The Effects of Continuous and High Intensity Interval Trainings on Plasma Betatrophin Level in Diabetic Rats Treated with Metformin

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Abstract

Objective: The study aimed to determine the effect of eight weeks high intensity interval (HIIT) and sub-maximal continuous trainings on plasma betatrophin level in diabetic rats treated with metformin.

Materials and Methods: In this experimental study, 42 diabetic wistar rats were divided into six groups (n=7): diabetic control (C), diabetic control + metformin consumption(C+M), diabetic HIIT, diabetic HIIT + metformin (HIIT+M), diabetic sub-maximal continuous training (SMCT), and diabetic sub-maximal continuous training + metformin (SMCT+M). Metformin was given 150 mg/kg/day by gavage every day, 48 hours after the end of the last training session, the rats were sacrificed. Then blood glucose and glycated hemoglobin (HbA_1c) levels were measured. One-way ANOVA test was used for statistical analysis of data.

Results: The level of plasma betatrophin was significantly different in the HIIT (*P*-value= 0.01) and C+M (*P*-value= 0.001) groups compared to C group. Blood glucose was significantly decreased in all training groups with or without betatrophin compared with the diabetic control group (*P*-value= 0.001). However, there were no significant changes between glucose levels in HIIT, HIIT+M, SMCT, and SMCT+M groups but SMCT showed most reduction in blood glucose.

Conclusion: Treatment with metformin did not change blood glucose but two types of exercise training with high and moderate intensity reduced blood glucose thus exercise can be a good alternative modality rather than taking medicine.

Keywords: Interval and continuous exercise, Betatrophin, Blood glucose, Diabetes

Introduction

Type 2 diabetes mellitus is due to the inability of beta cells to compensate for insulin resistance caused by hyperglycemia (1). Proliferation of beta-stimulating beta cells has been proposed as the treatment of type 2 diabetes mellitus (2). The new betatrophin hormone (ANGPTL8), which leads to the proliferation of beta cells in

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response to resistance to insulin, has attracted a lot of attention (3). Betatrophin is expressed primarily in the liver and adipose tissue and is released into blood (4,5). Its ability to reproduce 17 beta cells in response to insulin resistance suggests that betatrorphin can be used to treat type 2 diabetes mellitus and reduce the dependence of insulin injections (6). On the other hand, drugs used in diabetics, such as metformin, have many complications. Physical activity may be a good alternative to medication. There are not many studies about the effect of exercise on the level of plasma betatrophin. (7). Therefore, the present study was designed to investigate the effects of high intensity interval training (HIIT) and sub-maximal continuous training on the plasma betatrophin level in diabetic patients.

Materials and Methods

In this experimental study, 42 wistar male rats (average weight 256.9 ± 9.9 g) were randomly assigned to six diabetic groups diabetic control, diabetic control+ metformin consumption, diabetic high intensity interval training, diabetic high intensity interval training+ metformin, diabetic sub-maximal continuous training, and diabetic sub-maximal continuous training + metformin. The samples were 7 in each group. For induction of type 2 diabetes mellitus, nicotinamide and streptozotocin were used. After 12 hours of fasting, 45 mg / kg streptozotocin was dissolved in 300-300 μL of Physiologic Serum and injected intraperitoneally. For 15 minutes before streptozotocin injection, 110 mg / kg 110 solution of nicotinamide was injected into the physiologic serum. After 7 days, blood glucose was measured. To ensure the accuracy of the test, glucose tolerance test was performed. Blood glucose samples above 150 mg / dl were considered diabetic. For familiarization and preparation for one week and three alternate days, 15 minutes each day, at speeds of 10 m / min, were practiced on the treadmill. Interval training protocol include six minutes of warm up (50% to 60% vo2max), three severe periods (four minutes 90% to 100% vo2max intensity) between each severe period, a low intensity training (50% to 60% vo2max). At the end of 6 minutes, the cool down was carried out at 50% to 60% of vo2max. Continuous training started at a sub-maximal intensity with a 6-minute warm up (40 to 50 vo2max) and then the main training was performed with running from 65% to 75% of vo2max for 40 to 60 minutes. After the end of the main training, six minutes of cool down (40 to 50% of the vo2max) were performed. The activity of each training group (Interval and continuous) was performed one session a day, five days a week for eight weeks. According to Hoydal et al (2007) the warm-up stage of each rat was first performed for 10 minutes with 10 m / min severity, and then an increasing exercise began. The treadmill speed of 0.03 m / s automatically increased every two minutes until the time which samples were not able to continue. Considering the final rate obtained at the end of the maximum test, based on the study of these scientists, the speed was obtained at the intensity of the training program (8,9). To eliminate the acute effects of exercise and uncontrollable variables, 48 hours after the last session, observing ethical principles and using intraperitoneal injection, a combination of ketamine (30 to 50 mg / kg body weight) and xylacin (3,5) Mg / kg body weight) rats were anesthetized. Then, 10 ml of blood was taken directly from their hearts and centrifuged for 15 minutes at a speed of 3000 rpm. Glucose was measured by calorimetry method using the Pars Tesh (Pars Test - Iran) and Beta-trophin plasma kits using the German company Zalibo kit and ELISA method. The Kolmogorov-Smirnov test was used to check the normal distribution of data. One-way ANOVA and post hoc test were used to examine the differences between groups of each of the indices. P-values of < 0.05 were considered to indicate statistical significance. Data was analyzed using SPSS version 20.

Ethical considerations

This study was approved by Committee of Ethics in Ilam University of medical sciences,

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Results

Plasma betatrophin levels were significantly different in the diabetic control group with high interval diabetes (*P*-value< 0.01) and diabetes control with metformin (*P*-value< 0.001). Levels of betatrophin plasma were significantly reported in the diabetic with metformin group with high interval diabetic (*P*-value< 0.01), continuous diabetic with metformin (*P*-value< 0.001) and interval diabetes with metformin (*P*-value< 0.01). Plasma levels of betatrophin in the high interval diabetic group with metformin and continuous diabetic with metformin (*P*-value< 0.001) were significantly reported.

The blood glucose level in the diabetic control group with diabetic continuous exercise group (*P*-value< 0.001), diabetic continuous training + metformin (*P*-value< 0.001), diabetic interval training (*P*-value< 0.001) and diabetic interval training with metformin (*P*-value< 0.001) was significant. In addition, in the study of blood glucose, blood glucose in the diabetic control group with metformin with diabetic continuous training group (*P*-value< 0.001), continuous training group with metformin (*P*-value< 0.001), diabetic interval training (*P*-value< 0.001) and diabetic interval training with metformin (*P*-value< 0.001) was also significant. The mean plasma betatrophin levels and blood glucose (mg / dl) in the studied groups are shown in Table 1. Comparison of variables in different groups is represented as a graph (Figures 1 and 2).

Discussion

Betatrophin is a hormone that produced in the liver and adipose tissue that has a stimulating key role in the expression and beta cell proliferation. In many studies, high levels of betatrorphin in diabetics have been reported in comparison with non-diabetic patients. In another study, the association between betatrophin and glucose was significantly positive. Regarding the effect of exercise on the betatrophin level in diabetic subjects, observations have shown that the level of betatrophin in the obese group decreases significantly. The findings of this study showed that the level of betatrorphin increased in the training groups, which showed a significant increase in the interval diabetic group compared with the diabetic group,

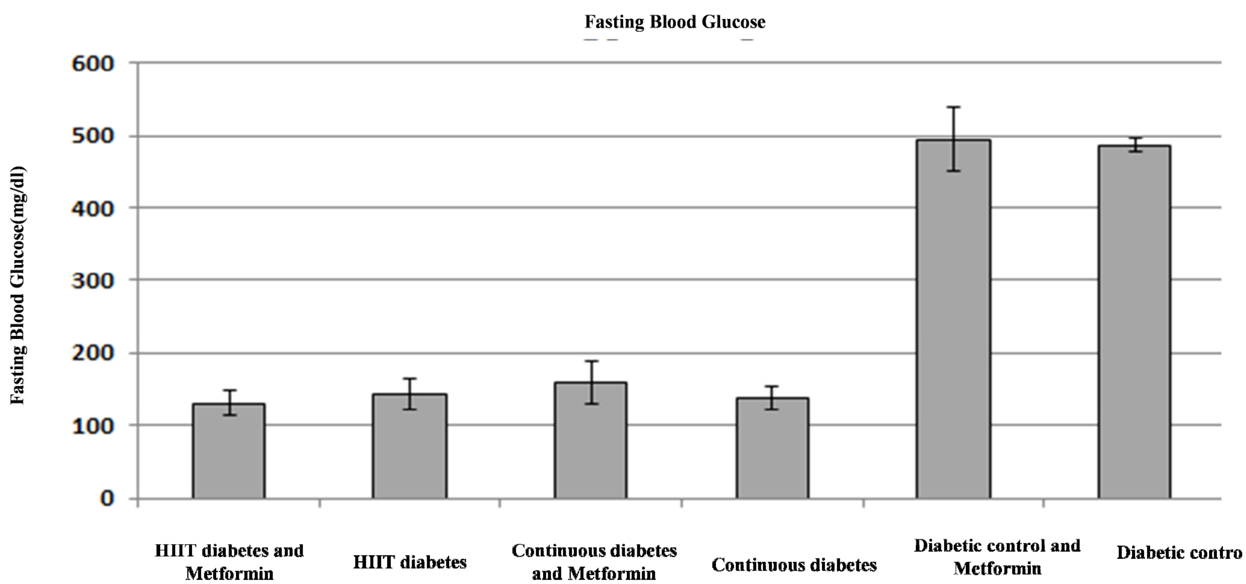

Figure 1. Difference in plasma fasting blood glucose levels between the groups

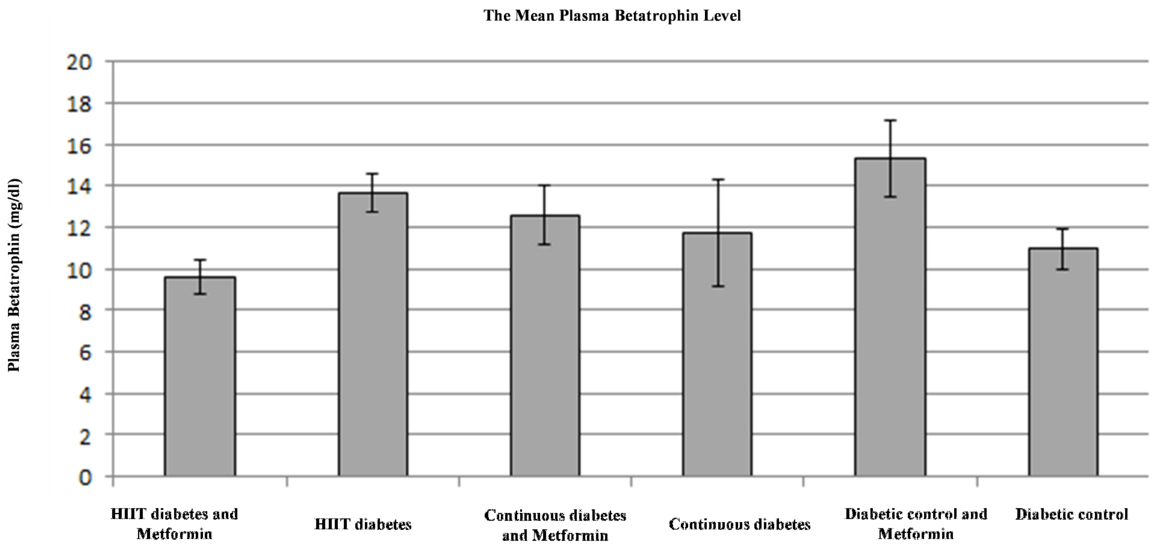

Figure 2. Difference between Plasma Betatrophin Levels in Groups

which contrasted with the data obtained from other researchers(7). The highest level of betatrophin levels was observed in the diabetic control with metformin group and its lowest level in the diabetic high interval with metformin group.

Further investigation is needed to discover the cause or the exact cause. Compared with the interval diabetic group, lower levels of betatrophin were reported in the continuous diabetic group, but it was not significant, although there was a need for more relevant variables and the relationship between these variables with betatrophin levels, But it seems that since the majority of studies conducted to increase the level of betatrophin, it has been shown that this increase is a kind of feedback for diabetes or obesity; in other words, the lower amount of betatorphin in the Continuous diabetic with metformin group, the need for betatrophin to express or along with it , ceases the proliferation of beta-cells. On the other hand, in order to study the low levels of blood betatrophin in diabetic control groups, more studies are needed.

The results of this study showed that doing eight weeks of high interval training and moderate continuous training results in a significant decrease in plasma glucose levels. The results of this study were consistent with Amitas et al. (10). Also, Gordon et al reported a significant decrease in plasma glucose levels in their study (11). Sports activities increase the number of glucose carriers (GLUT4) and, as a result, increase the transport of sugars into muscle cells and the consumption of sugars (12). Sports activities have an insulin-like effect and they send a lot of glucose into the cell to spend on energy production.

In this study, blood glucose levels in the diabetic HIIT group and moderate continuous training decreased significantly compared to diabetic control group. The diabetic continuous group caused a further decrease in blood glucose levels compared with the HIIT group. More interestingly, the efficacy of the diabetic continuous group in reducing blood glucose was even more than that of the continuous diabetic with metformin group. The difference between the results of various researches in different training groups can be attributed to the difference between the intensity and duration of the training program (13-15).

Conclusions

Compared with the diabetic interval group, the continuous diabetic group has a lower serum

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betatrophin level. Further investigation is needed to explain the cause of low levels of blood betatrophin in the diabetic control group compared with other groups. The most effective continuous diabetic group was reported to reduce blood glucose even more than the continuous diabetic with metformin group. This demonstrates the benefits of continuous exercise to bout of interval training and interval exercise with drug. Ultimately, this confirms that exercise can be a good alternative rather than taking medicine to lower blood glucose.

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