Journal of Sports Physiology and Athletic Conditioning (J.S.P.A.C) 2022; 2 (5): 73-81

Research Article

The Effect of 8 Weeks of High-Intensity Interval Training on the Expression of Lipasin in Diabetic Rats

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Received: 4 July 2022
Revised: 19 August 2022
Accepted: 30 August 2022

Abstract

Background: Diabetes is a metabolic disorder recognized as one of the most common diseases in the world. The disease has also increased dramatically in Iran.Today, there are many ways to treat diabetes, one of which is the increase in the level of pancreatic beta cells. The increase in these cells is done in several ways Several studies have demonstrated that the lipasin or betatrophin gene, a liver-expressed peptide hormone, increases the proliferation of beta cells, and that overexpression of this gene can increase the number of beta cells.

Materials and Methods: The study was conducted on 16 Wistar rats with a mean weight of 160 ± 10. They were induced by diabetes (seven months of diabetes mellitus was caused in rats). They then were divided into two groups of 6: Control (C) and High-Intensity Interval Training (HIIT). Eight weeks of exercise training was conducted on rats.The qRT-PCR technique was used to investigate changes in lipasin expression. An Independent t-test was used for data analysis, and Pearson correlation was used to determine the correlation between lipasin expression and insulin resistance index ($P < 0.05$).

Results: The results showed that expression of lipasin gene in the liver of rats in the training group was significantly higher than the control group rats after 8 weeks of training; Insulin resistance index of plasma, plasma insulin and plasma glucose decreased considerably after eight weeks of HIIT. Between lipasin expression and insulin resistance index in rats with type 2 diabetes in the training group, a consider correlation has been observed.

Conclusion: This study showed that an 8-week HIIT training period, with increased lipasin expression, could increase beta cells and also recover type 2 diabetes, which had been destroyed by these cells, and as a result of this increase in Insulin secretion and there is a way to prevent the disease.

Keywords:
HIIT training, insulin resistance, Lipasin, Type 2 diabetes

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1. Introduction

The prevalence of type 2 diabetes worldwide is rising rapidly due to the proliferation of this disease, insulin resistance, resulting in the destruction of the pancreatic beta cells and eventually disappearing, resulting in insulin not being secreted.

The pancreatic cells release insulin in two periods in this manner. In the first phase, insulin is released immediately in reaction to a rise in blood glucose, while in the second phase, newly created vesicles are released slowly and independently of blood glucose (2).

As long as stem cells continue to proliferate, the phenotype and duplication of beta cells in humans will be impossible (5). Beta cells are a vital receptor for blood glucose and release a little amount of insulin to manage glucose and energy balance (4).

Recent reports of a liver secreted protein have been responsible for liver signaling to beta cells. This protein is the same as betatrophin/ lipasin, which is the liver's expression in the pancreas and the function of the secreted protein in the pancreas. Lipasin It is an unknown gene that is called c19 or F80 in humans and GM6484 in rats, but several different names are used for this protein, including RIFL (Refeeding Induced Fat and Liver), ANGPTL8 (Angiopoietin-Like Protein 8), and betatrophin (7). It is a new protein but a member of the ANGPTL protein family, secreted from the liver. It participates in triglyceride metabolism, is a regulator of lipid metabolism (8), reduces TG (triglyceride) barriers by increasing serum TG content (4), and its levels are sensitive to food consumption (8), which means that it is stimulated by eating food and stopped by hunger. Most importantly, increases pancreatic β-cell proliferation (7).

Betatrophin/lipasin has recently received attention in preventing diabetes and as a β-cell regenerator, it has a potential role in type 2 diabetes (9). How insulin is returned to the cell by the pancreatic β-cell mass is incredibly beneficial for all people with diabetes (type 1 and 2), and the renewal of functional β-cell mass is valuable in that it is a crucial target for the prevention of diabetes (4).

Exercise is an essential part of preventing diabetes, primarily type 2 diabetes. Its benefits include improving physical fitness, preventing and reducing fat, improving the fat status and metabolic control of blood sugar, reducing the risk of coronary heart disease, and mental and social benefits: stress reduction and the possibility of reducing or eliminating diabetes medications for type 2 diabetes (1).

This study aimed to investigate the effect of eight weeks of High Intensity Interval training (HIIT) on lipasin expression in liver tissue in type 2 diabetic rats.

2. Materials and Methods

This study was performed on 16 Male Wistar rats with a mean weight of 160 ± 10 g. After induction of diabetes (feeding rats for seven months with food containing 30% animal fat and 25% fructose), rats were randomly divided into two groups, control, and HIIT. The training program was run for 8 weeks and 5 sessions per week on the treadmill running. Exercise with two periods (two-minute) of intense activity (80-90% of maximum oxygen intake) in the first week, with four replicates in the fourth week and at the end of the eighth week; between any two high-intensity alternatives, two minutes of Low Intensity regression (30% Maximum Oxygen intake).

The rats of the training group were placed on the treadmill for one week to familiarize themselves with the training protocol, with the utmost precision and calmness and at a low and uniform speed, and from the first week of training until the eighth week, they performed the corresponding protocol five days a week. They did it for eight weeks. The velocity maximum oxygen consumption (VO2max) was measured on the sixth day every two weeks. Due to the absence of availability to a direct instrument, such as a respiratory gas analysis equipment, an indirect technique with high precision was utilized (pilots have been conducted).

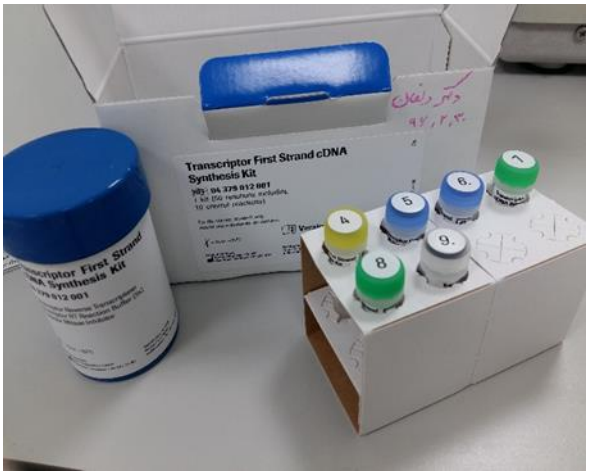
After three minutes of warming up at a speed of five meters per minute, the speed of the treadmill was increased once every two minutes by 4 meters per minute, the maximum speed was the maximum when the rats could not run at a constant speed for at least 1.3 minutes and Immediately after that, they were not able to run by increasing the speed (the incline of the treadmill was 0 degrees).

The control group did not participate in any sports activity program, but they were placed next to the treadmill to make them adapt to the environment and equalize the conditions with other rats.

In the HIIT training protocol, at the beginning, there was a three-minute warm-up with an intensity of 30 % of VO2max. After the warm-up, there was a high-intensity interval, with an intensity of 80 % of VO2max in the first week and 90 % of VO2max from the second week to the end of the eight week.

Low-intensity intervals were at 30 % of VO2max; The number of high-intensity interval was two repetitions in the first week, three repetitions in the second, third, and fourth weeks, and four repetitions from the fifth to the eight week. The high-intensity interval was two minutes and the low-intensity interval was two minutes. At the end, three minutes of cooling was done with an intensity of 30 % of VO2max. The incline of the treadmill was set to 0 degrees during the whole time of the exercise protocol.

Twenty-four hours after the last training session, the animals were sacrificed, and the lipasin gene expression from liver tissue was measured using the qPCR Real-Time method. An Independent t-test was used for data analysis, and Pearson correlation was used to determine the correlation between lipasin expression and insulin resistance index ($P < 0.05$).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3. Results

The results showed that after eight weeks of training, the expression of the lipasin gene expression in the liver of the rats in the training group was significantly higher than in the control group (P = 0.037); also, a significant negative correlation was observed between the expression of the lipasin gene and the insulin resistance index in the training group was compared to the control group (r = -0.568, P = 0.037).

In this study, the changes in the expression of the lipasin gene with the intervention of eight weeks of HIIT exercise as a preventive method for type 2 diabetic rats, by measuring plasma insulin, plasma glucose, insulin resistance index and expression of the lipasin gene in the liver of rats. The results of research indicate that HIIT workouts considerably enhance the expression of the lipasin gene compared to the control group, and that this increase has a good effect on the prevention of diabetic rats with the purpose of accelerating their recovery. Therefore, future study must investigate the impact of various training techniques in this area.

* Indicates the significance of the mean difference at the level of P<0.05

Sig.	standard error	Average group difference	Variable
0.016	0.34038	-0.92567*	HIIT, C

* Significant

Pearson Correlation Test Results

* Indicates the significance of the mean difference at the level of P<0.05

Sig.	Correlation with insulin resistance index	Variable
0.014	-0.568*	lipasin

* Significant

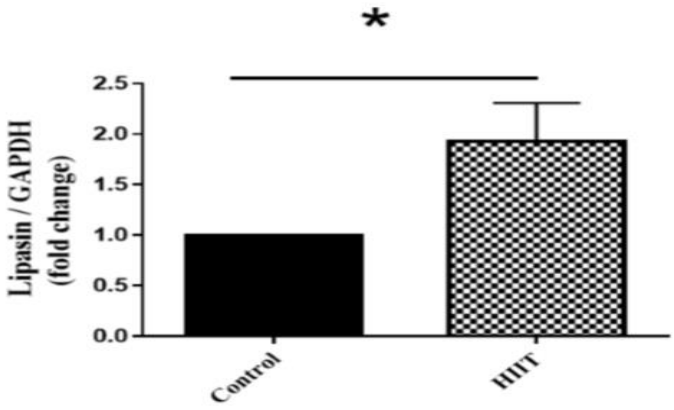

Figure 1: Comparison of significant levels of lipase expression in severe periodic exercise group (HIIT) and control group

* Significant

4. Discussion

By raising the expression of the lipasin gene, it appears that eight weeks of HIIT can increase the beta cells in diabetes patients and may be a beneficial non-pharmacologic intervention for reducing the disease's symptoms and consequences. Some studies have documented the therapeutic effect of this gene, and this therapeutic effect in diabetic patients will occur due to increased beta cell mass due to the overexpression of this gene.

A study on the claim was made by Daniel Espes et al. 2015. In this study, betatrophin in diabetics as an enhancer of beta cell proliferation is a target drug for the treatment of this disease (1). Collaborative studies have been conducted by Chen J et al. (2) that have been shown to improve glucose tolerance and insulin uptake, and studies conducted by Jonase Ah et al. (3), Lynnel et al (4), Chen et al. (5) and controversial reviews with this discussion have been made by Cox Aaron R et al. (6) and Victoria G et al. which have shown no increase and control of beta cells in the over expressive effect of this gene (7).

Yi et al. 2013, conducted a study on the betatrophin hormone that controls beta-cell proliferation. As a result of this study, the expression of betatrophin in the liver promotes beta-cell proliferation, promotes beta-cell mass development, and improves glucose tolerance. Therefore, betatrophin therapy can replace several insulin-producing cells instead of insulin injections in diabetics (8). Other investigations were conducted on Jonathan Ah's research on serum betatrophin in 2014, and as a consequence of this study, betatrophin will offer promise for the treatment of type 2 diabetes (3). Additionally, Zhu et al. did a study on the new insights of betatrophin about the therapy of diabetes and lipid metabolism. Showed that beta cells are known to respond to betatrophin stimulation, which modulates the mechanism of action between the liver and the fat by pancreas, and provides a way to treat diabetes with this approach (9).

There are many studies in line with this research, all of which have been conducted on serum lipasin in different conditions (pregnant women, children, obese people, etc.). The researches of Mohamed Abu-Farha et al., Shimin Wu et al., Chang-chiang chen et al., Natalia W et al., Onur Erol et al., Thomas Ebert et al., Yamada H et al., (10,12 ,11,13,14,15).

In study conducted by M Abu-farha et al., the opposite result was observed and there was no significant correlation between serum betatrophin/lipasin and insulin resistance index. Of course, these studies were conducted on serum lipasin and cannot be generalized to our research problem.

In a research conducted in 2017 by M Cahova et al., the findings of this research showed that the expression of the lipasin gene in white adipose tissue in Wistar rats has no significant correlation with insulin resistance, and this result is contrary to the current research and the reason Inconsistency is that measurements were made in adipose tissue (16).

In some studies, they also looked at the difference between lipasin gene concentration in obese and diabetic people. As a result of these investigations, it was shown that the serum betatrophin concentration is increasing in obese people, but no significant increase was seen in type 2 diabetics, and the reason for this inconsistency can be seen in the measurement of serum betatrophin (17).

Additionally, studies have been done by Cox Aaron R and colleagues (6) and Victoria G and colleagues (7) who have proven the lack of increase and control of beta cells due to the overexpression of this gene and the reason for this inconsistency These studies have been conducted on healthy people or rats.

۵. Conclusion

The results showed that expression of lipasin gene in the liver of rats in the training group was significantly higher than the control group rats after 8 weeks of training; Insulin resistance index of plasma, plasma insulin and plasma glucose decreased significantly after 8 weeks of HIIT, and between lipasin expression and insulin resistance index in rats with type 2 diabetes in the training group, Significant correlation has been observed. This study showed that an 8-week HIIT training period, with increased lipasin expression, could increase beta cells and also recovered in type 2 diabetes, which had been destroyed by these cells, and as a result of this increase Insulin secretion and there is a way to prevention the disease.

Acknowledgements

The authors would like to thank all athletes who participated in this research study. In addition, we thank the laboratory staff.

Funding

This study did not have any funds.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest in publishing this article.

Ethical approval the research was conducted with regard to the ethical principles (IR.SBMU.RETECH.REC.1395.883)

Informed consent Informed consent was obtained from all participants.

Author contributions

Conceptualization: S.S., N.KH.; Methodology: S.S., N.KH.; Software: S.S.; Validation: S.S., N.KH.; Formal analysis: S.S., N.KH.; Investigation: S.S., N.KH.; Resources: S.S., N.KH.; Data curation: S.S., N.KH.; Writing - original draft: S.S., N.KH.; Writing - review & editing: S.S., N.KH.; Visualization: N.KH.; Supervision: S.S.; Project administration: S.S., N.KH.; Funding acquisition: S.S., N.KH.

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