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Acute Response of Serum Interleukin-6 to cycling test in adult men with type II Diabetes

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ABSTRACT: A large body of evidence suggests that obesity is associated with systemic inflammation, type II diabetes and insulin resistance. In this study, we investigated the effect of a braked cycle ergometer test on serum Interleukin-6 (IL-6) in type II diabetes patients. For this purpose, fifteen untrained adult obese men (age: 43 ± 4.8 years, BMI: 30.7 ± 2.24) with type II diabetes that participated in study voluntary were completed a braked cycle ergometer test. Pre and post exercise blood samples were obtained for measure serum IL-6 in studied patients. Paired t test was used to determine the mean differences between pre and post-exercise values. P<0.05 was considered significant. No significant differences were found in serum IL-6 by cycling exercise with compared to baseline (from 2.15 ± 0.65 to 2.26 ± 0.60 pg/ml, p = 0.628). We conclude that there is no meaningful acute effect of short time exercise in inflammatory profile in type II diabetes patients.

Keywords: Inflammation, Diabetes, Exercise, Obesity

INTRODUCTION

It is well known that obesity and its associated abnormalities is spreading in not only developed or industrialized but also in developing countries and that, at present, obesity is one of the main causes of mortality and of some irreversible diseases. Therefore, obesity has received considerable attention from researchers in health and healthcare in recent decades. Obesity is accompanied by increases in some intermediary inflammatory substances such as C-reactive protein (CRP), Interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α) [1, 2, 3]. Impaired secretion, and low levels, of inflammatory markers, especially in obese people, are also accompanied by lipid disorders [4] and result in many chronic diseases such as hypertension, type 2 diabetes, and respiratory, hepatic and various cardiovascular diseases all of which are also associated with obesity [5].

Among peptide mediators, IL-6 has inflammatory properties and plasma IL-6 levels affect energy homeostasis and regulation of lipid levels [6, 7]. Some scientific sources have pointed out that increased systemic levels of this cytokine are a predictive index for death in old people [8]. Increased levels of plasma IL-6 are accompanied by reduced muscle mass or decreased muscular movement [9, 10, and 11). Some previous research also reported its role in glucose homeostasis; and studies on animal models showed that IL-6 injections resulted in increased glucogenesis that led to increased blood glucose (hyperglycemia) and, eventually, in high blood insulin levels (hyperinsulinemia) [12].

Scientific studies indicate that balanced inflammatory cytokines resulting from exercises and diets lead to improvement in metabolic risk factors [13]. The role played by exercises in reducing systemic levels of inflammatory cytokines was studied numerous times, and exercise programs had different effects on these pro- or anti-inflammatory indices and also on other risk factors for cardiovascular diseases [14, 15]. Each of these studies, depending on the intensity, duration, and type of exercises, reported a different response [16, 17,18], while some stated short- or long-term exercises had no effect on inflammatory factors that influence the development of obesity [19, 20]. Furthermore, most research in this field investigated responses of inflammatory cytokines such as IL-6 to long-term exercises with the purpose of determining their responses to weight reduction resulting from exercise programs, and less frequently investigated the immediate response of these cytokines to one session of, or to short-term, exercise programs. Therefore, this study was conducted with the purpose of determining immediate responses of IL-6 levels to one session of(or to short-term) cycling exercises with average intensity in men with type 2 diabetes who had a life-style with low levels of physical activities.

MATERIAL AND METHOD

A. Study patients

Subjects were fifteen sedentary adult obese men with type II diabetes aged 43 ± 4.8 years, BMI: 30.7 ± 2.24kg/m^2 that participated by accessible sampling in this study. The study protocol was approved by the local Research Ethics Committee of Islamic Azad University and written informed consent was obtained.

B. Inclusion and exclusion criteria

Participants were included if they had not been involved in regular physical activity/diet in the previous 6 months. Inclusion criteria for study group were determined as existing type 2 diabetic for at least three years and having a BMI of 30 or above. In addition, exclusion criteria included inability to exercise and supplementations that alter carbohydrate-fat metabolism. Those patients unable to avoid taking hypoglycemic drugs or other therapeutic drugs within 12 hours before blood sampling were excluded. We also excluded those with history of other chronic diseases addition to diabetes.

C. Anthropometrical measurements

Apart from the biochemical measurements, additional variables for this report included age, height and weight, body mass index (BMI). Body weight and height were measured with the subject wearing light clothes. Abdominal obesity was determined as waist circumference measured in a standing position. The BMI was calculated as the weight in kilograms divided by the square of the height in meters. All anthropometric measurements were made by the same trained general physician and under the supervision of the same pediatrician following standard protocols.

D. Laboratory and physical exercise

Blood samples were withdrawn 5 min before the start and immediately after of the cycling test. All participants refrained from any severe physical activity 48 h before measurements. Serum separated by centrifugation. These samples were analyzed to determine concentrations of serum IL-6 by ELISA method, using an Enzyme-linked Immunosorbent Assay for quantitative detection of human IL-6. The Intra-assay coefficient of variation and sensitivity of the method were 3.4% and 0.92 pg/mL, respectively. Cycling exercise test was a YMCA standard test on leg ergometry cycle (Tunturi, made in Finland). This protocol was performed in 5 continues stage without rest between stages. Each stage lasted 3 minute [21].

E. Statistical analysis

After calculation of the mean and the standard deviation, the statistical analysis was conducted using the SPSS software version 15.0. Kolmogorov-Smirnov test was used to determine of normal status of the data. Student's t-tests for paired samples were performed to determine significance of changes in serum IL-6 by exercise test in patients. A p value of less than 0.05 was considered as statistically signigcant.

RESULTS

In this study, acute response of serum IL-6 to a short time cycling test was measured in diabetes patients. Anthropometric and physiological characteristics of the study participants are described in Table 1.

There was no statistically significant difference in serum IL-6 between pre and post exercise (from 2.15 ± 0.65 to 2.26 ± 0.60 pg/ml, p = 0.628, Fig. 1). Exercise test resulted significant decrease in glucose concentration in studied subjects (from 200 ± 60 to 198 ± 54 mg/dl, p = 0.000, Fig. 2).

Table 1: Mean and SD of anthropometrical and clinical markers on studied patients

Variable	Mean	Standard deviation
Age (years)	43	4.8
Weight (kg)	92	6.7
Height (cm)	173	5.2
Systolic blood pressure (mmHg)	130	19
Diastolic blood pressure (mmHg)	84	9
Abdominal circumference (cm)	103	6.9
Hip circumference (cm)	102	4.2
Body mass index (kg/m^2)	30.76	2.24
Body fat (%)	28.9	3.91
Visceral fat	13.1	1.75
Insulin (µIU/ml)	8.1	1.79
Glucose (mg / dl)	220	60
Insulin resistance (HOMA-IR)	4.32	1.30
Interleukine-6 (pg/ml)	2.15	0.65

Table 2: Information of Paired Samples Test of IL-6 and glucose in response to cycling test in patiebts

		Paired Differences			t	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean		
Pair 1	Interleukin 6 (pre) - Interleukin 6 (post)	-.1133	.8863	.2288	-.495	.628
Pair 2	Glucose (pre) - Glucose (post)	21.867	15.556	4.016	5.444	.000

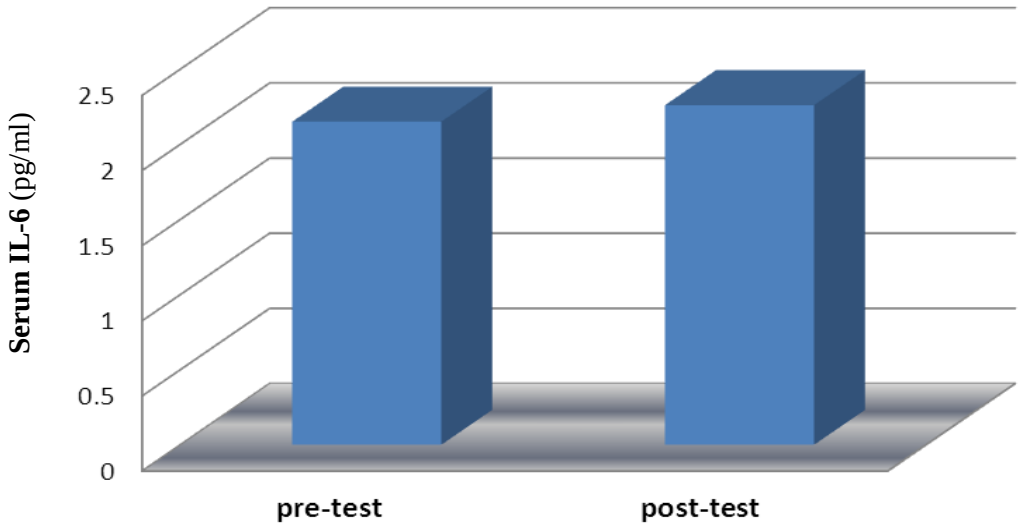

Fig. 1. The change of serum IL-6 by cycling test in diabetes patients.

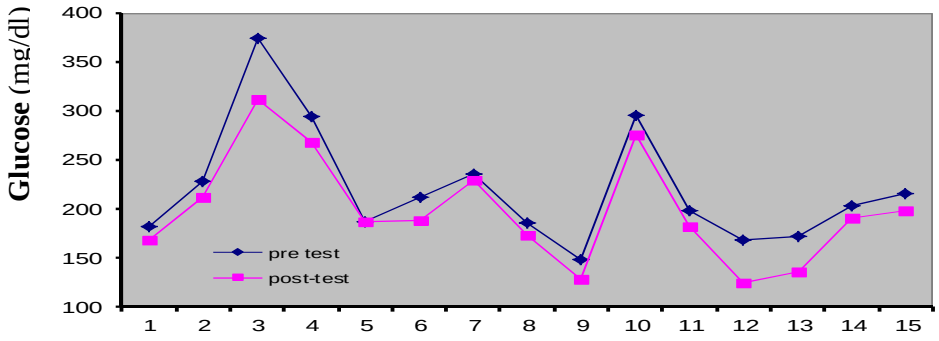

Fig. 2. The change of glucose concentration by cycling test in studied patients. Cycling test resulted significant decrease in glucose concentration.

DISCUSSION

Although some previous studies stated that short-term exercises could also influence pro-and anti-inflammatory cytokines (depending on the duration and intensity of the exercises), the findings of this research indicated IL-6 did not respond to one session of short-duration cycling in diabetics. In other words, based on these findings, it is concluded that one session of short duration cycling with average intensity did not affect serum IL-6 levels in men with type 2 diabetes but, nevertheless, significantly lowered blood glucose.

Mechanisms effective on energy balance such as inflammation and release of some adipokines determine pathophysiology of metabolic abnormalities in diseases associated with obesity. Scientific studies have repeatedly reported increased serum inflammatory cytokine levels in obese people and in diseases associated with them compared to healthy people with normal weights [22, 23, 24]. Exercise has been introduced as a non-drug treatment for reducing the spread of obesity and its complications. However, findings regarding the effects of physical activities on the levels of these variables (inflammatory cytokines) have so far been varied with no comprehensive or definitive results. Moreover, some researchers have reported considerable immediate response of these variables to exercises, especially to short-or long-duration one-session exercises [25, 26].

Immediate response of IL-6 to exercise is reported in this study, while some previous research reported decreased or increased levels of inflammatory cytokines following short- and long-term training exercises in various populations. For example, in a recent study, one session of exercise in the form of high intensity interval training led to significant increases in serum IL-6 and TNF-α levels in active young men. However, no changes were observed in the mentioned cytokines in these men in response to a 2-week training program in the form of 6 HUT sessions, which makes these results somewhat contentious [27]. In another study, 60 minutes of running on a treadmill with the intensity of 60-70(5) $VO2_{max}$ led to significant increases in IL-6 and some other inflammatory cytokines in men who engaged in endurance exercise [28]. On the other hand, in another study different from ours in time of performing the exercises but with findings similar to ours, one session of endurance exercise did not result in significant changes in IL-6, TNF-α, or IL-1β levels in women with metabolic syndrome [29]. Nevertheless, our study indicated IL-6 did not respond immediately to one session of exercises with average intensity, while blood glucose level significantly declined in response to these exercises. Short duration of exercises, and the fact that they were of average intensity, may be reasons for the lack of change in cytokine levels in our study. The grounds for this possibility is that, as shown in a review study, exercise-associated IL-6 levels depend on the intensity, and especially the duration, of the exercises while exercise type and the way it is carried out are not as effective or have limited effects [30].

Despite the fact serum IL-6 levels did not change in response to exercise test in our study, it is possible that the exercise led to changes in IL-6 expression or to its change in muscles involved in the exercise activity. It must also be mentioned that although there are several sources of IL-6 secretion in the body, skeletal muscles play the most important role in the production of IL-6 in blood flow in response to exercise [30]. Mechanisms such as changes in calcium homeostasis, damage inflicted by available glucose, and increases in active oxygen species can activate IL-6 synthesis pathways in response to exercise [30]. Nevertheless, considering skeletal muscles are not the only source of IL-6 production in the body, it is possible that IL-6 produced by active muscles and released into blood flow in response to the short duration exercise in our study did not lead to significant changes in its serum levels. This may explain why these serum levels did not change in the study. It is also possible that IL-6 responds to exercise with a short delay and not immediately after the exercise.

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