The Impact of Regular Aerobic Exercise on the Levels of Leptin, Fasting Blood Glucose, Insulin and Insulin Resistance in Patients with Diabetes Mellitus Type 2

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Abstract: Diabetes mellitus is a metabolic disease, characterized by chronic increased blood glucose levels, cardiovascular diseases and disorders in carbohydrate, fat and protein metabolisms. Leptin, which represents the amount of fat tissue in the body, plays an important role in overall body metabolic regulation and glucose homeostasis. This study has aimed to determine the effect of 12 weeks' moderate aerobic exercise, on levels of leptin and glucose homeostasis factors, in patients with diabetes mellitus type 2. In this quasi-experimental study, 40 patients with diabetes type 2, who had been referred to the Parsian clinic, Mashhad, were divided equally into two groups, namely, an experiment group and a control group. The experiment group participated in a twelve-week program (3 sessions a week and on average 40 minutes per session, with 60 to 70 percent intensity of heart rate reserve) in aerobic exercises on Treadmill. In this study, the factors, including leptin, fasting blood glucose, insulin and insulin resistance (HOMA) were measured before and after the exercise-period. A significant difference was observed in the plasma levels of leptin ($p = 0.000$), fasting blood glucose ($p = 0.010$), insulin ($p = 0.015$) and insulin resistance ($p = 0.035$) in the aerobic exercises group compared to the control group. Leptin can play an important role in reducing the cardiovascular risks and improving the process of glucose metabolism in diabetic patients. The process is aided through regular aerobic exercises, which has the effect on the one hand of reducing insulin resistance and increasing glucose metabolism, and on the other hand, of reducing serum.

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1. Introduction

The diabetes disease, sometimes known as the silent epidemic, is a disease in which the blood glucose levels are higher than normal. This disease is associated with increased urinary excretion and urinary glucose presence. Diabetes mellitus is a chronic metabolic disease that leads to damage to various organs of an infected person and reduction of longevity. According to the latest statistics, by the year 2025, the number of patients with this disease will reach to 135 million worldwide (1). In recent years, the prevalence and increase in obesity, diabetes and their related disorders are considered as the major health problems in Iran, and based on the same report, 58 percent of Iranian women and 75 percent of Iranian men suffer from overweight and obesity (2). In addition to this, 46 percent of mortality in Iran, caused by coronary vascular disorders, is due to hypokinesia, obesity and its complications - such as diabetes (3). The basic process is one where blood lipid disorders and increased fat tissue associated with central accumulation pattern are observed in diabetic patients (4). Insulin resistance is considered as fundamental to the properties of metabolic syndrome and early disturbance in the development of diabetes type 2. Reports also suggest the role of insulin resistance in the development of cardiovascular disease (5). It is only so far that the impact of physical activity has been known in the treatment of diabetes mellitus (6). Researchers having considered different approaches in treating diabetes and its complications through physical activity and exercise. Due to the importance of glucose metabolism and its related factors, most research has focused on effective factors in regulating blood sugar.

Although most of the conducted studies have reviewed aerobic exercises' impact on this

disease, there are many differences between the results obtained (7). For example, a study has shown that 12 weeks of aerobic exercise has no effect on the factors in these patients, including their insulin sensitivity, fasting blood insulin and fasting blood glucose (8). Also, an accurate intensity of physical activity for favorable changes in lipids, blood pressure, glucose levels and insulin resistance has not been determined, so that both the World Health Organization and the American College of Sports Medicine have recommended exercise intensity ranges as 55 percent to 80 percent (9, 10). Produced in fat tissue, leptin is a hormone that has a circadian pulse secretion, its rate reaching a maximum during the night and decreasing nearing the dawn (11). After passing the blood brain barrier, the hormone has influence on the hypothalamus and causes reduced appetite and energy intake (12). Leptin has a direct correlation with volume and size of fat cells (13); on the other hand, it has a direct relationship with certain hormones such as insulin, so that an increase in leptin levels is associated with increased insulin resistance and diabetes type 2 (11). Houmard et al. (2000) have shown in their research that a short-term aerobic exercises course (60 minutes with the 75 percent vo2 max intensity in seven consecutive days) does not cause a change in leptin levels in healthy males, both in young and older groups (14). Regarding the same subject, Kraemer et al. (1999) have found no change in leptin levels in obese women after 9 weeks of aerobic exercises (15). Meanwhile Kumru et al. (2005) have concluded that both short-term and long-term aerobic exercises reduce leptin levels significantly, and that such a reduction has been in parallel with reduced body mass index (BMI) (16). Given the inconsistencies in the studies conducted, and the lack of research on simultaneous homeostasis factors of glucose and leptin, this study has aimed to investigate the effect of regular aerobic exercises on leptin levels and the levels of glucose homeostasis factors (insulin, glucose and insulin resistance) in patients with diabetes type 2.

2. Material and Methods

2.1. Statistical population and the subjects

The research design used in the study was a quasi-experimental method. The research statistical population consisted of all patients with diabetes type 2 who had been referred to the Parsian Diabetes Clinic in Mashhad. Among these individuals, those who volunteered were 40 people in the 35-45 year age range. Blood sugar levels ranging from 150 to 250 (mg/dl) were selected, using screening methods once interview and review of medical records had taken place. The subjects were then randomly divided into two equal groups that comprised an aerobic exercises group and a control group. To avoid the influence of previous experience impacting on research results, only volunteers with no history of regular sports activity were selected. The conditions to be met in order to participate in the research included: female gender, diabetes type 2 both diagnosed by specialist physician and based on medical records, over 35 years old, and fasting blood glucose level ranging 150 -250 mg/dl. The exclusion criteria included: 1) currently suffering from other chronic diseases; 2) currently suffering from mental illness; 3) having maintained a regular exercise program over the past 3 months; 4i) a history of myocardial infarction (heart attack); 5) uncontrolled arrhythmias; 6) third-degree heart block; 7) high blood pressure (over 100/200 in under treatment patients); 8) diabetes type 1; and 9) diabetic complications such as diabetic foot ulcers, nephropathy and microalbuminuria.

2.2. Exercise protocol

The group that was subject of the experiment participated in a twelve weeks program (3 sessions a week and on average 40 minutes per session, with 60 to 70 percent intensity of heart rate reserve) in aerobic exercises on Treadmill. The exercise intensity was controlled using polar heart rate monitor device (s625x). The control group was advised to avoid participating in any type of sports exercises during the 12 weeks of the experiment.

2.3. Nutrition control

A questionnaire was given out three days before blood sampling. Participants were asked to note the amount and type of food that they consumed. The purpose of this survey was to consider the effect of nutrition on insulin resistance and to control the feeding of the subjects. The researchers measured the calories of the people's diet, and designed and repeated a similar 3-day diet for secondary blood sampling.

2.4. Blood factors measurements

All subjects in both groups were referred to the laboratory at the same point in the day (8-10 a.m.), where the subjects had been fasting for 12 hours and had undertaken no physical activity 24 hours before the testing. In the laboratory, 20 ml. of blood was taken from each subject's elbow vein. The samplings were conducted similarly before and after the exercises. The leptin concentrations measurement was performed by radio-immunoassay (RIA) method, using a diagnostic Biochem kit made in Hungary. For measuring insulin levels, the same method was used – a Gama counter device together with the Immuno tech company IM3210 kit, made in the Czech Republic. The measurement of blood glucose levels was conducted through an auto analyzer biochemistry Selectra device, built by Mann Company that used

the enzymatic method. Finally, insulin resistance was evaluated through a homeostasis evaluation method (HOMA-IR) and was calculated according to following formula (17):

HOMA-IR = fasting glucose [mmol / l] x fasting insulin [μU / ml] / 22.5

2.5. Measuring the body mass index (BMI)

The body composition analysis device, Tanita B_C418 model, was used for measuring body mass index and weight of the subjects.

2.6. Statistical Analysis

Research data was processed with the help of SPSS software, version 18 (SPSS Inc. Chicago Illinois, United States). The central trend indices and dispersion indices were shown through descriptive statistics. The Kolmogorov-Smrirnov test was used to review the data distribution types. To compare pre-test and post-test data means in each test group, the statistical correlated t test was used. All the statistical tests were performed at the 95 percent confidence level ($p < 0.05$).

3. Results

Forty people in two groups of the aerobic exercise group (20 subjects) and control group (20 subjects) performed the research pattern up to the end of 12 weeks, and the data obtained from them were analyzed. Descriptive information related to the age, weight, height, BMI, current drug-dose drug and disease-period of the subjects is given in Table 1. Following the exercise program being performed, the experiment group showed a significant decrease in weight ($p < 0.001$) and body mass index ($p < 0.002$) (Table 1). Furthermore, plasma levels of leptin ($p < 0.000$), insulin ($p < 0.015$) and blood glucose ($p < 0.010$), and, consequently, insulin resistance index ($p < 0.035$) had decreased significantly in the experimental group -compared to the control group (Table 2).

Table 1. Profile of subjects in two experimental and control groups

Group	n	Age (years)	Diabetes history	Medicine treatment before participating in the research	Height (Cm)	Weight (kg)		Body mass index (Kg/m^3)	
Test	20	40.4±5.11	5.38±3.4	2 tablets (1 Metformin, 1 Glibenclamide)	164.5± 5.5	B	78.7±7.84	B	29.3±3.45
						A	75.4±6.35	A	28.1±4.15
Control	20	38.3±2.45	5.2±2.4	3 tablets (1 Metformin, 2 Glibenclamide)	168.5± 6.5	B	80.3±6.35	B	28.47±5.2
						A	81.8±7.2	A	29±2.3

* Significance level ($p < 0.05$) ; A: After; B:Before

Table 2. Comparison of leptin, glucose, insulin and insulin resistance in two experimental and control groups

Group	Control			Test		
Variable	Pre-test	Post-test	P	Pre-test	Post-test	P
Leptin (ng/ml)	3.87±5.67	1.82±5.84	0.423	4.82±5.46	0.72±1.4	0.000*
Fasting glucose (mg/dl)	25.16±163.53	25.72±162.13	0.185	23.92±173	22.35±155.5	0.010*
Insulin (MU/ml)	6.74±11.89	11.18±13.62	0.367	4.98±13.85	2.01±10.04	0.015*
Insulin resistance (HOMA)	3.94±4.09	6.27±5.4	0.567	2.03±4.35	1.92±3.77	0.035*

* Significance level ($p < 0.05$)

4. Discussions

Based on the research results, blood insulin levels in patients of the experiment group had been significantly reduced. The results of this research are consistent with the results from the studies of Bruce et al. (18), but inconsistent with the results of the studies of Cauza et al. (7), Segal et al. (8) Massi et al. (19) and Esfehani et al. (20). The observed differences in outcomes could result from age and gender differences in the statistical samples and differences in intensity and duration of exercises in the different studies. Since blood insulin levels are reduced during exercise, the base insulin level and glucose-stimulated insulin level will reduce (21). Exercise also leads to reduced mRNA levels, required to produce pro-insulin mRNA and glucokinase mRNA in the pancreas. It seems therefore that there are at least two cellular mechanisms to reduce insulin secretion. The first reason for this supposition is that pro-insulin indicates the reduction of insulin mRNA synthesis in the liver. The second is that since the glucokinase presence in the liver is essential for the pancreatic beta cells' sensitivity to glucokinase mRNA insulin,

the reduction in glucokinase levels may lead to reduced sensitivity of these cells to insulin, and will reduce the amount of its secretion (22).

The most important finding of the present research was the reduced levels of insulin resistance in healthy middle-aged men, as a result of 12 weeks of aerobic exercises. The effect of exercises on insulin resistance has been studied through a wide range of research - which has mainly reported improvement in insulin resistance as a result of doing exercises (23-26). Carrel et al. reported that physical activity over 9 months, based on school physical fitness movements, improved insulin sensitivity as well as the levels of inflammatory markers such as adiponectine and TNF-α (tumor necrosis factor - alpha) in normal-weight children (25). Rubin et al. also reported that intense levels of physical activity have a direct relation to insulin sensitivity (26). Selected athletes, running an average of 48 miles per week, had less insulin resistance and more insulin sensitivity, compared to healthy people with low physical activity (23). However, there are also some studies that report exercise to have no influence on insulin sensitivity improvement (24). In a research paper that reported an increase in physical activity of men attempting 300 steps per day (approximately 30 minutes' walking), there were no significant effects on the hs-CRP levels, as well as insulin resistance level. The researchers stated that the reason had probably been the low duration and low intensity of the exercises (24).

The research results also showed that fasting blood sugar levels in the experimental group had reduced significantly after the ending of the interventions. The current research results are consistent with the results of Massi et al. (19), Bruce et al. (18), Esfehani et al. (20), and Duncan et al. (27), but inconsistent with the results of Segal et al. (8) and Cauza et al. (7). The reasons for these differences can be due either to variation in intensity of exercise, or to their intermittent or continuous patterns of practice. Our results' differences with those of Cauza et al. could for example stem from our study sample including only diabetic men over 35 years old, while older men and women had participated in their study; perhaps they could not perform the exercises with an intensity similar to those subjects of the current research - due to aging.

The studies show that muscle contraction has an insulin-like role, and sends a large amount of glucose into the cell, to be spent on energy production (28). The muscle contraction increases the membrane permeability to glucose, probably due to the increased number of glucose carriers in the plasma membrane (Glut4). When sports activities are undertaken, the amount of Glut4 in the exercised muscles increases, which improves the insulin action on glucose metabolism (29).

One of the most important results of this study is the significant reduction ($p = 0.000$) of leptin levels in the aerobic exercise group, compared to the control group. Considering the duration and intensity of performed exercises, the results of this study were consistent with many researchers, including Kumru et al. (2005) (16), Peeri et al. (30) and Oliveet al. (2001) (31). This would seem to imply that long-term exercise with moderate intensity leads to significantly decreased serum leptin concentrations. Despite the results obtained in this study, when Kraemer (2003) (32) reviewed the influence of intermittent exercises for progressive intensity effects on the leptin levels of individuals, no significant changes were observed. On the other hand, Zaccaria et al. (2002) (33) studied the effects of three endurance races on the leptin concentrations of 45 males, each of whom had participated in one of the three races. The results showed that only long-term endurance exercises, that required large energy consumption, were causing significantly reduced serum leptin levels, and no significant decrease was observed in half-marathon running and Nordic skiing.

In the present study, the reduced leptin levels can be attributed to the long-term (3 months) high caloric intake during exercises that were taken with the desired intensity. On the other hand, leptin represents the percentage of body fat and the balance of what is received and consumed as it is reduced in the body (34, 35). It has been observed in this study that, due to exercise, the body's mass index level and the weight of subjects in the test group, have been significantly reduced, and that this can be considered as one of the possible reasons for leptin reduction, as well as appropriate balance in internal body metabolism and caloric intake (36).

In summary, the research results showed that regular exercise can play an important role in the improvement of diabetes type 2, and also in the prevention of its development and complications. It can be inferred from the results that regular aerobic exercises may play an important role in reducing risks of cardiovascular diseases, and in improvement of the glucose metabolism in diabetic patients; this is due to reduced insulin resistance and increased glucose metabolism, as well as decreased leptin levels. Research into both the cell and the carriers of cellular glucose could be a good path by which to complete the findings of this research.

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