

Regular aerobic training improves insulin resistance but not pancreatic β -cells function in female patients with type 2 diabetes

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Abstract

Aim: Pancreatic β -cells function and insulin sensitivity resistance were impaired in type 2 diabetes. Exercise training may improves these impairs, however, this is **not** well known. The aim of present study was to examine the effect of 8 weeks aerobic training on pancreatic β -cells function and insulin resistance in female patients with type 2 diabetes.

Material & Methods: Twenty middle-aged women (age, 40 - 50 years) with type 2 diabetes participated as the subject. The subjects were randomly assign to control group (n=10) or the training group (n=10). The subjects in **the** training group performed 30 to 45 min aerobic training on the

treadmill with 60-75% of their maximum heart rate, 3 days a week for 8 weeks. The subjects in the control group were instructed to maintain their normal physical activity throughout the study.

Results: The results indicated that fasting blood sugar, fasting insulin and insulin resistance index decrease in the training group compare to the control group ($P < 0.05$); however, pancreatic β -cells function has no significant change after the intervention.

Conclusion: In summary, it seems that aerobic training utilized in this study improves glucose entry into cells but it had not effective on pancreatic β -cells function.

Key words: Type 2 diabetes, Aerobic training, Pancreatic β -cells function, Insulin resistance

1. Introduction

Globally, an estimated 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. The global prevalence (age-standardized) of diabetes has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population. Over the past decade, diabetes prevalence has risen faster in low- and middle-income countries than in high-income countries and diabetes caused 1.5 million deaths in 2012 (1). Type 2 diabetes (formerly called non-insulin-dependent or adult-onset diabetes) results from the body's ineffective use of insulin. Type 2 diabetes accounts for the vast majority of people with diabetes around the world (2).

Type 2 diabetes is sustained by insulin resistance and impaired insulin secretion. Impaired insulin secretion due to either β -cell dysfunction and/or β -cell loss is now recognized in the pathogenesis and progression of diabetes. The loss of β -cell mass and the progressive decline in β -cell function is an early feature of the natural history of diabetes and it is detectable prior to diagnosis (3). The United Kingdom Prospective Diabetes Study (UKPDS) showed that β -cell function, as evaluated by the homeostatic model assessment (HOMA-B) index, was already

decreased by 50% by the time of the diagnosis and that it continued to decline over the 6-year observation period, even with on-going hypoglycemic therapy (4). The relative increase of α -cells mass, another typical defect on Langerhans islets of diabetic subjects, may even precede β -cells loss, being already observed in normoglycaemic baboons with different degrees of obesity (5).

β -cell mass is influenced by a balance between proliferative and pro-apoptotic signals, which may be modulated by various growth factors, cytokines, and hormones, whose specific role in the rate of β -cell decline remains unclear. High levels of glucose and free fatty acids (gluco- and lipotoxicity), islet amyloid polypeptide deposition, and circulating inflammatory cytokines have been all implicated in β -cell apoptosis (5,6). At any rate, whenever it appears, impaired β -cell function leads to the progressive failure of islet cells to secrete sufficient amounts of insulin to overcome peripheral insulin resistance, ultimately resulting in failure to maintain normal glucose homeostasis over time. However, the rate of β -cell failure is unpredictable and not all persons with Type 2 diabetes will need insulin therapy to maintain their blood glucose levels (7).

Several factors may have a bearing on β -cell function, including healthy lifestyle – especially regular physical activity and exercise. Healthy life style provides clues to developing strategies to ameliorate the long-term management of Type 2 diabetes. The data on the effects of exercise training on β -cell function are not well known. Farbod et al. (2014), for example, reported that β -cell function improved and fasting glucose decreased after 6 weeks aerobic exercise (8). However, Mahmudzadeh et al. (2014) showed that 6 weeks of aerobic training had not significant effect on β cell function in streptozotocin-induced diabetic rats (9). Thus the aim of present study was to investigation of the effect of 8 weeks aerobic training on pancreatic β -cells function and insulin resistance in female patients with type 2 diabetes.

2. Materials and methods

Subjects

Twenty middle-aged women (age, 40 -50 years) with Type 2 diabetes participated in the present study as the subject. Participants were

inactive, non-smoker and nonpregnancy. All subjects were non-smokers and had not participated in regular exercise/diet programs for the preceding 6 months. The exclusion criteria were as follows: Patients with known history of acute or chronic respiratory infections, neuromuscular disease, and cardiopulmonary disease. In addition, exclusion criteria included inability to exercise and supplementations that alter carbohydrate and fat metabolism. The subjects were given both verbal and written instructions outlining the experimental procedure, and written informed consent was obtained. The study was approved by the Islamic Azad University, Marvdasht branch Ethics Committee. VO_{2peak} of the subjects was determined via Rockport walking test and the subjects were divided into training group ($n=10$) or control group ($n=10$) based on their VO_{2peak} .

Exercise training

The subjects in the training group performed 30 to 45 min aerobic training on the treadmill with 60-75% of their maximum heart rate, 3 days a week for 8 weeks. Each participant was equipped with a heart rate monitor (Polar, FS3c, Finland) to ensure accuracy of the exercise level. The subjects in the control group were instructed to maintain their normal physical activity throughout the study.

Anthropometric and body composition measurements

Height and body mass were measured, and body mass index (BMI) was calculated by dividing body mass (kg) by height (m^2). Waist circumference was determined by obtaining the minimum circumference (narrowest part of the torso, above the umbilicus) and the maximum hip circumference while standing with their heels together. The waist to hip ratio (WHR) was calculated by dividing waist by hip circumference (cm) (10). Body fat percentage was assessed by skinfold thickness protocol. Skinfold thickness was measured sequentially, in triceps, abdominal, and suprailiac by the same investigator using a skinfold caliper (Harpenden, HSK-BI, British Indicators, West Sussex, UK) and a standard technique (10).

Measurement of peak aerobic capacity

Rockport walking test was conducted 48 hours before taking blood sample and 48 hours after last session of aerobic training. $VO_{2\text{peak}}$ was calculated using the below formula (11):

$$VO_{2\text{peak}} = 139.68 - (0.388 \times \text{age}) - [0.077 \times \text{body mass (pound)}] \\ - [3.265 \times \text{time (min)}] - [0.156 \times \text{heart rate (bpm)}]$$

Blood samples and laboratory analysis

Fasting blood samples were collected at rest (before training) and after last session of training. All the subjects fasted at least for 12 hours and a fasting blood sample was obtained by venipuncture. Blood samples were kept in the temperature of -20°C . Glucose was determined by the oxidase method. Insulin was also determined by ELISA kit (Merckodia, Sweden). The intra and inter-assay coefficients of variation for glucose were $<1.3\%$ and a sensitivity of 1 mg/dl.

β -cell function was assessed with the HOMA-B model and insulin resistance was calculated using the HOMA-IR model (12,13).

Statistical analysis

Results were expressed as the mean \pm SD and distributions of all variables were assessed for normality. Data were analyzed using independent and paired sample t-test. The level of significance in all statistical analyses was set at $P < 0.05$. Data analysis was performed using SPSS software for windows (version 17, SPSS, Inc., Chicago, IL).

3. Results

Anthropometric and body composition parameters of the subjects are presented in Table 1. The results indicated that body weight, BMI and body fat percent were decreased and $VO_{2\text{peak}}$ was increased in the training group in compare to the control group ($P < 0.05$). For WHR no significant change was observed after the intervention.

Table 1. Anthropometric and metabolic characteristics (mean \pm SD) of the subjects before and after training

	Control (mean \pm SD)		Training (mean \pm SD)	
	Pretraining	Posttraining	Pretraining	Posttraining
Body mass (Kg)	77.3 \pm 10.9	78.5 \pm 11.0	77.6 \pm 9.1	76.0 \pm 9.0*
BMI (Kg/m ²)	31.9 \pm 3.6	32.4 \pm 3.5	32.5 \pm 3.6	31.9 \pm 3.5*
Body fat (%)	30.6 \pm 3.4	31.1 \pm 3.9	32.2 \pm 0.4	31.7 \pm 0.5*
WHR	1.0 \pm 0.1	0.98 \pm 0.07	1.0 \pm 0.08	0.99 \pm 0.09
VO _{2max} (ml.Kg ⁻¹ .min ⁻¹)	33.4 \pm 5.4	31.6 \pm 4.5	29.8 \pm 5.1	37.6 \pm 4.6*

*: P<0.05 for between-group differences.

†: P<0.05, pretraining *vs.* posttraining values.

Biochemical parameters of the subjects are presented in Table 2. The results indicated that fasting glucose, fasting insulin and insulin resistance determined by HOMA-IR improve after 8 weeks aerobic training (P<0.05), but these training had not significant effected on β -cell function determined by HOMA-B.

Table 2. Changes of the biochemical parameters of the subjects before and after training

	Control (mean \pm SD)		Training (mean \pm SD)	
	Pretraining	Posttraining	Pretraining	Posttraining
Fasting glucose (Kg)	146.9 \pm 58.0	153.8 \pm 59.0	146.2 \pm 53.1	129.6 \pm 48.5*
Fasting insulin (Kg/m ²)	8.4 \pm 3.6	9.1 \pm 6.0	8.3 \pm 2.1	5.4 \pm 2.3*
HOMA-IR	3.1 \pm 2.0	3.3 \pm 2.5	2.9 \pm 1.2	1.5 \pm 0.7*
HOMA-B	47.9 \pm 33.4	53.8 \pm 48.4	46.8 \pm 21.4	41.7 \pm 21.4

*: P<0.05 for between-group differences.

†: P<0.05, pretraining *vs.* posttraining values.

4. Discussion

Type 2 diabetes (formerly called non-insulin-dependent, or adult-onset) results from the body's ineffective use of insulin. Type 2 diabetes comprises the majority of people with diabetes around the world, and is largely the result of excess body weight and physical inactivity. Previous studies indicated that exercise training is a useful therapy for improving insulin resistance (14-16). The results of the current study in line with previous studies demonstrated that fasting glucose, fasting insulin and insulin resistance determined by HOMA-IR improve after 8 weeks aerobic training. Insulin resistance is marked by a decreased

responsiveness to metabolic actions of insulin such as insulin-stimulated glucose disposal and inhibition of hepatic glucose output (17). The exercise-induced increase in insulin sensitivity is believed to reflect adaptations in muscle insulin signaling (18,19), glucose transporter type 4 (GLUT4) protein expression, content and action (20,21) and associated improvement in insulin-stimulated glucose disposal and glycogen synthesis (18,19). This is accompanied and influenced by enhanced intramyocellular oxidative enzyme capacity and possibly changes in muscle architecture from fast-type to slow-type fibers (22,23).

Exercise increases insulin-mediated GLUT4 translocation to the sarcolemma and subsequent glucose uptake, which may reflect a transient elevation as a consequence of the "last bout" (20). The underlying increase in GLUT4 transcription and expression of GLUT4 mRNA has been shown to persist for 3 to 24 hours after exercise (21,24). In this way, regular exercise translates into a steady-state increase of GLUT4 protein expression, and subsequent improvement in glucose control over time (21). Similarly, enhanced whole-body insulin sensitivity has been shown to occur in the hours immediately following exercise, and evidence from a limited number of studies using hyperinsulinaemic-euglycaemic clamp and oral glucose tolerance test (OGTT) suggests that this may persist for up to 24 to 72 hours after the last bout (25-27).

The results indicated that our training had not significantly affected β -cell function determined by HOMA-B. There is still the issue of which between insulin resistance and HOMA β -cell precedes the occurrence of diabetes (28). In the case where insulin resistance is argued to be the primary cause, decline in the function of β -cell is the later response to the gradual increase in insulin secretion due to the insulin resistance. However, those who argue that the malfunction of β -cell as the primary cause of diabetes state that the reduction in the insulin secretion is the reason that normal blood sugar levels would increase (29). In addition, the HOMA-IR index seems to reflect insulin resistance, but there is still room for discussion regarding the correlation between HOMA β -cell index and the β -cell function of the pancreas.

Haffnet et al. (1996) noted that the β -cell malfunction is the primary cause of diabetes (30). Through regular exercise, less insulin can carry

the same amount of glucose to muscles and the liver. Therefore, β -cells in the pancreas do not have to excessively secrete insulin, resulting in decreased HOMA-IR and HOMA β -cell indexes (30). The mechanisms behind the improved pancreatic β -cell function to increase insulin action could be multifaceted, including perhaps an improved coordinated feedback loop between liver (decreased hepatic gluconeogenesis), muscle (attenuated insulin resistance) and pancreas (slowly wakening of β islets to secrete insulin). However, given that type 2 diabetes is a disease characterized by perturbations in several organs, anti-inflammatory cytokines secreted by both adipocytes (e.g. adiponectin) and myocytes (e.g. IL-6) could be involved in the improvement of pancreatic β -cell function (31). Although we had not measured the inflammatory and anti-inflammatory cytokines, not significant change in β -cell function might due to unchanged on these cytokines in the present study.

5. Conclusion

In summary, it seems that aerobic training utilized in this study improves glucose entry into cells but it had not effective on pancreatic β -cells function.

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Conflict of interests: No conflict of interests amongst authors.

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