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Response of Growth Hormones and Cortisol to One Session of Moderate-Intensity Endurance Exercise in Patients with Type 2 Diabetes: A Quasi-experimental Study

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Abstract

Background: Therapeutic interventions for diabetes are one of the main components of treatment and having proper physical activity in these patients is important from different physical, psychological, and social aspects. The benefits of exercise in these people include improved cardiovascular health and increased self-confidence, contributing to maintaining proper weight, controlling blood pressure, lowering blood lipids, and lowering insulin levels. The objective of this study was to assess the baseline levels of growth hormones and cortisol and the response of these 2 hormones to 1 session of moderate-intensity exercise in type 2 diabetic patients and to compare them with healthy individuals.

Methods: This was a quasi-experimental and applied study, with a pretest and posttest design and with 1 control group. Participants included 12 healthy people without diabetes and 12 patients with type 2 diabetes aged over 30 years who were referred to the Diabetes Clinic of Tohid hospital, Kurdistan, Iran. After describing the objectives and hypothesis of the study and the implementation method, informed consent was obtained from all participants. SPSS Version 22 software was used for data analysis and coding. The Shapiro-Wilk normality test was used to assess data distribution. A paired t test, an independent t test, the Wilcoxon test, and the Mann-Whitney U test were used to compare outcomes between the 2 groups before and after the intervention.

Results: A total of 24 individuals were included: 5 men and 7 women were included in the diabetic group and 7 men and 5 women were included in the healthy group. The mean duration of diabetes in the diabetic group was 7.82 years. The results showed that there was no reason for rejecting a relationship between 1 session of moderate-intensity exercise and increased growth hormone secretion in healthy individuals (p=0.010), but the relationship between this factor and increased growth hormone secretion in the diabetic participants could be strongly rejected (p=0.900). Also, 1 session of the moderate-intensity exercise was not significantly correlated with cortisol secretion in healthy and diabetic participants (p>0.05).

Conclusion: This study revealed that baseline growth hormone levels in healthy participants were higher than those of diabetic participants and 1 session of moderate-intensity exercise significantly increased the growth hormone secretion but did not significantly increase the cortisol secretion.

Keywords: Type 2 Diabetes, Growth Hormone, Cortisol, Moderate-Intensity Exercise

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Introduction

Diabetes is a group of metabolic diseases characterized by a chronic increase in blood glucose and impaired car-

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↑What is "already known" in this topic:
Various studies showed that the role of cortisol and growth hormone in coping with hypoglycemia attacks in diabetic patients has been proven. As a result, it's critical to investigate the link between cortisol and growth hormone and hypoglycemia control in Iran.

→What this article adds:
The baseline growth hormone levels in healthy participants were higher than those of diabetic participants and 1 session of moderate-intensity exercise significantly increased the growth hormone secretion but did not significantly increase cortisol secretion.

bohydrate, fat, and protein metab olism. It is one of the major health problems in many countries, especially in less developed areas (1-3). The International Diabetes Federation predicts that the number of people with diabetes around the world will reach 592 million by 2035. About 77% of diabetic patients are living in less developed areas (American Diabetes Association) (4-6). In Iran, based on the statistics reported by the Ministry of Health Center for Prevention of Non-Communicable Diseases Prevention, the prevalence of diabetes was estimated at 11.3% in 2011, equivalent to 4.5 million diabetic patients. These statistics have increased up to 35% compared with 2005. It is also estimated that about 9.2 million Iranians will have diabetes (7-11). Type 2 diabetes accounts for over 90% of diabetes and is caused by the resistance of target tissues to the effect of insulin on the body. In patients with type 2 diabetes, impaired cortisol secretion is one of the major factors involved in insulin resistance and metabolic syndromes, such as obesity, hypertension, dyslipidemia, type 2 diabetes, and cardiovascular events. Increased cortisol secretion causes diabetes and exacerbates the metabolic status of diabetes. Also, the relationship between cortisol levels, insulin resistance, and disease complications has long been investigated and there are still many ambiguities in this regard (12-15).

In this regard, therapeutic interventions for diabetes disease are one of the main components of treatment, and having proper physical activity in these patients is important from different physical, psychological, and social aspects. The benefits of exercise in these people include improved cardiovascular health and increased self-confidence, contributing to maintaining proper weight, controlling blood pressure, lowering blood lipids, and lowering insulin levels. Also, exercise with sufficient intensity can stimulate the secretion of counter-regulatory hormones, such as glucagon, catecholamine, growth hormone, and cortisol (12, 16, 17).

Cortisol and growth hormone are vital hormones in coping with hypoglycemia attacks in diabetic patients with a variety of mechanisms, including increased hepatic glucose synthesis and reduced glucose uptake by peripheral tissues leading to an increase in blood glucose level. Thus, impaired secretion of these hormones in diabetic patients can result in loss of one of the important mechanisms of the body in coping with hypoglycemia attacks (18-20). As growth hormone and cortisol secretion in response to physical activities in healthy individuals have been investigated in different studies and as the role of cortisol and growth hormone in coping with hypoglycemia attacks in diabetic patients has been proven, this study was conducted to assess the level growth hormone and cortisol levels and the response of these two hormones following a moderate-intensity exercise session in type 2 diabetic patients and compare it with healthy people.

Methods

This was a quasi-experimental study with a pretest and post-test design and a control group. Participants included 12 healthy individuals without diabetes and 12 patients with type 2 diabetes who were over 30 years old and referred to the diabetes clinic of Tohid hospital in Sanandaj, Iran, and were treated with oral blood glucose-lowering drugs. After describing the objectives of the study and the implementation method, informed consent was obtained from all participants to participate in the study. All participants were asked to avoid exercising and using caffeine, fatty foods, and alcohol at least 24 hours before the exercise test. All patients were studied at the start of the morning while they were fasting. They were randomly selected based on inclusion and exclusion criteria. Patients whose diabetes was confirmed by a specialist physician, patients who were treated with oral blood glucose-lowering drugs, and patients with desired maximal heart rate were included in the study. Patients with underlying, cardiovascular, and heart failure diseases, previous history of stroke, liver and kidney failure and amputation, hypoglycemia in the last 48 hours, bilateral blindness and cancer, consumption of caffeine and fatty foods, alcohol consumption 24 hours before exercise, and those who exercised 24 hours before the exercise test were excluded from the study. Before the test, demographic characteristics, including age, gender, duration of diabetes, used drugs, history of diabetes complications (cardiac, renal, ocular, nervous, foot ulcer, hypoglycemia, and liver failure), and body mass index were obtained from patients and recorded in the information collection checklist.

The instruments used in this study included a treadmill, a weighing scale, a height meter (Seca), a chronometer (manufactured in Japan), an electrocardiogram (ECG); a contour plus glucometer, a test tube, and a blood storage chamber. Before starting exercise, a proper intravenous line (IV line) was taken and a blood glucose sample was measured and recorded with a glucometer. If the glucose level was less than 100 before exercise, the oral carbohydrate level was given to the patient and the glucose level increased to over 100. Then, the protocol of the project was explained to the patient and the training needed to perform the exercise correctly was given to achieve desired MHR. Bruce protocol and exercise on a treadmill were used. Bruce maximal test on a treadmill is the most commonly used exercise test for estimating oxygen consumption. This test is performed in a maximum of 6 to 7 steps and lasts 3 minutes for each step. Increasing the intensity of the activity from one step to the criteria. The median for diabetic patients before the next step is associated with increased speed and slope. The first step starts at 1.7 miles per hour and a 10% slope, then, the speed and slope of the device increase at a constant ratio in each step. To modify the usual protocol due to the limitation in the activity intensity in the diabetic patients, the patients continued the exercise at the heart rate of 64% to 76% of maximal heart rate (MHR) up to the failure level, and then the exercise was stopped. According to the American College of Sports Medicine, moderate-intensity exercise is defined as the percentage of VO_2max 45% to 62% or a heart rate between 64% and 76% of maximal MHR. To measure the MHR, the formula age-220 in men and age-210) in women was used. During the exercise, the heart electric status was recorded by a 12-lid electrocardiogram (ECG), and blood pressure and heart rate status were recorded by digital monitoring. In the case of a drop in glucose <70 mg/dL, exercise was discontinued and 15 g of oral glucose was administered and the blood glucose was measured 5 to 15 minutes, and if the glucose level reached over 70, exercise did not start. Also, in the case of chest pain, excessive fatigue, and feeling of a light head or excessive fatigue, symptoms of hypoglycemia, or test syncope were stopped.

Blood samples were taken before and immediately after completion of the activity via the cubital vein. The samples were placed in an anticoagulant-containing tube (EDTA), and immediately centrifuged, and the obtained plasma was used to measure growth hormones and cortisol. To determine the growth hormone level of each blood sample, Kit-Siemens Immulite (No. 181 and Model 2000) through enzyme-linked immunosorbent assay (ELISA) was used. The level of cortisol hormone of each blood sample was also measured using the Mindray Mindray Kit (No. 2017060100, Model CL6000) through the ELISA method. The unit of cortisol measurement was µg/ dL and the unit of growth hormone measurement was ng/mL.

Statistical Analysis

SPSS Version 22 software was used for data analysis and coding (21). The Shapiro-Wilk normality test was used to assess the distribution of data. A paired t test was used to compare the values of cortisol hormone in pretest and posttest stages in both groups (healthy and diabetic participants). An independent t test was also used to compare the values obtained between the 2 groups. The Wilcoxon test was used to compare the data of growth hormone secretion in each group before and after 1 exercise session, and the Mann-Whitney U test was used to compare the levels of growth hormones between the 2 groups before and after the intervention. The significance level was considered at $P \leq 0.05$.

Results

In the present study, out of 24 participants studied, 5 men and 7 women were included in the diabetic group and 7 men and 5 women were included in the healthy group. Results showed that the mean duration of diabetes in patients was 7.82 years (Table 1).

The results also revealed that the mean of cortisol in the blood serum of diabetic patients before and after the intervention was 11.20 and 12.09, respectively, and the mean of cortisol in the blood serum of the healthy participants was 10.95 and 11.06, respectively (Table 2).

The results of investigating the relationship between independent variables and growth hormone and cortisol in the 2 groups revealed no significant relationship between age (p=0.666), weight (p=0.100), body mass index (p=0.450), duration of diabetes (p=0.120), complications of diabetes (p=0.200), and MHR (p=0.640). None of the relationships was statistically significant (Table 3).

The results of the Wilcoxon test at a significant level of.05 revealed that there is no reason to reject the relationship between 1 session of moderate-intensity exercise and an increase of growth hormone secretion in healthy participants (p=0.010). However, the relationship between this factor and growth hormone secretion in diabetic participants can be strongly rejected (p=0.900). Paired t test results showed that exercise was not significantly associated with cortisol hormone secretion in healthy and diabetic participants (p=0.200, p=0.830) (Table 4).

Discussion

The goal of this study was to compare the effects of 1 session of moderate-intensity exercise on the secretion of growth hormone and cortisol in patients with type 2 diabetes to healthy participants. In the present study, the percentage of relative changes in the serum levels of growth hormone and cortisol after 1 session of moderate-intensity exercise was not significantly different between men and women in each of the study groups. These results were in line with those of the study conducted by Jill et al (2001) who found no relationship between gender and hormone and cortisol secretion at baseline and after exercise (18). They are also in line with the results of the study conducted by Arthur et al in 2008 to investigate the effect of gender and body mass index on growth hormone and cortisol

Table 1. The Comparison of Demographic Characteristics in Diabetic Patients and Controls

Variable	Diabetes Group (n = 12)	Healthy Group (n = 12)
Age, y	51.00 ± 16.19	50.83 ± 10.75
Body mass index, kg/m^2	26.79 ± 4.82	26.53 ± 3.08
Maximal heart rate	140.36 ± 13.31	157.67 ± 14.45
Duration of diabetes	7.82 ± 5.65	-
Gender		
Male	5 (41.7)	7 (58.3)
Female	7 (58.3)	5 (41.7)

In this table, data are presented as mean (SD) or N (%).

Table 2. The Comparison of the Level of Hormones in Diabetic Patients and Controls

Hormones	Intervention	0.06 (0.04 - 0.10)	Healthy Group (n = 12)
Cortisol	Before	11.20 ± 3.83	10.95 ± 3.31
	After	12.09 ± 3.99	11.06 ± 2.80
Growth Hormone	Before	0.26 (0.07 - 0.74)	0.06 (0.04 - 0.10)
	After	0.31 (0.07 - 0.88)	0.07 (0.04 - 0.24)

In this table, data are presented as mean (SD) or median (P0.25, P0.75).

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Table 3. The Correlation Between Independent and Levels of Cortisol and GH

Variables	Growth Hormone (GH)		Cortisol	
	Correlation (r)	P Value	Correlation (r)	P Value
Age	-0.02	0.941	-0.15	0.666
Body mass index	0.16	0.630	0.52	0.100
Weight	0.28	0.390	0.25	0.450
Maximal heart rate	0.33	0.324	0.15	0.640
Duration of diabetes	0.30	0.370	-0.49	0.120
Complication	0.17	0.590	-0.42	0.200

Table 4. Response of Growth Hormones and Cortisol to 1 Session of Moderate-intensity Endurance Exercise in Patients with Type 2 Diabetes

Hormones	Groups		Mean ± SD Median	Z or T Statistics	P Value
Growth Hormone	Diabetic patients	Before	0.69 ± 0.990	-0.11*	0.900
		After	0.77 ± 1.321		
	Control	Before	0.06 ± 0.03	-2.42	0.010
		After	0.59 ± 1.25		
Cortisol	Diabetic patients	Before	11.20 ± 3.83	- 1.34**	0.200
		After	12.09 ± 3.99		
	Control	Before	10.95 ± 3.31	0.21	0.830
		After	11.06 ± 2.80		

*Wilcoxon Test, **Paired t test

secretion at baseline and during exercise. In this study, no association was reported between gender and the level of these hormones secreted during rest and exercise. Also, they are inconsistent with those of the study conducted by Pritzlaff et al (1999) who found that the response to growth hormone to exercise was higher in women than that in men (22). Sartorio et al (2004) investigated the impact of growth hormone on 99 athletes (61 men and 38 women) and the results showed that growth hormone was higher in women than that in men both at baseline and after exercise (23). This inconsistency in the results can be attributed to different sampling methods or the desired sample size. In the present study, there was no significant association between relative changes in the serum levels of growth hormone and cortisol and weight and body mass index in the healthy and diabetic participants. Also, based on the results of Wahl et al (24) and Weltman et al (25), the mean serum concentration of growth hormone was inversely associated with fat percentage and abdominal fat was associated with reduced growth hormone.

In the present study, no significant correlation was found between relative changes in growth hormone levels and cortisol and the age of healthy and diabetic participants. Based on the results of studies, the response of growth hormones and cortisol to exercise is reduced by increasing the age of participants. Weltman et al (1992) investigated the acute hormonal response to resistance exercises in the young and the elderly participants. The results showed a significant increase in blood growth hormone levels and young people showed a higher increase in hormones compared with elderly people (25). This study showed no significant correlation between relative changes in the serum levels of growth hormone and cortisol and the duration of disease in diabetic participants. Studies conducted on animal and human models have shown that growth hormone secretion is reduced in patients with type 2 diabetes. This is due to the increased secretion of somatostatin from the hypothalamus, and as a result, a reduction in growth hormone secretion from the pituitary. The effect of diabetes on growth hormone secretion varies depending on the etiology of diabetes. In type 1 diabetes, growth hormone secretion increases, and this increased secretion can cause significant metabolic and vascular complications in the patients.

The results of this study revealed that the MHR during the exercise in healthy participants was significantly higher than that of the diabetic patients. This result is in line with that of the study conducted by Owen et al (2002) who indicated that in diabetic patients, the response to cortisol and epinephrine hormones and physiological stimuli, including hypoglycemia, is impaired and the cortisol response returns to a normal level with insulin therapy (26). However, the epinephrine response does not return to normal eve with insulin therapy and remains impaired. In this study, the serum levels of growth hormone increased by about 2% in diabetic patients after 1 moderate-intensity exercise session, whereas it increased by about 35% in healthy participants. The difference in relative changes at this hormone level was not significant between the 2 groups at the borderline level.

Serum levels of cortisol increased by <1% in diabetic patients after 1 moderate-intensity exercise session and by 2% in healthy participants. There was no statistically significant difference in the percentage of relative changes in hormone levels between the 2 groups. In line with the results of the present study, Felsing et al (1992) also reported that growth hormone levels did not increase significantly after low-intensity exercises (27). Wahl et al (2010) also reported results similar to the results of this study (24). Eliakim et al (1998) also reported that although an increase in growth hormone levels occurred after 1 hour of volleyball exercise, no increase was observed in the levels of IGF-1 and proteins binding to it, IGFBP-3 (28). The discrepancies between studies can be linked to variances in exercise intensity, duration, and body mass index, which are all related to the participants' degree of fitness and body fat. The most powerful stimulation for growth hormone secretion is probably exercise. Exercise seems to affect the secretion of this hormone through a variety of mechanisms, such as nerve load, direct stimulation of catecholamine, nitric oxide, and lactic oxide, and changes in acid balance (29).

Gadfrey et al (2003) reported that increased levels of growth hormone secretion after moderate to high-intensity exercise could be attributed to increased nitric oxide and lactic acid and increased sympathetic activity (30). Nitric oxide is an essential intracellular and intercellular transmitter that regulates pituitary growth hormone release. Nitric oxide appears to help the pituitary release growth hormone.

Conclusion

The present study revealed that baseline growth hormone levels were higher in healthy participants compared with diabetic patients, and 1 moderate-intensity exercise session significantly increased growth hormone secretion in healthy participants but did not significantly increase the cortisol secretion. However, in diabetic patients, this type of activity did not significantly increase the secretion of growth hormone and cortisol.

Acknowledgment

Not applicable.

Ethical Approval

This research was approved by Sanandaj Branch, Islamic Azad University, Sanandaj, Iran (IR.IAU.SDJ.REC.1398.267).

Conflict of Interests

The authors declare that they have no competing interests.

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