

Effect of Eight Week Endurance Training on Serum Levels of Interleukin-2 and Interleukin-4 in Sedentary Men

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ABSTRACT: One of the factors that affect the immune system status and function is Physical activity. To find the response of cytokines to exercise, we examined the possible effects of an 8-week endurance training program on the serum levels of cytokines, including interleukin-2 and interleukin-4 in sedentary men. A total of 85 healthy young male volunteers were selected for this study. The training group followed a specific exercise protocol (running on a treadmill for 15-30 min at 50-70% maximal heart rate) for 8 weeks and the control group did not participate in any exercise program. Venous blood samples were collected 2 h before and 2 h after the exercise. Pair T test was used for statistical purposes. The serum levels of IL-2 and IL-4 were determined by ELISA. Non-significant ($p > 0.05$) Increases were observed in the serum levels of IL-2 and IL-4, after the 8-week endurance training program. The findings of present study indicate that an 8-week endurance exercise may affect non-significantly the serum levels of some cytokines.

Keywords: Cytokine, Endurance exercise, IL-2, IL-4.

INTRODUCTION

One of the most important products of the immune response, are cytokines. Cytokines are low molecular weight mediators secrete by cells of the innate and acquired immune, which affected on the many of the acquired and innate immune cells functions (Delves, Martin et al. 2011). We know that different stressor factors can influence on the immune system function such as physical activity that can affect the immune system status and function (Nieman, Davis et al. 2003), physiological state such as Pregnancy (Jahromi, Zareian et al. 2011, Jahromi, Shojaei et al. 2014) and also in some inflammatory diseases such as atherosclerosis (Jahromi, Shojaie et al. 2010).

Physical activity according to the severity, duration, type of activity have different effects on the immune system, among these parameters the exercise intensity of the most important factors that could affect the production and secretion of cytokines (Peake, Suzuki et al. 2005).

As mentioned, exercise can have different effects on the immune system, so that regular moderate exercise can improve the immune system function (Simpson, Lowder et al. 2012, Jahromi, Zar et al. 2014). In contrast, extreme and exhaustive exercise can weaken the immune system (Gillum, Kuennen et al. 2011, Walsh, Gleeson et al. 2011, Xiang, Rehm et al. 2014).

Cytokines are secreted by different types that included Th1, Th2 and T reg. Th1 cells are associated with cell-mediated immunity and play an important role in clearing intra cellular infections, While Th2 cells participate with humoral immunity and play a key role in the prevention of extracellular infection (Abbas, Lichtman et al. 2014).

Numerous studies have shown the influence of an acute bout of exercise on circulating levels of cytokines (Toft, Falahati et al. 2011, Kouda, Furusawa et al. 2012, Timmerman, Amonette et al. 2015). previous study has shown that exercise has different effects on cytokines. Timmerman et al showed that IL-10 increased after maximal aerobic exercise (Timmerman, Amonette et al. 2015).

Increased the serum level of IL-2, IL-4, and IL-10 were observed after acute aerobic exercise in human (LaVoy, Bosch et al. 2013). Sellar et al reported that IL-2 significantly decreased after 1 hour training program with 70% Vo₂ peak intensity rowing on a rowing machine (Sellar, Syrotuik et al. 2006). Alvandi and colleagues founded that 10 week resistance training can increase IL-4, but this increase is not statistically significant (Alvandi, Salehzadeh et al. 2014) or Balducci et al reported that a combination of aerobic and resistance exercise can reduce in serum levels of IL-4 (Balducci, Zanuso et al. 2010).

Several factors are participated in effects of various factors of the immune system included that exercise or physical activity parameters such as type, intensity, duration and various physical conditions (Pedersen and Febbraio 2005).

We use a human model to explore the role of endurance training on the some cytokine. Hence, the aim of this study was to investigate the effects of an 8-week endurance activity on the serum levels of interleukin (IL)-2, IL-4 in sedentary men.

MATERIALS AND METHODS

Subjects

A total of 85 healthy young male volunteers were selected for this study. Subjects with a history of heart disease, hypertension, diabetes, smoking and use of drugs were excluded from the study. Furthermore, the subjects were asked not to participate in any activities except the training program during the study period.

Research design and exercise program

The subjects belonging to the ET group underwent an 8-week endurance training program followed by a recovery period (Fig. 1). In brief, the subjects exercised on a treadmill three times a week for 8 weeks. Their running on the treadmill lasted for 15~30 min at 50~70% maximal heart rate. Venous blood samples were collected 2 h before and 2 after the exercise.

Anthropometric characteristics, including height, weight and body mass index (BMI) of all the participants, were measured using standard procedure before the beginning of the study, and resting blood samples were collected for cytokine assessment. In detail, 2 h before the beginning of the training Program and after a 10-h fasting period at 10:00 am, all the participants were asked to remain seated for 10 min, and first blood samples were collected. Subsequently, second blood samples were collected 2 h after recovery (end of the exercise training program). All the Participants were allowed to warm up for 5 min, and then they started to run on the treadmill (Table I).

Maximal heart rate

The heart rates of all the participants were recorded for the maximal heart rate calculation using Karvonen method (Jahromi, Zar et al. 2014) as follows: $HR_{target} = \% Intensity (HR_{max} - HR_{rest}) + HR_{rest}$

Cytokine concentrations tests

IL-2 was assayed by ELISA (Bendermed systems, Austria Ref NO: BMS221; It is based on the direct sandwich technique with biotin-Streptavidin, in which two monoclonal antibodies are directed against human IL-2. Human IL-2 present in the sample or standard binds to antibodies adsorbed to the microwells. A biotin-conjugated anti-human IL-2 antibody is added and binds to human IL-2 captured by the first antibody. Following incubation unbound biotin-conjugated anti-human IL-2 antibody is removed during a wash step. Streptavidin-HRP is added and binds to the biotin-conjugated anti-human IL-2 antibody. Following incubation unbound Streptavidin-HRP is removed during a wash step, and substrate solution reactive with HRP is added to the wells. A colored product is formed in proportion to the amount of human IL-2 present in the sample or standard. The reaction is terminated by addition of acid and absorbance is measured at 450 nm. A standard curve is prepared from 7 human IL-2 standard dilutions and human IL-2 sample concentration determined). Serum IL-4 was measured by ELISA (Bendermed systems, Austria Ref NO: BMS225/2) according to company instruction as the same method for serum IL-2.

Statistical analysis

For data analysis, Pair T test was employed using SPSS-12. The measurements were considered as statistically significant if $p < 0.05$. All the values were expressed as mean and standard deviation.

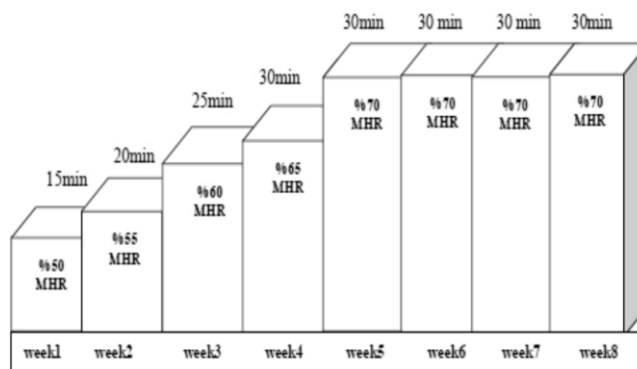


Figure 1. Eight-week endurance-training program.

Table 1. Duration and intense of training in an 8-week endurance Training

	Duration of running	Intense of training
Week 1	15 minutes	%50 maximal Heart rate
Week 2	20 minutes	%55 maximal Heart rate
Week 3	25 minutes	%60 maximal Heart rate
Week 4	25 minutes	%65 maximal Heart rate
Week 5	30 minutes	%70 maximal Heart rate
Week 6	30 minutes	%70 maximal Heart rate
Week 7	30 minutes	%70 maximal Heart rate
Week 8	30 minutes	%70 maximal Heart rate

RESULTS AND DISCUSSION

Results

Subjects

The baseline characteristics, of study group included age and BMI, 21.1 ± 1.8 years and 21.2 ± 2.4 kg/m², respectively.

Cytokine response to exercise

The serum levels of the cytokines IL-2 and IL-4 increased after the 8-week endurance training Program. However, mean serum IL-2 before and after the exercise were 3.40 ± 3.05 pg/ml and 4.13 ± 2.55 pg/ml, respectively. That this increase was not statistically significant ($P=0.125$). Mean serum IL-4 before and after the exercise were 2.64 ± 1.66 pg/ml and 3.16 ± 2.60 pg/ml, respectively. That this increase was not statistically significant ($P=0.117$) (Figure 2).

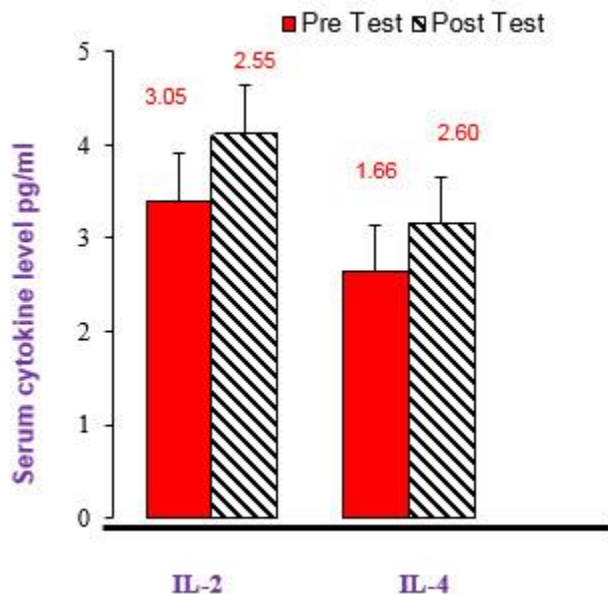


Figure 2. IL-2 and IL-4 serum level pre-exercise and post exercise.

Open bars: pre-exercise., solid bars: post exercise.

Discussion

In present research, we found that there are only limited studies about relation between low-intensity and low-duration aerobic exercise and cytokines.

In this study, the effect of endurance exercise on serum level of IL-2 and IL-4 as cytokines involved in the cellular immune response and in humeral immune response respectively, were evaluated by inactive People.

Eight week endurance training leads to a not statistically significant increase in IL-2 and IL-4 levels in sedentary men.

Previous studies on the effect of exercise on inflammation showed controversial results:

A significant increasing in the plasma levels of IL-4 after 4 weeks of McKenzie lumbar spine exercise was found in comparison with baseline (Al-Obaidi and Mahmoud 2014). Del Giacco et al., observed that IL-2 and IL-4 significant decrease after exercise training (Del Giacco, Scorcu et al. 2014). Other results demonstrate that aerobic conditioning reduces Th2 (IL-4) response (da Silva, Almeida et al. 2014). Serum level of IL-4 decreased after moderate intensity training (Gholamnezhad, Boskabady et al. 2014). Resistance training did not change serum il-4 level in human (Kjølhede, Dalgas et al. 2015) and after in rat (Jung, Ahn et al. 2015). Aerobic exercise did not change plasma level of IL-2 in asthmatic children and adolescents (de Andrade, Britto et al. 2014).

Exercise can causes intensity exercise dependent changes in immune system gene expression especially cytokines (Koch, 2010), and can temporarily change the levels of cytokines. These changes returned to normal level within a few hours. But people who long for a long time without adequate rest or doing heavy exercise may affect the immune response and inflammatory disease associated changes permanent (Koch 2010, Walsh, Gleeson et al. 2011).

The relationship between exercise and cytokines is complex and controversial. Exercise intensity, training conditions, location of cytokine measurement (e.g. tissue, plasma or urine), specificity and sensitivity of the methods of measurement and also type of cytokines participate in this relationship (Pedersen and Febbraio 2005). As we could not find any other similar studies with present research, it is necessary to distinctly examine the effects of each type of exercise on the immune system.

In conclusion, the results of the present study revealed that 8 weeks of insurance exercise cannot significantly affect the production of cytokines such as il-2 and il-4. To determine the effect of exercise and endurance training on cytokines and immune system further studies with larger sample sizes are recommended.

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CONFLICTS OF INTEREST

The authors have no financial conflict of interest.

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