

Moderate Versus High Intensity Aerobic Exercise Training on Glycemic Control and Anti-Inflammatory Effects on Non-Insulin Dependent Diabetic Patients

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Abstract: Chronic low-grade inflammation has recently emerged as the common denominator linking non-insulin dependent diabetes mellitus (NIDDM), insulin resistance and cardiovascular diseases. Aerobic exercise training is an accepted therapeutic strategy in the management of NIDDM because of its beneficial effects. Objective: The aim of this study was to compare changes in glycemic control and circulating levels of some inflammatory markers, including C-reactive protein (CRP), tumor necrosis factor (TNF) - α , interleukin-6 (IL-6), glycosylated hemoglobin (HbA_{1c}) and Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) index after moderate and high intensity aerobic exercise training in NIDDM patients. Thirty-six NIDDM patients of both sexes with body mass index (BMI) ranged from 25 to 30 Kg/m², non smokers, free from respiratory, kidney, liver, metabolic and neurological disorders were recorded in this study. Their age ranged from 40 to 55 years. The subjects were included into 2 equal groups; the first group (A) received high intensity aerobic exercise training. The second group (B) received moderate intensity aerobic exercise training for 3 months. The mean values of TNF- α , IL-6, CRP, HOMA-IR and HbA_{1c} were significantly decreased in group (A) and group (B). Also, there was a significant difference between both groups after treatment. High intensity aerobic exercise training is more appropriate than moderate exercise intensity in improving glycemic control and anti-inflammatory effects on NIDDM Patients.

Key words: Aerobic exercise • Glycemic control • Anti-inflammatory effects and Non- Insulin dependent diabetes

INTRODUCTION

Non-insulin dependent diabetes mellitus (NIDDM) is associated with insulin resistance. Adipocytes not only secrete free fatty acids but also release a variety of adipokines including leptin, tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6). These factors have paracrine/autocrine functions that include regulation of energy expenditure, in part, by modulating whole-body insulin sensitivity [1-4].

Tumor necrosis factor α (TNF- α) induced insulin resistance by interacting with insulin receptor signaling and through activation of lipolysis and inhibition of lipoprotein lipase. TNF- α was proposed to have preferentially paracrine effects and to be a regulator of insulin resistance at the tissue level [5]. C-reactive protein (CRP) was known to be produced primarily by the liver in response to inflammatory cytokines including interleukin (IL)-6 and TNF- α [6,7].

Exercise improves diabetic status and reduces the metabolic risk factors associated with cardiovascular diseases and improves insulin sensitivity [8,9]. Regular exercise increases maximum oxygen uptake, reduces insulin resistance, reduces obesity and prevents further weight gain and dampens the inflammatory markers, suggesting that habitual exercise plays an important role in the prevention and treatment of obesity, insulin resistance and coronary heart disease [3, 4,10].

Few studies have prospectively examined the effect of exercise on elevated levels of inflammatory biomarkers in diabetic subjects and found contrasting results in terms of efficacy and dependence on weight loss [11,12]. Moreover, the type, dose and intensity of physical activity needed to obtain a significant anti-inflammatory effect in this high-risk population are largely unknown.

This study was aimed to compare the effect of moderate and high exercise intensity on glycemic control and circulating levels of some inflammatory markers, including C-reactive protein (CRP) tumor necrosis factor (TNF)- α and interleukin-6 (IL-6), Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) index and HbA_{1c} in NIDDM.

MATERIALS AND METHODS

Subjects: Thirty-six NIDDM patients of both sexes with body mass index (BMI) ranged from 25 to 30 Kg/m², non smokers, free from respiratory, kidney, liver, metabolic and neurological disorders. Their age ranged from 40 to 55 years. The subjects were included into 2 equal groups; the first group (A) received high intensity aerobic exercise training. The second group (B) received moderate intensity aerobic exercise training. All patients performed three sessions / week (i.e. a total of 36 sessions per patient over a 3-month period). Informed consent was obtained from all participants. All participants were free to withdraw from the study at any time. If any adverse effects had occurred, the experiment would have been stopped, with this being announced to the Human Subjects Review Board. However, no adverse effects occurred and so the data of all the participants were available for analysis.

Methods

Evaluated parameters

Chemical Analysis: Blood sample after fasting for 12 hours was taken from each patient in clean tubes containing few mg of K₂EDTA, centrifuged and plasma was separated and stored frozen at -20° used for estimation of plasma TNF- α , interleukin-6 (IL-6), C-reactive protein (CRP) and glycosylated hemoglobin (HbA_{1c}) using colorimetric method. Homeostasis Model Assessment-Insulin Resistance (HOMA) index

for insulin sensitivity was computed following this equation: [fasting glycemia (mmol/L) [fasting insulin (mIU/L)]/22.5 [13].

The Aerobic Exercise Training Program: The aerobic treadmill-based training program (Track master 400E, gas fitness system, England) was at 75 % to 85% of the maximum heart rate (HRmax) achieved in a reference ST performed according to a modified Bruce protocol for group (A) who received high intensity aerobic exercise training, where group (B) received moderate intensity aerobic exercise training at 60% to 75% of the maximum heart rate (Hrmax) [14]. This rate was defined as the training heart rate (THR). After an initial, 5-minute warm-up phase performed on the treadmill at a low load, each endurance training session lasted 30 minutes and ended with 5-minute recovery and relaxation phase. All patients performed three sessions / week (i.e. a total of 36 sessions per patient over a 3-month period).

Statistical Analysis: The mean values of TNF- α , IL-6, CRP, HOMA-IR and HbA_{1c} obtained before and after three months in both groups were compared using paired "t" test. Independent "t" test was used for the comparison between the two groups (P<0.05).

RESULTS

Thirty-six NIDDM patients of both sexes with total body obesity (body mass index (BMI) 25-30 Kg/m², their age ranged from 40 to 55 years. The subjects were included into 2 equal groups; the first group (A) received high intensity aerobic exercise training. The second group (B) received moderate intensity aerobic exercise training for 3 months in order to compare the effect of moderate and high exercise intensity on glycemic control and circulating levels of some inflammatory markers, including TNF- α , IL-6, CRP, HOMA-IR and HbA_{1c} in patients with NIDDM.

Table 1: Mean value and significance of TNF- α , IL-6, CRP, HOMA-IR and HbA_{1c} in group (A) before and after treatment.

	Mean \pm SD		T-value	P-value
	Before	After		
TNF- α (pg/mL)	6.11 \pm 1.86	4.18 \pm 1.15	5.78	<0.05
IL-6 (pg/mL)	3.21 \pm 1.13	1.26 \pm 1.5	6.64	<0.05
CRP(mg/dl)	18.45 \pm 3.32	9.76 \pm 2.85	7.32	<0.05
HbA _{1c} (%)	7.88 \pm 1.26	6.14 \pm 0.96	5.15	<0.05
HOMA-IR	4.81 \pm 2.29	2.73 \pm 1.26	6.91	<0.05

TNF- α = tumor necrosis factor - alpha. IL-6 = Interleukin-6

CRP = C-reactive protein HbA_{1c} = glycosylated hemoglobin

HOMA-IR = Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) index

Table 2: Mean value and significance of TNF- α , IL-6, CRP, HOMA-IR and HBA_{1c} in group (B) before and after treatment.

	Mean \pm SD		T-value	P-value
	Before	After		
TNF- α (pg/mL)	6.24 \pm 1.95	5.11 \pm 1.87	3.25	<0.05
IL-6 (pg mL ⁻¹)	3.41 \pm 1.74	2.31 \pm 1.90	3.44	<0.05
CRP(mg/dl)	18.82 \pm 4.16	12.27 \pm 3.45	4.15	<0.05
HBA _{1c} (%)	7.92 \pm 1.36	7.12 \pm 1.06	3.11	<0.05
HOMA-IR	4.92 \pm 2.33	3.88 \pm 1.56	3.03	<0.05

TNF- α = tumor necrosis factor - alpha. IL-6 = Interleukin-6
 CRP = C-reactive protein HBA_{1c} = glycosylated hemoglobin
 HOMA-IR = Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) index

Table 3: Mean value and significance of TNF- α , IL-6, CRP, HOMA-IR and HBA_{1c} in group (A) and group (B) after treatment.

	Mean \pm SD		T-value	P-value
	Group A	Group B		
TNF- α (pg/mL)	4.18 \pm 1.15	5.11 \pm 1.87	3.10	<0.05
IL-6 (pg mL ⁻¹)	1.26 \pm 1.50	2.31 \pm 1.90	3.11	<0.05
CRP(mg/dl)	9.76 \pm 2.85	12.27 \pm 3.45	4.23	<0.05
HBA _{1c} (%)	6.14 \pm 0.96	7.12 \pm 1.06	3.02	<0.05
HOMA-IR	2.73 \pm 1.26	3.88 \pm 1.56	3.25	<0.05

TNF- α = tumor necrosis factor - alpha. IL-6 = Interleukin-6
 CRP = C-reactive protein HBA_{1c} = glycosylated hemoglobin
 HOMA-IR = Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) index

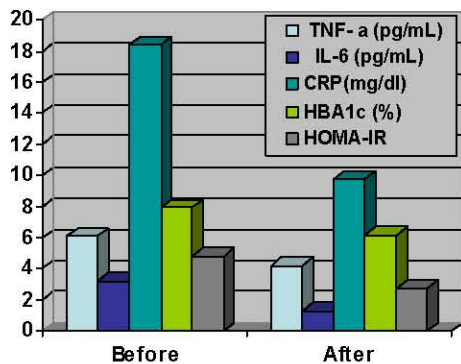


Fig. 1: Mean value and significance of TNF- α , IL-6, CRP, HOMA-IR and HBA_{1c} in group (A) before and after treatment

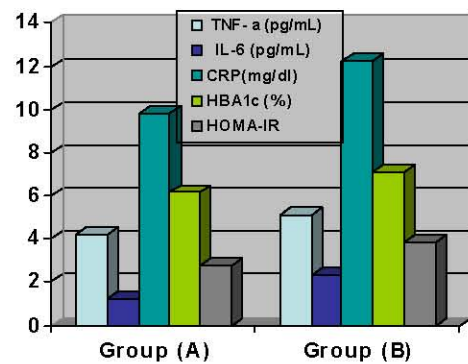


Fig. 3: Mean value and significance of TNF- α , IL-6, CRP, HOMA-IR and HBA_{1c} in group (A) and group (B) after treatment

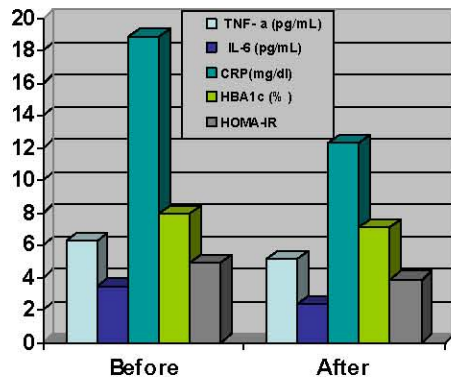


Fig. 2: Mean value and significance of TNF- α , IL-6, CRP, HOMA-IR and HBA_{1c} in group (B) before and after treatment

The mean values of TNF- α , IL-6, CRP, HOMA-IR and HBA_{1c} were significantly decreased in group (A) and group (B) (Table 1 and 2 and Figure 1 and 2). Also, there was a significant difference between both groups after treatment (Table 3 and Figure 3). So, high intensity aerobic exercise training is appropriate to improve glycemic control and anti-inflammatory effects on NIDDM Patients.

DISCUSSION

The aim of this study was to detect changes in glycemic control and inflammatory markers, including CRP, TNF- α and interleukin-6 (IL-6), HOMA-IR and

HbA_{1c} after moderate and high intensity aerobic exercise training in patients with NIDDM. The mean values of TNF- α , IL-6, CRP, HOMA-IR and HbA_{1c} were significantly decreased in group (A) and group (B). Also; there was a significant difference between both groups after treatment. This means that high intensity aerobic exercise training is more appropriate than moderate exercise intensity in improving glycemic control and anti-inflammatory effects on NIDDM Patients. Results of this study confirmed and agreed with many previous studies.

A twelve week thrice-weekly swimming training was associated with improved measurements of chronic inflammation markers as noted by an increase in the levels of adiponectin and a reduction in C-reactive protein. The improvements in insulin sensitivity resulting from swimming exercise appeared to be related to changes in these inflammatory mediators [15]. Several studies have shown that levels of physical activity and cardiorespiratory fitness are inversely correlated to CRP [16]. Also, regular exercise significantly reduces circulating levels of CRP and other inflammatory mediators [17,18].

Aerobic exercise training prevents the development of chronic inflammation associated with NIDDM by reducing the production of proinflammatory cytokines TNF- α and IL-6. The beneficial effects of regular physical activity in improving insulin resistance, dyslipidemia and levels of proinflammatory cytokines [19]. The potential mechanisms for the anti-inflammatory effect of exercise, including reduced percentage of body fat and macrophage accumulation in adipose tissue, muscle-released interleukin-6 inhibition of tumor necrosis factor- α and the cholinergic anti-inflammatory pathway [20].

There was no change in sIL-6R up to 24 hours following 3 hours of cycling exercise at a moderate intensity [21]. The contrasting findings be explained by the higher intensity and longer exercise duration [22].

High-intensity exercise training program induced an improvement of biomarkers of inflammation and insulin resistance, with a reduction of IL-6, TNF- α and leptin (associated with decreased insulin, C-peptide and HOMA-IR) and an increase of IL-4 and IL-10 thus indicating that exercise has a full anti-inflammatory and insulin-sensitizing effect. These results suggest that the beneficial effect of physical activity on CVD morbidity and mortality may depend, at least partly, on the anti-inflammatory effect of exercise, though it is unproven that reducing CRP and other inflammatory biomarkers is

effective in decreasing CVD risk [23]. Changes in inflammatory biomarkers in the high-intensity exercise were paralleled by improvements though, to a lesser extent in HbA_{1c} [18].

Circulating inflammatory biomarkers originate from multiple sources, particularly visceral adipose tissue, where excess fat promotes macrophage recruitment and both adipocytes and macrophages secrete numerous cytokines (adipokines), including IL-6, TNF- α and leptin [23]. Skeletal muscle is another source of cytokines, called myokines, among which IL-6 is considered to play a dual role: anti-inflammatory and pro-inflammatory, the latter by inducing production of CRP. High-intensity training of long duration may significantly influence myokine production, thus driving the anti-inflammatory effect of exercise [24].

CONCLUSION

High intensity aerobic exercise training is more appropriate than moderate exercise intensity in improving glycemic control and anti-inflammatory effects on NIDDM Patients.

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