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Effects of exercise on glycaemic control and insulin action in type II diabetes mellitus

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Abstract

Exercise training is widely used for improving glycemic control and insulin action in diabetic patients. This study aimed to investigation effect a single bout and long exercise training program on glycemic indicators in type 2 diabetic patients. A 32 adult males with type 2 diabetic placed randomly in two control and experimental groups. For measuring of glucose and insulin concentration, a venous blood sample was collected after an overnight fast, immediately a single bout exercise and after three months aerobic exercise program in experimental group or control group (detraining in all stages). From insulin and glucose data used for calculation insulin sensitivity, insulin resistance and ß-cell function. Anthropometric indices in both groups were measured before and after prolonged exercise. Statistical analysis was performed using independent-paired T test ($p < 0.05$). There were no significant changes in insulin sensitivity and insulin resistance after single bout exercise compared to baseline levels, but long-time exercise program improved significantly these variables($p < 0.05$). Glucose concentration decreased significantly and b-cell function increased significantly in response to either single bout or long-time exercise ($p < 0.05$). None of the variables in the control group changed ($p \geq 0.05$). Our findings indicate that the reduction in blood glucose concentrations after exercise in patients with diabetes is due to improvement of insulin action and beta cell function.

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Introduction

Diabetes is a chronic metabolic disease that is created by the inability of pancreatic cells to produce sufficient insulin and/or the sensitivity of glucose-metabolizing tissues to insulin decreases. The main feature of the onset of type II diabetes is insulin resistance phenomenon (DeFronzo *et al.,* 1992). In people with insulin resistance, the severity of diabetes does not increase if they have sufficient insulin secretion capacity to compensate for insulin resistance (Park *et al.,* 2007). However, chronic hyperglycemia is associated with impaired insulin secretion and its function . In healthy individuals, insulin secretion from the pancreas through a postulated negative feedback loop that is associated with insulin sensitivity enabling beta cells to compensate for any changes in whole-body insulin resistance or sensitivity of cells to insulin due to increased secretion of insulin (Retnakaran *et al.,* 2005). But in type II diabetes, beta cell adaptation to increased insulin secretion in response to the phenomenon of insulin resistance ultimately leads to hyperinsulinemia phenomenon and excessive insulin resistance and the adaptation period, eventually leads to impaired function of these cells (Király *et al.,* 2008). In the pathogenesis of type II diabetes, destruction or progressive impairment of beta cell function, leads to inability to secrete insulin to compensate and overcome insulin resistance (Bergman *et al.,* 2002; Weyer *et al.,* 1999). Longitudinal studies have shown that impaired beta cell function is of particular importance in increasing the severity of the disease in infected people (Weyer *et al.,* 199). Some other studies attribute the prevalence of type II diabetes in obese people, particularly the disruption of hormonal mediators and circulation cytokines.

These studies suggest that prolonged exposure of beta cells to inflammatory mediators such as leptin, resistin, tumor necrosis factor alpha and some of interleukin is associated with impaired function of these cells (Stumvoll *et al.,* 2005; Andersson *et al.,* 2001, Maedler *et al.,* 2004; Nayak *et al.,* 2010). Recent studies have suggested that exercise as a none-pharmologicel treatment plays an important role in the regulation and reduction of inflammatory cytokines associated with beta cell function (Tang *et al.,* 2005; de Salles *et al.,* 2010). These studies also discuss reduction of blood glucose levels and insulin resistance in response to short-and long-term exercise training (Sheu *et al.,* 2008; Boulé *et al.,* 2001; Tokmakidis *et al.,* 2004). But, so far few studies have reported independent response of pancreatic beta cells function to different exercise activities. For this reason, this study aims to determine the effect of a short-and long-term exercise on beta cell function and some other diabetic indicators such as blood glucose levels and insulin sensitivity

Material and Methods

Subjects

This randomized controlled trail study performed on a group of adult men with type II diabetes in the age and weight range of (41 ± 6 years, 103 ± 9 kg) placed randomly in two control (n = 16) and experimental(n = 16) groups. Informed consent was obtained from each subject after full explanation of the purpose, nature and risk of all procedures used. The patients studied were sedentary and did not regularly participate in sports activities. The review of their medical records showed that all patients had a diabetes history of at least 5 years.

Exclusion criteria

All subjects were non-smokers. Subjects with a history or clinical evidence of recent myocardial infarction, congestive heart failure, active liver or kidney disease, growth hormone deficiency or excess, neuroendocrine tumor, anemia were excluded. Participants were included if they had not been involved in regular physical activity in the previous 6 months. Patients were in reasonable physical condition with no movement or orthopedic disorders.

Anthropometric measures

Anthropometric measurements of height, weight, percent body fat, and circumference measurements were taken in beginning of study. Height was measured without shoes (0.5 accuracy), and weight with light clothes and without shoes (100 g accuracy). Waist circumference was measured after a normal expiration under the midline of the subject's armpit, at the midpoint between the lower part of the last rib and the top of the hip. The body weight, body mass index and body fat percentage were measured by body composition monitor (OMRON, Finland) and recorded.

Blood sampling and Exercise program

For measuring of glucose and insulin concentration, a venous blood sample was collected from all the subjects who came after a 12-h overnight fast. Blood sampling was also repeated immediately after a one-session exercise test on a cycle ergometery according to Astrand submaximal protocol (Mullis *et al.,* 1999). Serums were immediately separated and stored at -80° until the assays were performed. Then, the experimental group performed an aerobic exercise program in 60–70% maximal heart rate. Exercise training duration was 3 months (3 times, weekly). Typical exercise sessions consisted of a 5-min warm-up; 45 min of aerobic training consist of running on treadmill or stationary cycling, and 5–10 min of cool down activity. Polar heart rate (HR) monitors were worn by the subjects during every exercise session. Finally, 48 hours after the last exercise session, the blood sampling was performed in the fasting state. Also, blood sampling at all time stages was performed on the control group except that they did not participate in the one-session test and the long-time aerobic exercise program. Glucose oxidase method (Pars Azmun, Tehran, Iran) was used for measuring blood glucose and insulin was measured by ELISA method (Demeditec, Germany). Insulin sensitivity, insulin resistance and beta cell function were calculated by using fasting glucose and insulin (Marita *et al.,* 2005). The anthropometric variables were measured again after a 3-month training period.

Statistical analysis

All results are expressed as means ± SD. Independent samples t-test was used to compare baseline levels of anthropometric and biochemical variables of control and experimental groups. Paired Student t test was used to determine significance levels of changes in any of the variables compared to baseline conditions after exercise interventions (SPSS, Version 15). P value of <0.05 was accepted as significant.

Results

In this study, the effect of one session and three months of aerobic exercise on blood glucose levels, beta cell function, insulin sensitivity and insulin resistance in diabetic patients was investigated. Table 1 presents all anthropometrical and biochemical characteristics in the baseline and follow by exercise interventions of two groups. There were no significant inter-group differences in all variables or duration of diabetes. Information related to the baseline levels of body mass index and body fat percentage showed that patients studied are in the obese diabetic class. The three-month training program brought about a significant reduction in anthropometric indices such as weight, body mass index and body fat percentage ($p <0.05$). The statistical findings showed that there is no significant difference in baseline levels of blood glucose, beta cell function and insulin sensitivity index and other variables between control and experimental groups ($p \geq 0.05$). There are not significant change in anthropometric and biochemical variables follow up detraining interventions (one-session or three month detraining) compared to baseline levels in the control group ($p \geq 0.05$).

In experimental group, increase in insulin sensitivity index after a one-session exercise test was not significant, but after a three-month training program significantly increased compared to baseline levels (p

<0.05). The results showed that beta cell function in response to an exercise session and after three months of aerobic exercise significantly increased compared to baseline levels (p <0.05, Fig 1). In addition, there were no significant changes in insulin resistance after one-session exercise test. But three month exercise training decrease this variable significantly (p <0.05). The statistical test also showed that blood glucose levels in the experimental group following a one-session exercise and a three-month training program significantly decreased compared to baseline levels (p <0.05, Fig. 2).

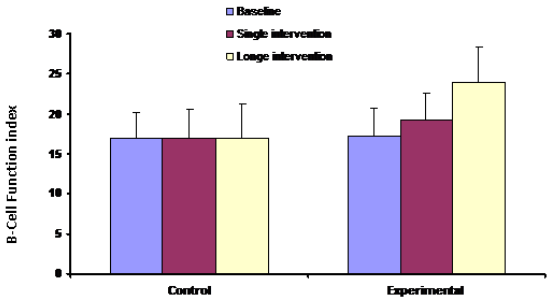

Fig. 1. The changes pattern of ß-cell function index in baseline and by interventions in two groups. The results showed that beta cell function in response to single bout exercise and after three months of aerobic exercise significantly increased compared to baseline levels (p <0.05).

Table 1. Anthropometrical and biochemical characteristics in the baseline and follow by interventions of two diabetic groups.

Variable	Experimental			Control		
	Baseline (detraining)	single(detraining)	long	Baseline	single exercise	long exercise
Weight (kg)	103 ± 9	103 ± 9	98 ± 7 *	102 ± 8	102 ± 8	102.23 ± 11
WC (cm)	106 ± 11	106 ± 11	100 ± 9 *	105 ± 9	105 ± 9	106 ± 11
BMI (kg/m2)	34.02 ± 4.23	34.02 ± 4.23	32.36 ± 4.11 *	33.69 ± 3.26	33.69 ± 3.26	33.77 ± 3.61
BF (%)	33 ± 3.42	33 ± 3.42	29 ± 4.11 *	32.60 ± 3.12	32.60 ± 3.12	32.81 ± 3.65
glucose(mm/L)	13.01 ± 2.36	12.21 ± 3.03 *	10.27 ± 2.43 *	13.28 ± 3.68	13.21 ± 3.14	12.98 ± 4.12
Insulin(µIU/ml)	8.21 ± 2.43	8.43 ± 2.11	8.13 ± 1.68	8.33 ± 2.86	8.23 ± 1.14	8.06 ± 1.39
HOMA-IR	4.74 ± 0.48	4.57 ± 0.68	3.71 ± 0.36 *	4.90 ± 1.31	4.83 ± 1.21	4.65 ± 1.44
HOMA-IS	0.49 ± 0.09	0.50 ± 0.12	0.52 ± 0.09 *	0.49 ± 0.08	0.49 ± 0.11	0.49 ± 0.10
HOMA-BF	17.26 ± 3.44	19.35 ± 3.26*	24.01 ± 4.36 *	17.03 ± 3.24	16.95 ± 3.69	17 ± 4.28

Data represent mean ± standard deviation.

* represent significant changes compared to baseline levels.

WC = Waist Circumference. BMI = Body Mass Index, BF = Body Fat Percentage,

HOMA-IR = Insulin Resistance Index, HOMA-IS = Insulin Sensitivity Index, HOMA-BF = ß-Cell Function Index

Discussion

Beta cell dysfunction reflects the presence of chronic insulin resistance (Retnakaran *et al.,* 2005). The findings of this study showed that short-and long-term exercise leads to improvement of beta cell function accompanied with a significant reduction in fasting glucose concentration in adult men with type II diabetes. Impairments in ß -cell compensation for insulin resistance and ß-cell sensitivity to glucose have been found in people with impaired glucose tolerance (Chang *et al.,* 2006). Type II diabetes is not defined only by decreased hepatic and peripheral insulin action, but the defects or loss of beta cell function also contribute to prevalence the increased severity of the disease and in fact, are responsible for the discrepancy between insulin-resistant obese nondiabetic and type 2 diabetic patients (Király *et al.,* 2008). For example, one study found that people with type II diabetes

represent a 40 to 60 percent reduction in beta cell mass compared with non-diabetic hyperinsulinemia control group (Westermark *et al.,* 1978). The question that what phenomenon is the precipitating factor of beta cell dysfunction in diabetics and in not in obese insulin resistant individuals has not yet been explored sufficiently. In subjects with type II diabetic, this adaptive period of ß-cell compensation is short-lived and may fail altogether (Westermark *et al.,* 1978). However, clinical studies suggest that increased activity of beta cells to overcome insulin resistance in type II diabetic patients in a prolonged period of time is associated with reducing the mass of these cells and with their reduced performance (Király *et al.,* 2008). Some studies, however, have suggested that loss of beta cell function has a strong correlation with decreased expression of glucose transporters (GLUT2) (Pick *et al.,* 1998; Tanaka *et al.,* 1999).

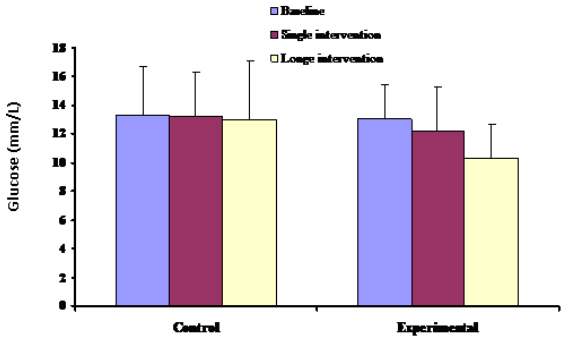

Fig. 2. The changes pattern of glucose concentration in baseline and by interventions in two groups. Blood glucose levels in the experimental group following a one-session exercise and a three-month training program significantly decreased compared to baseline levels ($p < 0.05$).

In obese rodent models such as the Zucker rat, calorie restriction (Ohneda *et al.,* 1995), decreased fat mass (Gabriely *et al.,* 2002) and increased regular exercise (Okada *et al.,* 2010; Pold *et al.,* 2005) can improve insulin sensitivity and inhibit the spread of hyperglycemia. Pharmacologic and non-pharmacologic treatment methods such as diet or regular exercise have been proved to lead to increased insulin sensitivity and reduce the demand for insulin and apoptosis of beta cells (Király *et al.,* 2008). Some studied reported that exercise training alone in absence to diet improve insulin resistance or sensitivity (Short *et al.,* 2003; Poehlman *et al.,* 2000). However, exercise effects on ß-cell function have not been examined. Our study showed that although one session of exercise does not bring about any significant change in insulin resistance or insulin sensitivity, long-term exercise training significantly improved these variables accompanied with decreased blood glucose concentration.

Given the potential role of reducing body fat in increasing insulin action (Gabriely *et al.,* 2002), it seems that increased insulin sensitivity or decreased insulin resistance in response to prolonged exercise can be attributed to reduced weight and reduced body fat in patients studied. Increased insulin sensitivity in response to exercise-induced weight loss has been observed in some other studies (Hays et al., 2006; Hays *et al.,* 2006). Confirming the findings of this study, other studies have also reported the role of different training methods such as activity on the treadmill and swimming in preserving beta cell function and mass (Pold *et al.,* 2005; Bloem *et al.,* 2008; Rhodes *et al.,* 2002).

However, the temporary and modest elevation of insulin resistance has been shown to lead to an increase in pancreatic ß-cells (Jetton *et al.,* 2005; Rooman *et al.,* 2002), which occurs as a result of hypertrophy and the neogenesis of precursor cells (Jetton *et al.,* 2005). But, long-time and severe insulin resistance has been shown to decrease the proliferation of ß -cells. Scientific evidence suggests that exercise increases beta cell mass through the process of hyperplasia and hyperplasia is brought about by increased beta cell proliferation and decreased apoptosis (Park *et al.,* 2007).

It is possible that exercise training or exercise-induced weight loss indirectly and by affecting biochemical mediators or peptide hormones the expression of genes or the presences of the receptors of which in pancreatic cells have been reported (Stumvoll *et al.,* 2005; Andersson *et al.,* 2001; Nayak *et al.,* 2010; Goldberg,

2009), improve insulin sensitivity or beta cell function that is associated with reduced blood glucose levels in diabetic patients. Some studies in the field suggests improvement of cytokines related to insulin performance, such as adiponectin, leptin, resistin and other cytokines in response to short or long term exercise (Tang *et al.,* 2005; de Salles *et al.,* 2010).

Although study findings on the direct effect of exercise on insulin resistance or adaptation of pancreatic beta cells is unclear, but this study shows that short-or long-time aerobic exercise improves beta cell function and is associated with reduced Hyperglycemia and insulin resistance. The mechanisms contributing to decline in ß-cell function and how exercise may improve ß -cell function cannot be determined merely from the current study and required extensive studies in this area.

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