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Serum C-reactive protein and glycosylated hemoglobin in response to aerobic training in diabetic patients

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Abstract

Accumulating evidence indicates that obesity and overweight are associated with chronic low grade inflammation. The aim of our work was to study the effect aerobic exercise training on glycosylated hemoglobin and acute phase C-reactive protein (CRP) in diabetic patients. Thirty-eight sedentary, nonsmoking, type II diabetic (BMI: 30–35 kg/m2) men, aged 38–46 years, were recruited to participate to study and divided in to exercise (3 months, 3 sessions/weekly) and control (no training) group by randomly. Pre and post training CRP, glycosylated hemoglobin and anthropometrical parameters were measured in exercise and control groups and compared with each other. Aerobic exercise training resulted in significant decrease in body weight, body mass index and body fat percentage in exercise group (p<0.05). Glycosylated hemoglobin levels were significantly decreased in response to exercise training when compared with baseline levels (p=0.033). But, serum CRP did not change with aerobic exercise training. All variables in control group remained without changes. We conclude that there are no meaningful chronic effects of exercise on serum CRP, even in presence a improving in glycosylated hemoglobin in diabetic patients.

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Introduction

Accumulating evidence suggests diabetes as a metabolic -disorder with inappropriate hyperglycemia either due to an absolute or relative deficiency of insulin secretion or reduction in the biologic effectiveness of insulin or both. (Safiullah *et al.,* 2010). Accumulating evidence indicates that low-grade inflammation as an independent predictor of diabetes.

C-reactive protein (CRP) is an inflammatory cytokine produced by the liver under the stimulation of cytokines such as tumor necrosis factor-α and interleukins 1 and 6(Wang *et al.,* 2007). Recent epidemiologic studies have demonstrated that that CRP is a strong independent predictor of future cardiovascular events, including myocardial infarction, ischemic stroke, peripheral vascular disease, and sudden cardiac death among individuals without known CVD (Ridker, 2003; Ridker, 2001). On the other hand, There is considerable evidence have established elevated CRP levels to be predictive of the development of insulin resistance, metabolic syndrome, and type 2 diabetes (Pradhan *et al.,* 2003; Ndumele *et al.,* 2006).

A large body of evidence suggests that increased CRP is a significant predictor of diabetes risk even after adjusting for body mass index, family history of diabetes mellitus, smoking, and other factors (Pradhan *et al.,* 2001). Additionally, some Previous investigations have described a positive association of CRP with fasting plasma glucose and HbA1c in diabetic patients (Li *et al.,* 2004; Pradhan *et al.,* 2001), although the physiopathological mechanisms underlying these associations are largely unknown. The health benefits of an active lifestyle are well recognized. It is generally accepted that physical inactivity is increasingly recognized as modifiable behavioral risk factors for a wide range of chronic diseases. On the other hand, physical activity is a major modifiable risk factor of obesity and related diseases, therefore offers a potential therapeutic approach to modulate low-grade inflammation.

Although, the role of exercise training on glucose and other indicative markers of type II diabetes were studied at previous, but its role on HbA1C and CRP are not completely understood. Therefore, the present study aimed to evaluate the significance of a long term aerobic exercise on serum CRP and HbA1C in type II diabetic patients.

Subjects and methods

Subjects were thirty two sedentary adult obese men with type II diabetic aged 38–46 years, (BMI 30–35 kg/m2) that divided randomly into exercise group and control groups (no training). 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 two years. In addition, exclusion criteria included supplementations that alter carbohydrate or fat metabolism. Presence of previous coronary cardiac disease, chronic airway disease, and impaired hepatic dysfunction and presence of any acute disease and having symptoms that may be indicative of ischemia in electrocardiography were determined as exclusion criteria. All participants were informed verbally and in writing, as to the objectives of the experiments, together with the potential associated risks.

The aim of this study was to determine the effect of 12 weeks of aerobic exercise training (60 min, 3 days/week for 12 weeks) on serum fasting CRP and glycosylated hemoglobin in a group of adult males' type 2 diabetic patients and compared with control subjects.

Measurements

Anthropometric measurements of height, weight, percent body fat, and abdominal and hip circumference measurements were performed at baseline. Body weight and height were measured with a standard physician's scale and a stadiometer, respectively when subjects were in a fasting state when the participant had thin clothes on and was wearing no shoes. Body mass index was calculated as

body mass (in kilograms) divided by height squared (in square meters). In addition, blood samples were collected an overnight fast for measuring serum CRP and glycosylated hemoglobin in two groups. All participants refrained from any severe physical activity 48 h before measurements. Serums were immediately separated and stored at -80° until the assays were performed. Serum CRP was determined by ELISA method (Diagnostics Biochem Canada Inc. High sensitivity C - reactive protein (Hs-CRP)). The Intra- assay coefficient of variation and sensitivity of the method were 5% and 10 ng/mL, respectively. Finally, all measurements consist of fasting blood sampling, anthropometric measurements and Blood pressure repeated 48 h after last exercise session.

Table 1. Mean and standard deviation of anthropometrical and biochemical characteristics before and after intervention in studied groups.

Variables	Control diabetic		Exercise diabetic	
	Pretest	post-test	Pretest	post-test
Age (year)	42 ± 3.4	42 ± 3.4	41 ± 4.2	41 ± 4.2
Height (cm)	175.5 ± 6.8	175.5 ± 6.8	176.1 ± 5.9	176.1 ± 5.9
Weight (kg)	99.3 ± 7.9	100.1 ± 9.21	100 ± 10.3	96.3 ± 11.3
Waist circumference (cm)	107 ± 8.4	107 ± 10.3	108.9 ± 7.6	104.2 ± 9.8
Hip circumference (cm)	105.3 ± 9.4	105 ± 8.7	106.3 ± 10.1	101.2 ± 6.4
BMI (kg/m2)	32.23 ± 3.1	32.49 ± 2.6	32.24 ± 3.11	31.05 ± 2.13
Body fat (%)	31.2 ± 3.12	31.6 ± 3.32	32.1 ± 3.56	29.2 ± 3.23
HbA1C	8.98 ± 1.65	8.83 ± 2.64	8.86 ± 2.13	7.11 ± 2.32
CRP (ng/ml)	1262 ± 311	1196 ± 219	1193 ± 213	1092 ± 273

Exercise program

Exercise training program lasted 3 months (3 days/wk) 60 to 80 percent of maximum heart rate. Each session started by 15 min of flexibility exercises, 30-40 min of aerobic exercise and 5–10 min of cool down activity. Aerobic exercises in each session included walking on a treadmill and stationary cycling. Initially, subjects exercised at low intensity and the intensity of exercise was gradually increased to 80% of peak heart rate in next sessions. In this 12-week period, participants in the control group were barred from participating in any exercise training.

Statistical analysis

Statistical analysis was performed with the SPSS software version 15.0 using an independent paired t-test. Normal distribution of data was analyzed by the Kolmogorov-Smirnov normality test. An Independent sample T-test was used to compare all variables between exercise and control groups at baseline. Student's t-tests for paired samples were performed to determine significance of changes in variables by exercise program in exercise group and comparing to control group. Significance was accepted at $P < 0.05$.

Results

Baseline and post training anthropometric and biochemical characteristics of patients are shown in Table 1. At baseline, there were no differences in the age, body weight, BMI, serum CRP and glycosylated hemoglobin between the two groups (see Table 1).

Compared to pre-training, body decreased significantly after exercise program ($p = 0.023$). BMI levels were significantly decreased in response to aerobic exercise program when compared with baseline levels in exercise group ($p = 0.032$) but in control group was not changed ($p = 0.312$). After exercise intervention, body fat percentage decreased

in exercise group (p = 0.026) but not to control group (p = 0.226). Compared with pre interventions, serum CRP was not changed in both exercise and control groups (p ≥ 0.05). Glycosylated hemoglobin was decreased significantly with aerobic exercise program (p = 0.033) whereas it was not changed in control group (p = 0.162, Fig 1).
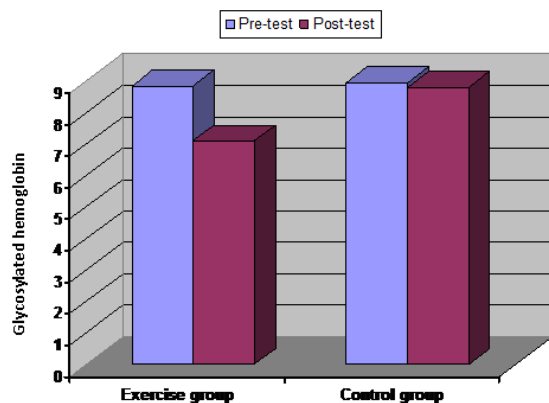

Fig. 1. The changes pattern of Glycosylated hemoglobin in control and exercise groups of studied subjects. Aerobic exercise leads to significant decrease in Glycosylated hemoglobin in exercise group, while this variable remained without change in control group.

Discussion

No significant change in CRP in response to the exercise program is one of the main findings of this study. These findings were observed while aerobic exercise program significantly decreased HbA1C in the diabetic subjects.

The precursor value of this inflammatory hormone for CVD in men and women or smokers and non-smokers and those with diabetes and even non-diabetic populations has been repeatedly confirmed. In a study on a multitude of Greek women and man, it was found that CRP alongside age, hypertension and diabetes are the most important factors associated with cardiovascular diseases (Panagiotakos *et al.,* 2008).There are conflicting studies regarding the effects of exercise on CRP, as some studies have not observed any effect after a 12-week exercise program (Kim *et al.,* 2008), yet some others have observed reduced levels of CRP after 6 months of training (Campbell *et*

al., 2008). Although most previous studies have reported a significant reduction of CRP in response to long-term training programs, the statistical findings of this study showed that three months of aerobic exercise would not lead to any significant changes in serum CRP levels.

Researchers have revealed that the training program, once associated with associated with a significant reduction in weight or percentage of body fat, would reduce serum CRP levels (Ouchi *et al.,* 2003). In this context, the findings of a recent study showed that 6 months of exercise training with average 2.5 sessions per week would significantly decrease CRP (Smith *et al.,* 1999). While some studies have reported a significant decrease in the levels of inflammatory cytokines due to physical activity despite BMI or body fat levels remaining unchanged (Kohut *et al.,* 2006; Stewart *et al.,* 2005), in several recent studies physical intervention has brought about no changes in levels of CRP or other inflammatory cytokines (Hammett *et al.,* 2006; Fischer *et al.,* 2004; Bautmans *et al.,* 2005; Marcell *et al.,* 2005). Moreover in some other studies no significant connection between levels of physical activity and CRP levels has been observed even after BMI synchronization, indicating that measuring inflammation is not the only factor determining the beneficial effects of exercise (Pischon *et al.,* 2003). In another study, researchers deduced from their findings that physical activity would probably reduce CRP levels in those with higher baseline CRP levels to a greater degree independent of changes in weight or body fat, indicating that the baseline levels of inflammation is an important factor in its response to exercise (de Visser *et al.,* 2006).

The fact that fasting and non-fasting blood glucose levels in the diabetic patients are higher than non-diabetic individuals is a major feature of type II diabetes. Glycolized hemoglobin or HbA1C represents the average blood glucose levels over a period of 2 to 3 months. Exercise is considered a useful non-drug therapy in controlling blood sugar levels and weight loss in type 2 diabetic patients,

although clinical studies regarding the effects of exercise on diabetes have provided conflicting results. In this context, some studies have reported no change in blood glucose or HbA1C in response to exercise. In one study, 6 weeks of exercise 60 to 80 percent VO2max intensity did not lead to significant changes in glucose and insulin sensitivity (Glans *et al.,* 2009). Also in another study 20 weeks of exercise training in form of 3 to 5 sessions a week with intensity of 70% VO2max did not result in any change in HbA1C (Vancea *et al.,* 2009). Despite these findings, in this study a three-month aerobic exercise program significantly reduced HbA1C the subject diabetic patients.

In a recent study, in the face of no change in body mass due to prolonged aerobic exercise in patients with type II diabetes, glycolized hemoglobin significantly decreased compared to the control group (Boulé *et al.,* 2011). In another study, 4 and 16 weeks of endurance and strength training (2 endurance sessions + 2 strength sessions per week) significantly reduced fasting glucose and HbA1C and insulin function (Tokmakidis *et al.*, 2004). In another study, 12 weeks of exercise including three 60-minute walking sessions a week resulted in a significant reduction in fasting glucose and HbA1C (Goldhaber-Fiebert *et al.,* 2003). In another study, after 6 months of aerobic and resistance exercises higher improvement in HbA1C was observed in those patients with greater intensity of activity (Glans *et al.,* 2009).

In a general summary, unlike most previous studies, the findings of this study showed that although a three-month program of aerobic exercise would not lead to a significant change in CRP serum in patients with type II diabetes it does lead to a significant reduction in HbA1C that is a leading indicator in diagnosis of type II diabetes. It can be determined based on these findings that changes in blood glucose levels in response to a variety of sporting activities can be achieved independently of changes in systemic inflammation of these patients.

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