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The 10-week of aerobic-functional training improves fasting blood sugar, insulin resistance, and lipid profile in patients with diabetic peripheral neuropathy: A randomized controlled trial

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Abstract

Study aim: This study aimed to investigate the effect of a 10-week of combined training course on concentrations of blood sugar, Insulin Resistance (HOMA-IR), and lipid profile in patients with diabetic peripheral neuropathy.
Materials and methods: This clinical trial was performed in diabetic neuropathy women and men (30–60 years old). Participants were randomly assigned to two groups: exercise (EG; n = 10) and control (CG; n = 10). The EG performed 10-week programme with one session of aerobic exercises (40% to 70% of $HR_{Reserve)}$ and one session of functional exercises (60–90 min/day) at the same day for four days/week and the CG performed their daily activities. The Blood glucose, IR, and lipid profile were measured initially and after the intervention.
Results: Repeated-measures ANOVA showed significant decrease in fasting blood sugar ($p < 0.01$) and HOMA-IR ($p < 0.01$), and greater improvements in TG ($p < 0.05$) and LDL ($p < 0.05$) in EG than CG, but. HDL concentration did not show significant changes.
Conclusion: The 10-week of aerobic-functional training improves fasting blood sugar, IR, and lipid profile in patients with diabetic neuropathy.

Key words: Combined exercise – Insulin Resistance (HOMA-IR) – Lipid profile – Diabetic neuropathy

Introduction

Diabetes is one of the largest metabolic diseases in the world, which is highly prevalent in developed and developing countries [14]. The disease can cause a number of neurological, blood vessel, and lymphatic vessel disorders [8]. The most common complication of diabetes is Diabetic Peripheral Neuropathy DPN [14, 33]. DPN is a common disorder of the peripheral nervous system that may be associated with a variety of weaknesses, autonomic changes, and sensory changes [13]. The International Diabetes Federation estimates that 425 million people worldwide have diabetes, of which more than 50% have neuropathy and this is the biggest global epidemic of the 21st century [12, 29]. Without successful intervention, it is estimated that out of the expected population of 9.7 billion by 2050, one-third will have diabetes, and half of this population will have neuropathy [12]. The exact mechanisms in the pathogenesis of DPN are still unknown due to the multifactorial nature of the disease. However, chronic hyperglycemia with Insulin Resistance appears to be at the forefront of DPN causes [14, 28].

Common risk factors for vascular disease in diabetics, especially type 2 diabetes, include hyperglycemia, insulin resistance, lipid dysfunction, hypertension, and tobacco use and obesity [11]. Insulin resistance IR indicates the relative insensitivity of peripheral tissues such as muscle, liver and adipose tissue to the effects of the insulin hormone [27]. Previous research has shown that Insulin Resistance IR, low levels of High-Density Lipoprotein HDL and high triglycerides TG are significantly effective in the

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prevalence and development of peripheral neuropathy [7]. Despite regular blood sugar control, diabetic neuropathy can be affected by insulin resistance, and in patients with insulin resistance, the control of dyslipidemia can prevent the development of diabetic neuropathy or slow its progression [7]. Non-pharmacological treatment of diabetes mellitus is based on lifestyle changes including physical activity, diet and smoking habits [6, 16]. In addition, in people with diabetes, regular physical activity reduces the use of anti-diabetic drugs and insulin doses [31].

Most of the benefits of the exercise and management of type 2 diabetes are related to improving insulin function [10]. Exercise and diet are the cornerstones of diabetes treatment [15, 24 ,26]. Various studies have investigated the effects of exercise on blood sugar indices, insulin resistance, and lipid profile in patients with type 2 diabetes. Some of these studies have reported a significant reduction in insulin resistance following aerobic as well as aerobic-resistance training [1, 30]. In contrast, Tatjana et al. [30] reported that after 12 weeks of aerobic, resistance, and combination exercises in type 2 diabetic patients, despite a decrease in fasting blood sugar, no significant reduction in insulin resistance was observed in these groups [30]. The Bello et al. (2011) study following 8 weeks of aerobic exercise in diabetic patients also did not report significant changes in HDL, Low Density Lipoprotein LDL, and FBS levels [3].

Medication has beneficial effects on the risk of sequelae, but it is not enough to reverse the sequelae of diabetes [6]. Despite the effectiveness of exercise on blood sugar control and insulin resistance in some studies [11, 30], the effectiveness and response methods of exercise in people with DPN are not known [17].

Few studies have examined the effect of weight-bearing exercise on blood sugar control and insulin resistance due to fear of foot injuries and foot ulcers in patients with DPN neuropathy. While it has recently been reported that these patients can use weight-bearing exercises such as walking and running [18, 25]. Therefore, considering the contradictory exercise recommendations in physical activity prescription and the lack of studies performed in patients with DPN, the present study aimed to investigate the effect of a combined training course on blood sugar, insulin resistance and lipid profile in patients with diabetic peripheral neuropathy.

Material and methods

Participants

Among the patients referred to the Research Institute of Endocrinology and Metabolism of Iran University of Medical Sciences (men and women), 48 patient volunteers (age, 30–60 years) with type 2 diabetes and peripheral neuropathy were selected and introduced for further assessment. Inclusion criteria included: (Diagnosis of type 2 diabetes for more than five years, glycosylated hemoglobin in between 6.6% to 12%, lack of regular exercise, lack of specific medical conditions such as the history of heart attack, stroke, no medical prohibition from exercise, report of diabetic peripheral neuropathy in medical records, presence of clinical signs of diabetic peripheral neuropathy in the questionnaire by Michigan questionnaire).

Design

The research was a quasi-experimental two-group study (Exercise and Control) with pre and post-intervention measurements. The present study was approved by the Committee of Ethics in Research at Tehran University and registered in the Iranian Clinical Trial Registration Center (IR.UT.SPORT.REC.1400.014).

After careful examination, 20 (11 women and 9 men) people (51.55 ± 5.57 years, 167.12 ± 9.54 cm height, 76.72 ± 10.92 kg weight) were selected as a sample based on inclusion criteria. Initially, a clinical examination of the subjects' feet was performed by a technician to diagnose the loss of protective sensation (LOPS) in the foot clinic of the Endocrine and Metabolism Research Institute of Iran University of Medical Sciences, which included: (10 g monofilament, 128 HZ tuning fork, pinprick sensation, ankle reflex, foot temperature (cold-warm test). Nerve conduction studies NCS were then performed by a neurologist on the right leg of the subjects to diagnose diabetic peripheral neuropathy more accurately. Participants were randomly assigned to exercise (EG = 10) and control (CG = 10) groups. The CG was then be asked to maintain their normal diet, daily activities and medication intake during the 10-week research period. They were also asked to notify the researcher in the event of any changes. The subjects of EG, besides their regular diet such as the control group, performed exercises four times a week for ten weeks in the morning during the training days in the gym with proper air conditioner and temperature. The intensity and duration of the exercises were adjusted according to the training protocol (Table 1). Each training session was started with 10 minutes of warm-up, including walking and stretching exercises, followed by aerobic exercises on the treadmill and then special lower extremity exercises based on the protocol. At the end of each session, 10 minutes of cool-down training were performed. The aerobic exercise intensity for each individual was determined using the Carvonen equation. A Polar heart rate monitor was used to observe the subjects' heart rate during each session. Also, to prevent possible consequences and hypoglycemia, the subjects' blood sugar was measured in the training sessions before and after the training using a glucometer. The participants were asked to stop that session if the blood sugar levels were inappropriate,

Blood sample

Twenty-four hours before the start of training and 48 hours after the last training session, the subjects went to the laboratory observing the fasting conditions. The sampled blood was placed in a tube that was not treated for anticoagulation and was then centrifuged at 3,000 rpm using a centrifugal separator for 10 minutes. After extracting the serum from the cellular components, the serum was put in a storage tube and stored in the refrigerator at –70ºC until analysis. Blood lipid profiles Triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and glucose were measured with Biolis 24i, Tokyo, Japan, with the method of Calorimetry (Pars Azmoon kit made in Iran), insulin by ELISA method using ELISA reader and by Mono kit (kit made in Iran), and Insulin Resistance index based on the following formula [20, 27]:

$$\text{HOMA-IR} = \frac{\text{fasting glucose [mg/dl]} \times \text{fasting insuline [µU/ml]}}{405}.$$

Exercise protocol

The exercise group first performed aerobic exercises and then unilateral special exercises for the lower limb. The intensity and duration of the exercises were applied during the research according to the training protocol Table 1. Each session began with 10 minutes of warm-up exercises, including walking and stretching. Then the subjects performed aerobic exercises on the treadmill and then special unilateral exercises on the right leg. These exercises were performed under the direct supervision of an exercise physiologist. The aerobic exercise intensity was stored at 40% to 70% of the heart rate reserve and was calculated using the Carvonen equation.

Statistical analysis method

Data were analyzed using SPSS for Windows version 26. Distribution of data was assessed for normality using Shapiro-Wilk test. The data were normally distributed, therefore, were analyzed using parametric methods. Repeated-measures analysis of variance was applied to analyze the changes between groups, with significant time × group interaction showing significant inter-group differences. Paired t-test was also used to compare the pre-test (week 0) and post-test (week 10) values.

Results

Mean and standard deviation of demographic information, fasting blood sugar, insulin, insulin resistance index, and lipid profile are presented in Table 2. There was no significant difference between the groups before the intervention $p \geq 0.05$. Based on the information in Table 2, there was significant difference in weight and body mass index between groups ($p = 0.01$, $p = 0.03$, respectively). Fasting blood glucose, insulin, and insulin resistance index HOMA-IR significantly decreased compared to the control group following Repeated measure analysis ($p = 0.004$, $p = 0.002$, $p = 0.001$, respectively). Changes in triglyceride ($p = 0.02$). and LDL ($p = 0.03$) levels were significant and showed a significant decrease compared to the control group (Table 2). Ten weeks of aerobic-functional training

Table 1. Exercise training protocol

Aerobic exercises				Functional exercises	Set × repetition
Weeks	Time	Intensity (%HRR)	Sessions per week		
1st and 2nd weeks	20	40–55%	4	1. Dorsi flexion side lying	3 × 5
3rd and 4th weeks	25	50–55%	4	2. Plantar flexion on gym ball	3 × 5
5th and 6th weeks	30	55–60%	4	3. Raise the heel for 20 seconds	1 × 5
7th and 8th weeks	35	60–65%	4	4. Stand on one foot for 15 seconds	1 × 5
9th and 10th weeks	40	65–70%	4	5. unipedal wobble board	1 × 3
				6. inversion	3 × 5
				7. eversion	3 × 5
				8. toe extension on the step	3 × 5
				9. toe flexion on the step	3 × 5
				10. tennis ball rolling	1 × 5
				11. ankle rotation	3 × 5

Table 2. Mean ± SD demographic information and anthropometric indices after(post) the intervention among groups

Variables	Control		Exercise	
	Pre	Post	Pre	Post
Gender (Female/Male)	(5 Female 5 Male)		(6 Female 4 Male)	
Age [years]	51.2 ± 6.5		51.9 ± 4.7	
Height [cm]	169.1 ± 8.3		165.1 ± 10.64	
Weight [kg]	77.95 ± 10.85	78.14 ± 10.88	76.48 ± 11.98	75.31 ± 11.36*,**
[1]BMI [kg/m^2]	27.12 ± 1.86	27.19 ± 1.69	27.96 ± 2.99	27.54 ± 2.8 1*,**
[2]FBS [mg/dl]	171.1 ± 44.28	174 ± 39.87	174.1 ± 34.01	145.9 ± 19.04*,**
Insulin [μU/ml]	8.81 ± 3.42	9.08 ± 2.8	8.46 ± 3.36	5.98 ± 3.06*,**
[3]HOMA-IR	3.70 ± 1.45	3.87 ± 1.37	3.53 ± 1.40	2.09 ± .87*,**
[4]TG [mg/dl]	187 ± 62.1	193.3 ± 56.13	179 ± 47.48	146.8 ± 21.89*,**
[5]HDL [mg/dl]	53.1 ± 9.6	54.5 ± 8.92	54 ± 13.5	59.5 ± 14.69
[6]LDL [mg/dl]	107.5 ± 25.1	110.1 ± 20.96	109.2 ± 35.6	95.1 ± 26.89*,**

* Significantly ($p < 0.05$) different from pre-test to post-test values. ** Time × group interaction is significant ($p < 0.05$). [1] – Body Mass Index, [2] – Fasting Blood Sugar, [3] – Homeostatic Model Assessment, [4] – Triglyceride, [5] – High Density Lipoprotein, [6] – Low Density Lipoprotein.

did not also cause a significant difference in HDL between the groups ($p = 0.2$).

Discussion

Performing ten weeks of aerobic-functional training in patients with diabetic peripheral neuropathy caused a significant change in weight, fasting blood sugar, insulin resistance HOMA-IR and a change in the lipid profile of these patients.

Fasting blood glucose, insulin and HOMA-IR were significantly reduced compared to the control group following analysis. These results were consistent with the findings of Nadi et al. [22] Tatjana et al. [30], and Motahari-Tabari et al. [21]. Nadi et al. [22] compared the effect of two types of exercise in patients with mild to moderate diabetic neuropathy. They showed a significant reduction in fasting blood sugar in both groups after performing 12 weeks of special lower extremity training and resistance training with 30% intensity. Also, Tatjana et al. [30] examined the effect of 6 months of aerobic exercise 3 to 5 sessions per week. At the end of the study, the exercise group showed a significant decrease in fasting blood sugar and HOMA-IR index compared to the control group. In contrast, Jorge et al. [15] compared the effects of 3 different modalities of exercise on metabolic control, insulin resistance, inflammatory markers, adipocytokines, and tissue expression of insulin receptor substrate (IRS)–1 among patients with type 2 diabetes mellitus. Despite of a significant reduction in blood sugar, no reduction in HOMA-IR was observed between groups. In this study, which was performed for 12 weeks and three sessions per week, compared three methods of aerobic, resistance and combined training on men and women with type 2 diabetes. Reasons for contradiction with the results of the present study include 60 minutes vs. 90 minutes of training and also the number of sessions per week 3 sessions versus 4 sessions per week. In the present study, 10 weeks of aerobic-functional exercise reduced blood sugar and reduced insulin resistance. Exercise acutely increases muscle glucose uptake by up to 5-fold through insulin-independent mechanisms and can therefore be used as one of the mechanisms for lowering blood sugar [10]. Also, insulin resistance can cause various physiological disorders by reducing the insulin response in target tissues such as liver, muscle and fat tissue. It has recently been reported that insulin resistance is independently associated with peripheral neuropathy in patients with type 2 diabetes [7]. Therefore, reducing insulin resistance can be used as a tool to prevent or slow the development of diabetic neuropathy. Exercise can reduce insulin resistance by increasing insulin sensitivity in skeletal muscles as well as increasing the expression of insulin receptors [4, 15, 32]. Skeletal muscle accounts for approximately 75–95% of whole-body glucose disposal [2]. During exercise, muscle contraction increases glucose uptake by skeletal muscle independent of insulin, and this mechanism is active even in diabetics with insulin disorders [5, 9]. In the present study, exercise also decreased triglyceride and LDL content, while it had no significant effect on the increasing high-density lipoprotein HDL. These results were consistent with the results of several studies [15, 19, 23]. However,

our findings were inconsistent with the results of a study by Jorge et al. [15]. Several studies have recently reported the role of dyslipidemia in developing microvascular and macrovascular complicationsin diabetic neuropathy. Lipid control is a new treatment strategy in patients with type 2 diabetes. Previous studies have reported that excessive fat delivery due to elevated triglycerides to mitochondria increases reactive oxygen species and alters cellular redox potential and can ultimately lead to insulin resistance [7]. Increased fat oxidation as an energy substrate, both during exercise and during recovery, is the main mechanism of exercise activity in lipid profile improvement and reducing triglyceride content [23].

Conclusion

According to the present study results, ten weeks of aerobic-functional training has a significant effect on reducing fasting blood sugar, HOMA-IR, and triglycerides. Insulin resistance and dyslipidemia independently affect the development of diabetic neuropathy. Therefore, based on the results of the this study, the use of aerobic-functional exercise could be effective in the treatment of these patients.

Conflict of interest: Authors state no conflict of interest.

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