ORIGINAL ARTICLE

Serum Glucagon-Like Peptide-1 Changes in Women with Type 2 Diabetes Following a Four Weeks Aerobic Exercise

Mehrzad Shaabani[1], Farzaneh Abolfathi[1], Ali Akbar Alizadeh[1*]

1. Department of Exercise Physiology, Shahid Chamran University of Ahvaz (Islamic Republic of Iran), Ahvaz, Iran.

***Correspondence:**
Ali Akbar Alizadeh, Department of Exercise Physiology, Shahid Chamran University of Ahvaz (Islamic Republic of Iran), Ahvaz, Iran.
Tel: (98) 918 143 6507
Email: aliakbar.alizadeh1984@gmail.com

Received: 10 December 2016

Accepted: 08 February 2017

Published in March 2017

Abstract

Objective: The objective of this study was to investigate the effect of four weeks aerobic training on serum glucagon-like peptide-1 (GLP-1) in women with type 2 diabetes mellitus (T2DM).

Materials and Methods: Twenty T2DM patients (33-53 years) were randomly assigned into control (n=10) and experimental (n=10) groups. The main intervention included running on treadmill, reaching 55 to 80% of the maximum heart rate (five times by week) done for 30 minutes in the first session and increasing gradually to 60 minutes by the end of the fourth week.
Blood samples were collected before and after 4 weeks, and the concentrations of serum GLP-1 and insulin were determined using separate ELISA and the glucose concentrations was determined by biochemical methods.

Results Statistical analysis showed that after four weeks of aerobic training, the serum levels of GLP-1, glucose and insulin related to the experimental group had no significant difference in comparison with control group (P>0.05).

Conclusion: The results indicate that doing the aerobic training five times a week during four weeks with 55 to 80 percent of maximum heart rate has no effect on GLP-1 serum levels, glucose and insulin in T2DM women.

Keywords: Aerobic exercise, GLP-1, Type 2 diabetes.

Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disease in which the glucose, protein and fat metabolism is altered, and as a result, the plasma glucose levels are elevated. T2DM is also known as adult-onset diabetes, since it develops gradually (1). Eighty percent of T2DM patients are obese (2). The most important risk factors of T2DM development are obesity, genes, eating habits and sedentary life style (3). These factors are believed to affect the individual´s insulin resistance, blood glucose levels and eventually also the individual´s pancreatic β-cell function (3). Both insulin resistance and the pancreatic β-cell dysfunction are thought to be central factors for the development of T2DM (3).

Glucagon-like peptide-1 (GLP-1) is produced primarily by the intestine in response to caloric intake mainly from carbohydrates and fat. It increases insulin secretion in a glucose dependent manner, an effect that led to the development of GLP-1 mimetic compounds for the treatment of T2DM (4). GLP-1 plays a physiological regulatory role in controlling appetite and energy intake in humans (5) and animals (6). GLP-1 is considered as a therapeutic agent in the treatment of the hyperglycemia of T2DM because of its various biological effects, (7). In T2DM patients the incretin effect is either greatly impaired or absent which make these patients disable to adjust their insulin secretion to their needs. The secretion of GIP is generally normal in T2DM patients but the secretion of GLP-1 is reduced. The effect of GLP-1 is preserved whereas the effect of GIP is severely impaired (8).

Less is known about the response of other gut hormones to exercise. Recently the effect of exercise on the incretin hormones changes is considered (9). Acute exercise and aerobic training such as incretin GLP-1 secretion is affected. These findings suggest that exercise may be a physiological regulator to function or secretion of the incretin (10). Some researchers examined the effect of exercise on the levels of GLP-1. Yoda et al (11) reported that the levels of GLP-1& PPY increased after exercise. Insulin changes and improvement of insulin action following exercise may be due to modulation of incretin hormones (10). Exercise training produced GLP-1 L and alpha cells of the pancreas to the intestine which increase and improve insulin secretion (12). It is assumed that aerobic exercise causes increased secretion of GLP-1, Insulin and decrease glucose in diabetic patients. The aim of this study was to investigate the effect of 4 weeks aerobic training on serum GLP levels, Insulin and Glucose in T2DM women.

Materials and Methods

Twenty patients with T2DM among the woman admitted to Ahwaz Golestan hospital were selected by random sampling. They were between 33-53 years old. The inclusion criteria was, having blood glucose in the range of 140-250 mg/dl, not smoker and any other drugs addiction or medication, no particular disease such as cardiovascular, respiratory, kidney, and hypertension diseases, not insulin use and having no diabetes complications such as peripheral vascular disease and diabetic foot ulcers. The participants were randomly assigned into two groups, including aerobic exercise (n=10) and control (n=10). Before and after the main activity, anthropometric measurements (weight and height) and body composition (body mass index (BMI), body fat percentage) were done for each subject in the laboratory. Subject's fat percentage measured with bioelectrical impedances (BIA) made in South Korea using bioelectrical method.

Aerobic exercise protocols

The experimental group carried out the aerobic exercise five sessions a week for 4 weeks. These exercises included warm up, main training, and cool down. Subjects warmed up by stretching and jogging for 10 minutes. The main training included running on treadmill, reaching 55 to 80% of the maximum heart rate done for 30 minutes in the first session and increasing gradually to be 60 minutes by the end of the four week. Cooling down included the static stretching movements. The performance of the subject was controlled by a physical education expert and the heartbeat was constantly checked by the polar device, and control group remained sedentary in this period.

Blood sampling and laboratory measurements

Forty-eight hours before starting the exercise program, while all the subjects were fasten; 5 cc of blood was taken from their brachial vein. In order for preventing the data of being interrupted by the circadian rhythm of the hormone, all blood sampling were done from 8a.m to 9a.m. Also, 48 hours after finishing the 4-weeks exercise program, post-testing

blood sampling was done under the same conditions. All the samples were rapidly put in EDTA- containing tubes and kept in the refrigerator until they were centrifuged. Centrifuge was done at the gravity of 3000, temperature of -4◦ C, for 15 minutes, and the separated serum was kept at the temperature of -80◦ C. Serum GLP-1 was measured using ELISA kits (Mediagnost, Reuttlinger, Germany) for insulin. The intra- and inter assay coefficients of variation were respectively 3.9, 8.6% for GLP-1, and 3% and 5% for insulin. Also Serum glucose was measured (using glucose kit, Pars Azmoon Company, Iran with internal measurement degree of 1.28 and sensitivity degree of 5 mg/dl).

Statistical analysis

Normality of the data was tested using Shapiro-Wilk test and the equality of the variances of the groups in different factors was tested using leven's test. After being assured of the normality and equality of the groups, variance analysis test measuring was used to study the differences between the mean amounts. Statistic calculations of this study were done by the software SPSS, Ver.17. Significant change was accepted at *P*-value ≤0.05.

Results

Anthropometric and hormonal indicators of the subjects, before and after the training program are shown in table 1. After 4 weeks of aerobic exercises, the experiment group showed no significant decrease in weight and BMI.

Figure 1 to 3 demonstrated the plasma levels of GLP-1, glucose, and insulin in experimental and control groups before and after aerobic exercise. In control group there was no significant difference before and after exercise ($P<0.05$). However, in experimental group, insignificantly higher levels of GLP- and lower levels of glucose and insulin were found after as compared with before aerobic exercise ($P>0.05$).

Discussion

The aim of this study was to evaluate the effect of 4 weeks aerobic training on serum GLP-1 concentration changes in T2DM. Our findings revealed that after 4 weeks of aerobic training GLP-1 serum levels, glucose, insulin, body weight and BMI of the experimental group showed no significant change in comparison with the controls.

Toghi Eshghi et al (13) demonstrated effects of aerobic exercise with or without Metformin on Plasma incretins in T2DM. Our study showed that aerobic exercise did not acutely increase total GLP-1 and GIP levels in patients with T2DM. As opposed to previous studies in healthy participants (14,15), our study in T2DM patients did not observe an increase in GLP-1 concentrations after exercise. Most of the studies on the effect of physical activity on incretin hormones have been conducted with healthy subjects, athletes or obese participants (14,16).

Table 1. Anthropometric and hormonal indicators of the subjects, before and after the training program

Variable	Control group (mean ± SD)		Experimental group(mean ± SD)	
	Before	After	Before	After
Age	45.25±6.86	-	47.58±4.52	-
Height(cm)	157±5.29	-	156.92±8.45	-
Weight (kg)	68.84±0.80	69.48±1.07	66 ±3.35	65.71±2.99
BMI	26.86±1.36	27.74±1.34	27.06±1.62	27.83±1.33
GLP-1	49.72 ±1.58	58.25 ±1.65	64.58 ±4.01	77.38 ±10.9
Glucose	208. ±28.44	214.50±26.34	167.25±39.32	156.25±18.16
Insulin	0.62±0.24	0.48±0.42	0.77±0.48	0.43±0.16

* The results are showed in the form of mean ± standard deviation.

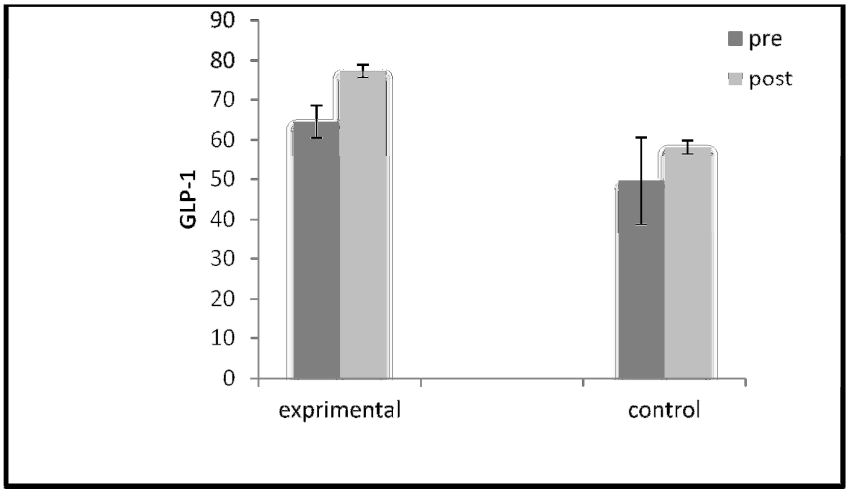

Figure 1. The GLP-1 changes in experiment and control groups

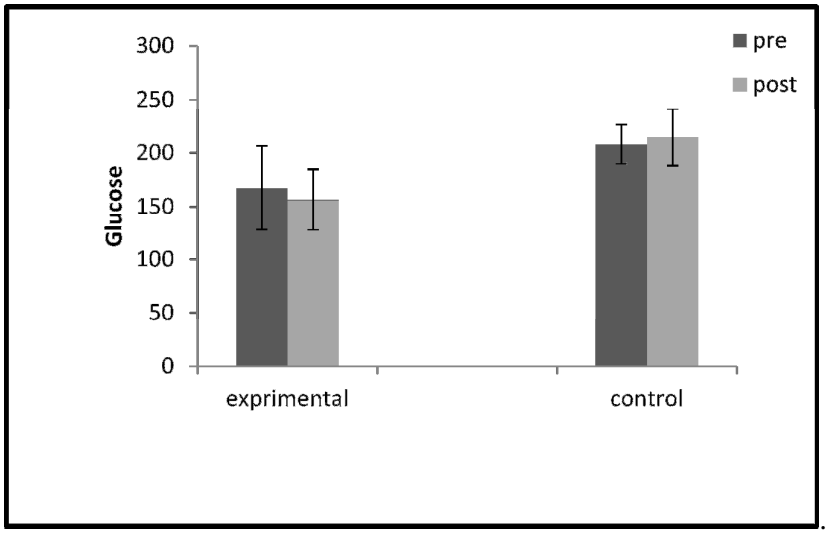

Figure 2. The glucose changes in experiment and control groups

O'Connor et al (14) showed prolonged exercise (running on a treadmill for 2 hours at 60% VO2max) with and without subsequent glucose ingestion can significantly increase GLP-1 and GIP levels in healthy people. GLP-1 concentration increased after a marathon and remained increased for at least 30 minutes (16). One-hour cycling on 65% maximum heart rate in 12 healthy normal weight volunteers increased GLP-1 as well. The GLP-1 levels began to increase during exercise and stayed higher than baseline after exercise (15). So, it is possible that there are no significant differences in serum GLP-1 levels in this study due to the study sample. Most of the GLP-1 studies are on the athletes and healthy people. Additionally, many studies have shown that a significant increase in serum GLP-1 levels following weight loss (17,18). But our present finding did not show significant differences in weight after 4 weeks regular exercise.

Our study exercise training program did not affect significant differences in serum GLP-1 levels. A further possible reason for not observing significant differences in serum GLP-1 levels is high intensity exercise training (19) which was not done in our study due to our study sample.

Our study has several limitations. First, we only studied female with T2DM. We could not

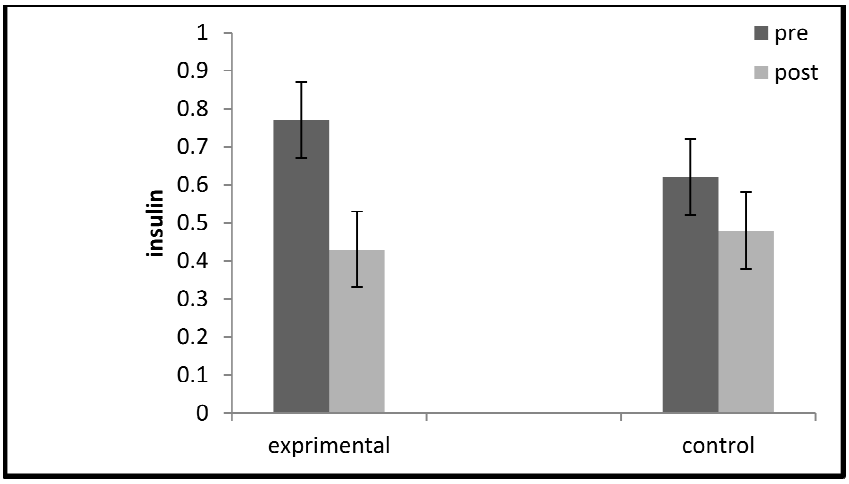

Figure 3. The insulin changes in experiment and control groups

rule out possible effects of gender on basal as well as on stimulated GLP-1 levels. Second, the exercise intervention was relatively short and no high intensity.

Conclusions

In summary, according to findings of other studies, it seems that evaluation of changes in serum GLP-1 levels need more studies with longer time follow up and greater number of subjects.

Acknowledgements

The authors of this paper wish to acknowledge all participations of this study.

References

1. Hall JE, Guyton AC. Guyton and Hall textbook of medical physiology. 12th ed. Philadelphia, PA: Saunders/Elsevier; 2011.
2. Pittas AG, Joseph NA.Greenberg AS. Clin Endocrinol Metab. 2004;89(2):447-52.
3. Agardh C, Berne C editors. Diabetes. 4th ed. Stockholm: Liber; 2010.
4. Meier JJ, Nauck, MA. Glucagon-like peptide 1(GLP-1) in biology and pathology. Diabetes Metab Res Rev. 2005;21:91-117.
5. Flint A, Raben A, Astrup A, Holst JJ. Glucagon-like peptide 1 promotes satiety and suppresses energy intake in humans. Clin Invest. 1998;101:515-20.
6. Tang-Christensen M, Larsen PJ, Goke RA, Fink-Jensen D, Jessop S, Moller M, et al. Central administration of GLP-1-(7-36) amide inhibits food and water intake in rats. Am. J. Physiol. 271 (Regulatory Integrative Comp. Physiol. 40) 1996;848-56.
7. Byrne MM, Goke B. Human studies with glucagon-likepeptide-1: potential of the gut hormone for clinical use. Diabet. Med.1996;13:854-60.
8. Vilsbøll T, Holst JJ. Incretins, insulin secretion and Type 2 diabetes mellitus. Diabetologia 2004;47:357-66.
9. Broom DR, Batterham RL, King JA, Stensel DJ. Influence of resistance and aerobic exercise on hunger, circulating levels of acylated ghrelin, and peptide YYin healthy males. Am J Physiol Regul Integr Comp Physiol. 2009:296,29-35.
10. Burmeister MA, Bracy DP, James FD, Holt RM, Ayala J, King EM, et al. Regulation of glucose kinetics during exercise by the glucagon-like peptide-1 receptor. J Physiol. 2012:590,5245-55.
11. Ueda S, Yoshikawa T, Katsura Y, Usui T, Nakao H, Fujimoto S. Changes in gut hormone levels and negative energy balance during aerobic exercise in obese young males. J Endocrinol. 2009:201,151-9.
12. Ellingsgaard H, Hauselmann I, Schuler B, Habib AM, Baggio LL, Meier DT, et al. Interleukin-6 enhances insulin secretion by increasing glucagon-like peptide-1 secretion from L cells and alpha cells. Nat Med. 2011:17:1481-9.
13. Eshghi SR, Bell GJ, Boulé NG. Effects of Aerobic Exercise with or without Metformin on Plasma Incretins in Type 2 Diabetes. Canadian Journal of Diabetes. 2013;37:375-80.
14. O'Connor AM, Pola S, Ward BM, Fillmore D, Buchanan KD, Kirwan JP. The gastroenteroinsular response to glucose ingestion during postexercise recovery. Am J Physiol Endocrinol Metab. 2006;290:1155-61.

15. Martins C, Morgan LM, Bloom SR, Robertson MD. Effects of exercise on gut peptides, energy intake and appetite. J Endocrinol 2007;193:251-8.
16. O'Connor AM, Johnston CF, Buchanan KD, Boreham C, Trinick TR, Riddoch CJ. Circulating gastrointestinal hormone changes in marathon running. Int J Sports Med. 1995;16:283-7.
17. Dekker MJ, Graham TE, Ooi TC, Robinson LE. Exercise prior to fat ingestion lowers fasting and postprandial VLDL and decreases adipose tissue IL-6 and GIP receptor mRNA in hypertriacylglycerolemic men. J Nutr Biochem. 2010;21(10):983-90.
18. Timothy DH, Ying L, Monica LK, Youngmin P, Kevin CD, Tom RT, et al. Prior exercise and postprandial incretin responses in lean and obese individuals. Med Sci Sports Exerc. 2013;45(10):1897-905.
19. Lee SS, Yoo JH, So YS. Effect of the low- versus high-intensity exercise training on endoplasmic reticulum stress and GLP-1 in adolescents with type 2 diabetes mellitus. J. Phys. Ther. Sci.2015;27:3063-8.