

THE EFFECT OF EXERCISE ON GLUCOSE AND INSULIN RESISTANCE IN ASTHMA PATIENTS

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ABSTRACT

Asthma can be considered as a chronic inflammatory disease and has been related to subclinical markers of metabolic syndrome or diabetes. The significant role of long term exercise training on metabolic or clinical markers in chronic diseases is well known, but the role of acute exercise has not drawn much attention. In this study, the acute and recovery response of glucose and insulin sensitivity to one exercise test (45 min run) was determined in fourteen adult men with mild to moderate asthma. Participant were inactive and non-smokers. For this purpose, the concentration level of glucose, insulin and insulin sensitivity were measured before, 0 and 60 min recovery of exercise test. Comparisons of data in each variable between 3 blood samples were analysed by the repeated measures ANOVA model. Data analysis showed that exercise test was associated with acute and recovery response of all variables. On the other hand, serum insulin, glucose and insulin sensitivity decreased immediately and 60 min recovery to exercise when compared with pretest. The finding of present study indicates that an increase in energy expenditure by exercise test can be affect diabetes markers in asthma patients.

KEYWORDS: Asthma, Exercise, Insulin action, Recovery.

INTRODUCTION

Asthma is a disease characterized by the narrowing of the respiratory airway along with the obstruction of respiratory pathways and wheezing symptoms (Settin *et al.*, 2008). One of the most important characteristics of asthma is the hyperresponsive of respiratory pathways which causes the narrowing of the pathways in response to stimulant drugs or agents (Weiss *et al.*, 2003). Although asthma is generally associated with inflammation of the respiratory pathways, there exists much evidence to support the presence of a systemic inflammation and introduce it as a disease with systemic inflammation (Castro-Rodríguez *et al.*, 2007; McMurray *et al.*, 2005). Most studies have reported an increase in the inflammatory cytokine levels, not only in respiratory pathways cells, but also in the blood circulation of asthmatic patients (Cristina *et al.*, 2005). For instance, mast cells are one of the main tissues responsible for allergic and asthmatic responses (Theoharides *et al.*, 2006), however, some studies have shown that these cells are also important in obesity-related diseases and type 2 diabetes (Settin *et al.*, 2008). The mice lacking mast cells or those exposed to drugs or inhibitors of mast cells (cromolyn or etotifen) are fully protected against type 2 diabetes (Barnes *et al.*, 2007). However, the relationship between asthma and type 2 diabetes have been reported by the literature (Enfield *et al.*, 2009; Arshi *et al.*, 2010) as insulin resistance have been reported in asthmatic patients (Thuesen *et al.*, 2009). There is also some evidence of the increased blood glucose levels in asthmatic patients (Arshi, 2010) which is associated to the insulin function as well as the insulin sensitivity of the target cells. Scientific evidence has shown that apart from medical treatments, exercise, as a non-pharmacological therapy, is of particular importance in improving pulmonary function in asthmatic patients (Chanavirut *et al.*, 2006; Chang *et al.*, 2008).

However, few studies are conducted on measuring the response of diabetes-related indicators, such as glucose, insulin or insulin sensitivity to short or long-term aerobic training in asthmatic patients. Exercise has been identified as a factor in increased insulin sensitivity and improved insulin function in insulin-resistant humans and animal models (Perrini *et al.*, 2004). Some studies have shown that short-term exercise increases insulin sensitivity in healthy subjects (Richter *et al.*, 1999). Given the limited studies on the effect of exercise, particularly short-term exercise, on glucose levels and insulin sensitivity in the patients, this study aimed at examining the effect of a relatively long-term aerobic exercise on the levels of these variables in asthmatic patients.

MATERIALS AND METHODS

Patients

Fourteen non-trained men (37.4±5 years mean ± standard deviation) with mild to moderate asthma participated in the study by voluntary. A history of asthma for three year was main inclusion criteria. The diagnosis of asthma and its severity was made by spirometry test. All subjects were non-smokers and had not participated in regular exercise

programs for the preceding 6 months. Those with other chronic or metabolic diseases were excluded. All subjects gave their informed consent to participate in the study.

Blood samples were obtained for biochemical assays, and anthropometric measurements were taken, including measurement of height and weight and spirometric factors in accordance with American Thoracic Society standards.

Anthropometry

Weight and height were measured in the morning, in fasting condition, standing, wearing light clothing and no shoes. BMI was calculated by dividing body mass (kg) by height in meters squared (m²). Abdominal and hip circumference were measured in a standing position at the end of normal expiration and ratio between them (AHO) was calculated for each subjects.

Forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) and FEV1/FVC were measured three using a portable spirometer (Minispire, Italy). Subjects were instructed to take maximum inspiration and blow into the pre-vent pneumotach as rapidly, forcefully and completely as possible for a minimum of 6 seconds, followed by full and rapid inspiration to complete the flow volume loop. The best of the three trials was considered for data analysis.

Blood Collection and protocol

Blood samples were collected prior to exercise, at the end of exercise, and at 60 min following exercise. Exercise test lasted 45 min included run with a moderate intensity equivalent to %70 of HRmax. Blood samples were analyzed for serum insulin, glucose and insulin sensitivity. Glucose was determined by the oxidase method (Pars Azmoon kit, Tehran) and serum insulin was determined by ELISA method. Insulin sensitivity was assessed using the homeostasis model assessment for insulin sensitivity formula derived from fasting insulin and glucose levels (McAuley *et al.*, 2001).

Statistical analysis

Data were analyzed by computer using SPSS software version 15.0. Given normal distribution of the data, which was analyzed by Kolmogorov-Smirnov test, subsequent analysis was performed by repeated measures ANOVA. A p-value less than 0.05 were considered statistically significant.

RESULTS

As mentioned previous, this study aimed to evaluate acute and recovery response of insulin, glucose and insulin resistance to exercise test in males with asthma. Exercise test included 45 min running without slope. Body weight and other anthropometrical characteristics are shown in Table 1. Table 2 presents the clinical parameters before, 0 and 60 min after exercise test. Based on repeated measure analysis, we observed acute ($p < 0.001$) and recovery ($p < 0.01$) responses in glucose concentration to exercise test when compared with pretest in studied patients (Fig 1). Serum insulin was also decreased significantly immediately ($p < 0.001$) and 60 min recovery ($p < 0.001$) after exercise test compared to pretest (Fig 2). We also observed a significant decrease in insulin sensitivity at 0 ($p < 0.001$) and 60 min recovery ($p < 0.001$) to exercise test compared with pretest (Fig 3).

Table 1: Characteristics for anthropometrical and spirometrical markers of studied patients.

	Minimum	Maximum	Mean	Std. Deviation
Age (year)	37	60	45.79	7.934
Height (cm)	172	179	175.07	2.056
Weight (kg)	79	118	93.21	11.383
Abdominal (cm)	90	132	104.57	12.094
Hip (cm)	91	126	103.79	10.101
WHO	.88	1.11	1.0079	.05820
BMI (kg/m ²)	26.1	36.8	30.371	3.3123
Body fat (%)	24.3	38.1	29.929	3.8185
Visceral Fat	9	26	13.43	4.274
FVC (%)	70	92	81.57	6.745
FEV1 (%)	65	84	77.07	6.330
FEV1 / FVC (%)	64.0	91.0	69.929	6.3666

Table 1: Mean and standard deviation of clinical markers before, 0 and 60 min after exercise test

Variable	Pre-test	Post-test	Recovery (60 min)
Fasting glucose (mg/dl)	87 ± 7.7	79 ± 6.8	82 ± 5.9
Serum insulin (μIU/ml)	16.4 ± 3.8	10.7 ± 3.6	12.1 ± 2.2
Insulin sensitivity (HOMA-IS)	0.53 ± 0.03	0.60 ± 0.04	0.58 ± 0.04

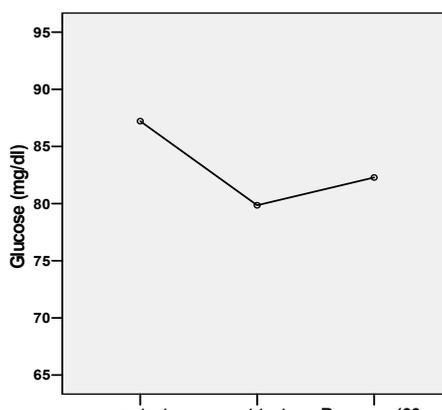


Fig 1: Acute and recovery response of glucose to exercise tes

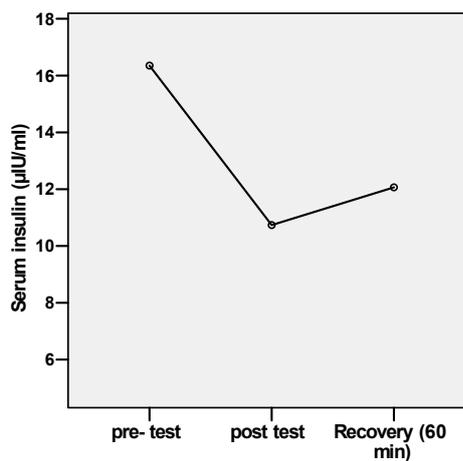


Fig 2: Acute and recovery response of insulin to exercise tes

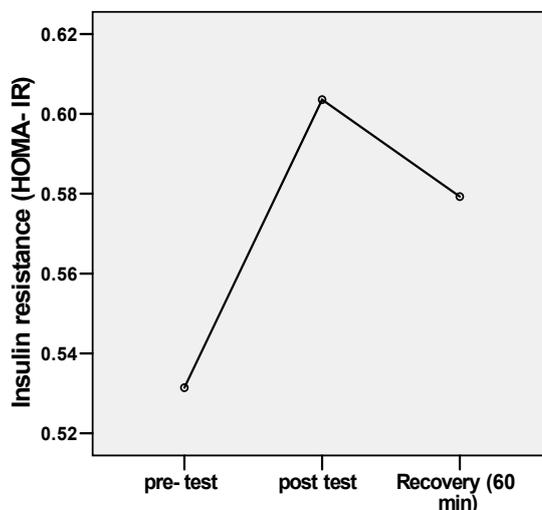


Fig 3: Acute and recovery response of insulin sensitivity to exercise test

DISCUSSION

A session of exercise in the form of intense running with a relatively moderate duration reduced insulin levels in asthmatic patients. Reduced insulin was also associated with improvements in blood glucose levels. Although several epidemiological studies have reported the concurrent prevalence of chronic diseases, such as diabetes and asthma (Enfield *et al.*, 2009; Arshi *et al.*, 2010), the molecular mechanisms of the relationship between these diseases are not fully understood yet. The close relationship between lung function impairment and increased glucose levels and diagnosis of diabetes has been reported. These studies have also reported the poor lung function in diabetic compared to non-diabetic patients (Walter *et al.*, 2003). Some other studies have supported a relationship between asthma and diabetes (Yun *et al.*, 2012). Longitudinal studies have noted that treated diabetics have higher lung function compared to other diabetics (Davis *et al.*, 2004).

Although improvement in diabetes-related indicators through short-term training have been reported too (Bloem *et al.*, 2008), it is thought that substantial improvement in these variables in different healthy or patient populations until achieving a normal condition require studies on long-term exercise. However, the findings of this study showed that even an aerobic exercise with a relatively moderate intensity had an improving effect on these indicators in patients with mild to moderate asthma. Positive response of these variables to exercise, albeit temporary, is of particular clinical importance. The available evidence on the effects of exercise on insulin levels is not consistent. Some studies have indicated that regular exercise reduces the secretion of insulin through its stimuli (King *et al.*, 1990), however, some other studies have suggested that long-term exercise increases the glucose-dependent insulin secretion in humans and animal models with type 2 diabetes (Dela *et al.*, 2004). A number of studies have shown that exercise improves the glucose homeostasis by increasing glucose uptake in skeletal muscle and adipose tissue (Berggren *et al.*, 2005; Corcoran *et al.*, 2007). In addition, some studies reported that exercise reduces hepatic insulin symptoms by reducing the release of hepatic glucose in the hyperinsulinemia condition (Perseghin *et al.*, 2007). However, in this study, one session of aerobic exercise led to the acute reduction in insulin levels in asthmatic patients. Effects of exercise on insulin sensitivity are well known (Cris *et al.*, 2009). Some studies have pointed out to the reduced lung function in diabetics and the prevalence of determinant symptoms of diabetes, such as insulin resistance and blood glucose, in asthmatic patients (Arshi *et al.*, 2010; Walter *et al.*, 2003). Generally, in the present study, the blood glucose levels decreased in response to exercise, while the serum insulin level was significantly reduced compared to the baseline

levels. Hence, it appears that despite a significant reduction in insulin, reduction in blood glucose is rooted in the reduced resistance of cells to insulin, or in other words, increased insulin sensitivity of cells, especially muscle cells. In support of this hypothesis, findings showed that insulin sensitivity was also significantly increased in response to exercise. However, apart from increased insulin function and increased insulin sensitivity, reduced blood glucose levels in asthmatic subjects may be attributed to other hormonal factors such as increased inflammatory cytokine, e.g., adiponectin. For example, most findings indicate that increased levels of adiponectin in response to short or long-term training programs leads to a decrease in blood glucose levels through affecting the insulin resistance or insulin sensitivity or inhibiting the hepatic gluconeogenesis process (Yamauchi *et al.*, 2002; Lindsay *et al.*, 2002). Some recent studies have shown that reduced adiponectin affects blood glucose levels by affecting insulin levels and beta-cell function (Eizadi *et al.*, 2012). Since there are adiponectin receptors in smooth muscle cells of the respiratory pathways, this hypothesis has been suggested by some researchers that reduced concentrations of adiponectin in obese individuals is effective in increasing the number smooth muscle cells of the respiratory pathways in asthma (Shore *et al.*, 2006). In non-diabetic adults prone to type 2 diabetes, the low levels of anti-inflammatory or anti-diabetic mediators, such as adiponectin, were associated with the destruction of glucose tolerance (Thamer *et al.*, 2006). However, some other studies have suggested that blood circulation levels of peptide mediators, such as adiponectin and leptin, are individually a predictor of insulin sensitivity, but these mediators do not affect the secretion of insulin or beta-cell function (Koebnick *et al.*, 2008).

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