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The effect of Endurance Exercise on the Inflammatory Cytokine Interleukin-6 in Serum of Inactive Allergic Asthma Participants

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Abstract

The aim of this study was to evaluate the effects of endurance training on serum cytokine – interleukin IL-6 (IL-6) levels in adult asthma patients. For this purpose, pre and post aerobic training (3 times-weekly/ 3 months) blood samples were taken after overnight fast in 32 adult men with asthma patients that was randomly divided to exercise and control groups. Anthropometrical indexes were also monitored in two occasions. All data were compared by t - tests. At baseline, there were no differences in the serum IL-6, body weight and other anthropometrical indexes between the two groups. Compared to pre-training measurements, the IL-6 levels did not change significantly subsequent to the endurance training in both groups ($p > 0.05$). We observed a significant decrease in all anthropometrical indexes in the exercise group. Thus, we conclude that the endurance exercise activity has no effect on the systemic inflammation in asthma patients.

Keywords: Asthma Patients, Endurance Exercise, IL-6.

It has been shown that lung diseases are on the rise popularly, and this issue denote an important cause of mortality and morbidity[20]. To date, the current management of asthma centers on the optimal control of airway inflammation as a central component of asthma control. Asthma is a disorder characterized by inflammation of the airways, and inflammation cytokines plays an important role in this disease[7,24]. Other studies have indicated that asthma is a complex syndrome with many clinical phenotypes[12,24]. Its major characteristics include a variable degree of airflow obstruction, bronchial hyper-responsiveness, and chronic airway inflammation. Allergic asthma is a chronic inflammatory illness that happens in response to of the airways that occurs in response to breathed in allergens like dust mites in the house, cat dander etc.[12]. In some inflammatory diseases similar to asthma serum concentration of Interlukine-6 (IL-6) has been shown to be increased[9,28]. Hence, the IL-6 has been stated an indicator of inflammation together with other classical inflammatory

cytokines (TNFα and IL-1β)[9,20,26]. The concentration of IL-6 has been increased in asthmatic participants compared with the concentrations in healthy nonsmoker participants[26], suggesting that IL-6 may perhaps play a part beyond participants who had allergic asthma that only represents approximately 50% of all asthmatics. Also, it has been demonstrated that the IL-6 secretion from alveolar macrophages is augmented in participants with asthma, typically in participants displaying a dual asthmatic response[6]. Some longitudinal studies have revealed that physical activity decreases the systemic inflammation in chronic diseases[13,22-24]. But, there is still restricted evidence on IL-6 responses to exercise in asthma patients. Thus, the present study aims to evaluate the significance of a long term aerobic exercise on serum concentration of IL-6 in adult men with asthma.

This study was approved by the Ethics Committees of Islamic Azad University, Parand Branch. The objective of this experimental study was to evaluate serum IL-6 response to endurance exercise program in group asthma patients. For this purpose, 32 adult asthmatic men (age = 39±5 years, BMI=29.06±3 $Kg.m^{-2}$) participated in this study by accessible sampling, and randomly separated into exercise (3 days/ 12 weeks) and control (no exercise) groups. Spirometry tests (Minispire model, Made in Italy) was performed in order to asthma diagnosis as well as to determine the asthma severity. FEV1 and forced expiratory volume in 1 s / forced vital capacity (FEV1/FVC) were measured. All patients were asked to avoid having tea or coffee as well as other airways dilator food for at least 4 hours prior to spirometry test. Before signing a consent form, all participants received written and verbal explanations about the nature of the study. All subjects were inactive, and none reported engaging in systemic (more than one time per week) sport activities before the study. Inclusion criteria for study group were determined as existing asthma for at least 2 years. Exclusion criteria included medications that alter carbohydrate metabolism, diabetes, inability to exercise, and history of hypertension or heart disease. All participants of both groups completed the anthropometrical measurements and blood samples before and after the exercise protocol. Height (m) and weight (kg) of the participants were measured with the barefoot and dressed in shorts and shirt. With these measures, the body mass index (BMI = $weight.height^{-2}$) was calculated. Visceral fat, and body fat percentage was determined using body composition monitor (OMRON, Finland).

All participants were advised to avoid any physical activity 48 hours prior to the blood sampling. Blood samples (5 mL) were taken between 8:00 am to 9:00 am subsequent to 10 to 12 hours overnight fast to measure serum concentration of the IL-6 from brachial vein in sitting position. Serums were immediately separated and stored at – 80 °C until the assays were performed. In fact, fasting blood samples were taken pre-training (pre-test) and 48 h after the training (post-test). Serum IL-6 was determined using the ELISA method (Diagnostics Biochem Canada Inc.). Exercise training program was performed at 60 to 80 percent of maximum heart rate of the participants. The endurance exercise was walking or running, and cycling on an ergometer. The exercise intensity was controlled by the heart rate monitor (Polar, Finland). All participants in the control group were barred

from contributing in any exercise. Finally, all measurements consist of fasting blood sampling; anthropometric measurements repeated 48 h after the last exercise session.

Statistical analysis:

The Kolmogorov-Smirnov test was used to determine the variables with normal distribution. Independent sample *t*-test used to observe group mean difference at baseline. Pre- to post training changes were determined by two-tailed *t*-tests, and the level of significance was set at $p < 0.05$. All data were analyzed using the Statistical Package for Social Sciences (IBM SPSS Statistics version 22.0).

At baseline, two groups were considered homogeneous regarding the IL-6 serum concentration (Fig. 1). The IL-6 serum concentrations after the post-test were not significantly changed. However, the serum concentration of the IL-6 was increased in the exercise group of asthmatic participants.

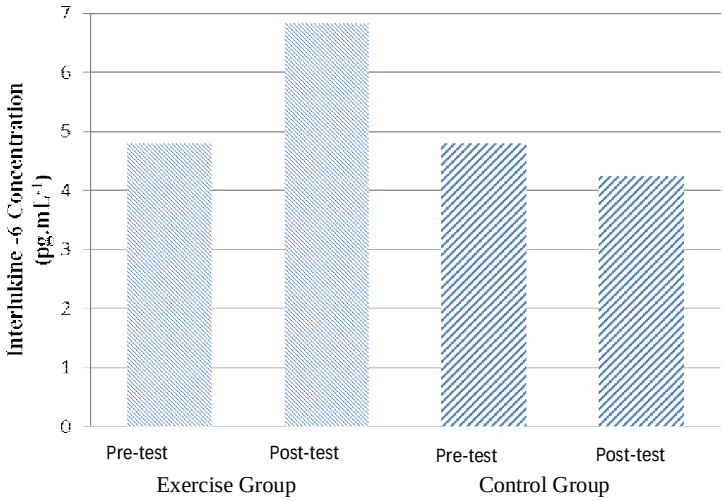

Figure 1. The changes pattern of serum concentrations of IL-6 at pre- and post-test.

Table 1. Mean and standard deviation of anthropometrical variables at baseline and after trial.

Variables	Control group		Exercise group	
	Pretest	post-test	Pretest	post-test
Age (years)	39 ± 5		40 ± 4	
Height (cm)	174 ± 8.8		175 ± 9.5	
Weight (kg)	88 ± 9.6	89 ± 5.6	90 ± 11	86 ± 12*
Body fat (%)	27.4 ± 4.1	27.6 ± 3.8	28 ± 3.2	26 ± 3.11*
Body mass index ($kg.m^{-2}$)	29.06 ± 2.9	29.36 ± 3.4	29.83 ± 2.6	28.08 ± 3.14*

**Significantly changed* $p < 0.05$

It can be seen from the data in the table 1 that the anthropometrics variables improved significantly after the endurance exercise in the exercise group. BMI levels were significantly decreased in response to exercise program when compared with baseline levels (p = 0.021). Also, we found that the endurance exercise program decreased the body fat percentage, body weight and visceral fat in exercise group (p > 0.05).

The current study was designed to determine the effect of 12 weeks of endurance exercise on serum concentration of IL-6 in the allergic asthma patients. This experiment did not detect any evidence for the impact of endurance exercise on the IL-6 in both groups. Another finding was that a decrease in the anthropometric variables after aerobic training in the exercise group. Adipose tissue secretes a variety of bioactive mediators including adipocytokines such as adiponectin, leptin, resistin or classical cytokines such as IL-6 [8,25].

One of the chronic inflammatory disorders is asthma that characterized by episodes of reversible decrease of lung function and airway hyper-responsiveness to a number of stimuli[4]. In this disorder, allergy is the main reason of asthma symptoms mainly in children, while a lot of grown person have asthma with no involvement of an allergic factor[10]. Environmental causes, including air pollution and smoking, provide the development of asthma. The production of some cytokines like IL-6 is changed during exercise, and it is produced by many different cells, but the principal sources are stimulated monocytes/macrophages, fibroblasts and vascular endothelial cells[1]. In physical activity, IL-6 is formed in larger quantities than other cytokine, and it has been established that contracting muscles synthesize IL-6 [17]. During physical activity, the blood concentration of IL-6 depends on intensity and duration of the training[17]. However, some studies concluded that the most important factor is intensity and not the duration of exercise[27]. In short intense training the IL-6 concentration was increased[11,14]. Also, the serum concentration of IL-6 was elevated during or following endurance exercise.

Thirteen male participated in a study, and they pedaled a total distance of 468 km over 6 days[21]. It was concluded that IL-6 concentration was raised up instantly after exercise on Day 1 but was unchanged at rest for the duration of the event. Training 5 times per week for 2 months the blood IL-6 concentration was increased in diabetic and non-diabetic rats[3]. Recently, in a study fifty-seven no diabetic participants (17 lean and 40 obese) were enrolled in a 3-month supervised exercise[2]. The concentrations of the inflammatory markers TNF-α or IL-6 were decreased following exercise. In another study, the serum concentration of IL-6 of participants following exercise remained unaffected, but there as a reduction in the local skeletal muscle[5]. In the last decade, it has been shown that the concentration of IL-6 may use inhibitory impacts on TNF-α [18]. This cytokine prevents lipopolysaccharide-induced TNF-α production both in human, and IL-6 in the blood is involved in the regulation of TNF-α levels[15]. IL-6 in the blood stimulates the secretion of soluble TNF-α receptors, but not IL-1 and TNF-α, indicates that IL-6 have anti-inflammatory properties[15,16].

Based on our study, the design of endurance exercise is important when asthmatic participants are training, and has to be designed separately, with moderate to high intensity. However, exercise in asthmatic participants cannot improve the lung functions, but can increase cardiorespiratory condition by effects on the muscles and the heart. It has been shown that exercise in asthmatics supports decrease ventilation in training[19]. Hence, it lessens the possibility of inducing an asthma attack while physical activity.

In conclusion, twelve weeks of endurance exercise improves anthropometrical indexes in participants with asthma, and the pro-inflammatory indicator of IL-6 did not increase after the 3 months of training. Exercise was well tolerated among participants, and patients with stable asthma should be stimulated to join in regular training programs, with no fear of symptom exacerbation. More investigation is required to recognize the mechanisms by which physical activity effects asthma management.

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References :

1. Akira, S., T. Taga and T. Kishimoto (1993). *Adv Immunol, 54:* 1-78.
2. Baturcam, E. and J. Abubaker, (2014). Physical Exercise Reduces the Expression of RANTES and Its CCR5 Receptor in the Adipose Tissue of Obese Humans. 627150.
3. Bonyadi, M., R. Badalzadeh, M. Mohammadi, S. Poozesh and I. Salehi (2009). *Saudi Med J, 30*(11): 1390-4.
4. Giavi, S. and N. G. Papadopoulos (2010). *Adolesc Health Med Ther, 1:* 129-36.
5. Gielen, S., V. Adams, S. Möbius-Winkler, A. Linke, S. Erbs, J. Yu, W. Kempf, A. Schubert, G. Schuler and R. Hambrecht, (2003). *Journal of the American College of Cardiology, 42*(5): 861-868.
6. Gosset, P., A. Tsicopoulos, B. Wallaert, C. Vannimenus, M. Joseph, A. B. Tonnel, and A. Capron (1991). *J Allergy Clin Immunol, 88*(4): 561-71.
7. Heidenfelder, B., M. Johnson, E. Hudgens, J. Inmon, R.G. Hamilton, L. Neas, and J. E. Gallagher (2010). *J Asthma, 47*(1): 106-11.
8. Hotamisligil, G.S. (2006). *Nature, 444*(7121): 860-7.
9. Kishimoto, T. (2010). *Int Immunol, 22*(5): 347-52.
10. Kroegel, C. (2009). *Expert Rev Clin Immunol, 5*(3): 239-49.
11. Luheshi, G. N., J. D. Gardner, D. A. Rushforth, A.S. Loudon and N.J. Rothwell (1999). *Proceedings of the National Academy of Sciences, 96*(12): 7047-7052.
12. Maslan, J. and J. W. Mims (2014). *Otolaryngol Clin North Am, 47*(1): 13-22.
13. Meyer, A., G. Wendt, K. Taube and H. Greten (1997). *Pneumologie, 51*(8): 845-9.
14. Moldoveanu, A. I., R. J. Shephard and P. N. Shek (2000). *J. Appl Physiol (1985), 89*(4): 1499-504.
15. Neveu, W. A., J. B. Allard, O. Dienz, M. J. Wargo, G. Ciliberto, L.A. Whittaker and M. Rincon (2009). *J. Immunol, 183*(3): 1732-1738.

16. Pedersen, B. K. (2006). *Essays Biochem, 42:* 105-17.
17. Pedersen, B. K., A. Steensberg, and P. Schjerling (2001). *J. Physiol, 536*(Pt 2): 329-37.
18. Petersen, A.M. and B.K. Pedersen (2005). *J Appl Physiol, 98*(4): 1154-62.
19. Ram, F.S., S.M. Robinson and P. N. Black (2000). *British Journal of Sports Medicine, 34*(3): 162-167.
20. Rincon, M. and C. Irvin (2012). *Int J Biol Sci, 8*(9): 1281-1290.
21. Robson-Ansley, P., M. Barwood, J. Canavan, S. Hack, C. Eglin, S. Davey, J. Hewitt, J. Hull and L. Ansley (2009). *Cytokine, 45*(2): 111-6.
22. Rohrer, V. and A. Schmidt-Trucksass, (2014). *Ther Umsch, 71*(5): 295-300.
23. Shimwela, M., J. C. Mwita, M. Mwandri, G. M. Rwegerera, Y. Mashalla and F. Mugusi (2014). *BMC Public Health, 14:* 387.
24. Tarmast, D., A. Zand, G. Faraji and H. Parsian (2012). *Int. J. Biosci., 2*(6): 159-164.
25. Tilg, H. and A. R. Moschen (2006). *Nat Rev Immunol, 6*(10): 772-83.
26. Tillie-Leblond, I., J. Pugin, C.H. Marquette, C. Lamblin, F. Saulnier, A. Brichet, B. Wallaert, A.B. Tonnel and P. Gosset (1999). *Am J. Respir Crit Care Med, 159*(2): 487-94.
27. Wallberg, L., C. Mikael Mattsson, J. K. Enqvist and B. Ekblom (2011). *Eur J Appl Physiol, 111*(6): 1081-8.
28. Yokoyama, A., N. Kohno, S. Fujino, H. Hamada, Y. Inoue, S. Fujioka, S. Ishida and K. Hiwada (1995). *Am J Respir Crit Care Med, 151*(5): 1354-8.