral Energy Balance: Ghrelin and Adiponectin. Experimental Biology and Medicine **232,** 184-194.

Rotsides DZ, Goldstein IF, Canfield SM, Perzanowski M, Mellins RB, Hoepner L. 2009. Asthma, allergy, and IgE levels in NYC head start children. Respiratory Medicine **104(3),** 345-55. http://dx.doi.org/10.1016/j.rmed.2009.10.016

Schmidt A, Maier C, Schaller G, Nowotny P, Bayerle-Eder M, Buranyi B. 2004. Acute exercise has no effect on ghrelin plasma concentrations. Hormone Metabolic Research Journal **36(3),** 174-7. http://dx.doi.org/10.1055/s-2004-814342

Tajima D, Masaki T, Hidaka S, Kakuma T, Sakata T, Yoshimatsu H. 2005. Acute central infusion of leptin modulates fatty acid mobilization by affecting lipolysis and mRNA expression for uncoupling proteins. Experimental Biology and Medicine (Maywood) **230(3),** 200-6.

Tong J, Prigeon RL, Davis HW, Bidlingmaier M, Kahn SE, Cummings DE. 2010. Ghrelin suppresses glucose-stimulated insulin secretion and deteriorates glucose tolerance in healthy humans. Diabetes **59(9),** 2145-51. http://dx.doi.org/10.2337/db10-0504

Vestergaard ET, Dall R, Lange KH, Kjaer M, Christiansen JS, Jorgensen JO. 2007. The ghrelin response to exercise before and after growth hormone administration. Journal of Clinical Endocrinology & Metabolism **92(1),** 297-303. http://dx.doi.org/10.1210/jc.2006-1435