

The Effect of 8 Weeks Aerobic Training on Serum Levels of Pro-inflammatory Cytokines (IL-17) and Immunoglobulins (IgA, IgM, IgG and IgE) Levels in Patients with Type 2 Diabetes

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Abstract

Sports activities play an important role in immune system function. Multiple short- long-terms, intense, endurance and regular exercise have different effects on immune system. In this study the effect of eight weeks aerobic training on serum levels of pro-inflammatory cytokines (IL-17) and immunoglobulins (IgA, IgM, IgG and IgE) in patients with type 2 diabetes were examined. **Methods of study:** 60 male type II diabetic patients age ranges from 30 to 50 years old with fasting blood glucose between 150-250 mg/dl were selected by cross-sectional clinical trial study. An eight-week program of aerobic exercise three hours per week, each week one hour training session was performed for them. Then 5 ml blood sample before starting the first session and 24 hours after eight weeks of training was taken. Serum levels of immunoglobulins E, G, M, A and IL-17 in patients before and after exercise were measured by ELISA method and the results were analyzed using statistical tests. **Results:** The results showed that serum immunoglobulin levels of patients after 8 weeks of aerobic exercise significantly altered but the serum levels of IL-17 was not significantly changed. **Conclusion:** Significant changes in the levels of serum immunoglobulin levels of athlete's diabetic patients hoping that exercise can improve their immune systems function. No significant changes in IL-17 after 8 weeks of training were due to the low-intensity exercise that requires further investigation.

Keywords: 8 weeks aerobic training; Serum levels of pro-inflammatory cytokines (IL-17); Immunoglobulins (IgA, IgM, IgG, IgE) levels; Type 2 diabetes

Introduction

The human immune system is always influenced by multiple harmful factors that to get rid of them, it is recommended that to do physical activities such as exercising regularly. [1] Researches have shown that regular and moderate intensity exercise play an important role in the prevention and treatment of many diseases, including immune system diseases, cardiovascular diseases, obesity, diabetes type II, hypertension and osteoporosis. [2] Investigate the effects of short-term exercise, intense, long-endurance activities and regular light exercise on immune system function and on the percentage of CD16 monocyte subset in obese individuals have extensively application in the development of public health. [3,4] In 2016 Gihan S Mohamed and Mona M Taha [5] reported the different effect of aerobic and resistive training on immunoglobulins in obese women. They showed that regular moderate aerobic training has been significantly increased IgM and IgG levels and improved immunity in response to aerobic training in comparison with resistive training group. The role of

aerobic training on improving of immune system of many infectious, non-infectious disease and quality of life in Individuals with type 2 diabetes has been well illustrated. [6,7] One of the diseases which are severely is under the effect of exercise training is type II diabetes as a metabolic disorder that based on statistics estimation about five to eight percent of adults population worldwide are affected with the disease. The disease is often referred to as insulin resistance or non-insulin dependent diabetes mellitus and decreased insulin sensitivity is called Type 2 Diabetes Mellitus (T2 DM) mellitus. [8] In 2011 International

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Diabetes Federation reported the number of people with type II diabetes about 285 million and predicts that by 2030 this may raise to 438 million.^[9] In 2010 Balducci et al. reported anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome that was dependent on exercise modalities and independent of weight loss.^[10] Later on numerous pro-inflammatory or anti-inflammatory factors such as IL-6 - IL-1, TNF- α and IL-17 has been introduced that they play a role in the pathogenesis of disease.^[11] These cytokines especially IL-17 are producing by many inflammatory cells like macrophages, lymphocytes and microglia cells as reported in the pathogenesis of osteoarthritis.^[12,13] Many of these cytokines are produced during strenuous sports activities. Evidence showed that IL-17 can be considered as reinforcement for granulopoiesis, the accumulation of neutrophils, activation of neutrophils in the lung, joint space, central nervous system and intestinal tissue taken.^[14,15] According to some researchers serum levels of IL-17 may be a useful biomarker for induction of acute inflammation.^[16]

On the other hand, intense training has a significant impact on the balance of cytokine activities and may cause changes in the distribution of these cells and causes temporarily suppression and weakened of immune system.^[17] In this regards, there are a few studies on the effects of exercise on these cytokines in diabetic patients. On the other hand, some documents suggested that during exercise changing in immune system components can be seen that may due to the intensity, exercise duration and sequence of exercise.^[18]

There is conflicting results on the effect of intense exercise on immunoglobulin levels. As Hans and colleagues and Keyvan Hejazi, reported that plasma levels of IgA, IgG, IgM in the first hours after the marathon race and in the recovery returned to normal and when any variation on amount of plasma was evaluated, only IgA was significantly increased.^[19,20] American Diabetes Association and American College of Sports Medicine confirmed that the rehabilitation program for diabetics patients is better to be aerobic exercise or a combination of aerobic and resistance training.^[21]

Due to lack of research on the base of impact of exercise on the immune system of diabetics patients, we design a study to know the effect of 8 weeks aerobic training on serum levels of pro-inflammatory cytokines (IL-17) and immunoglobulins (IgA, IgM, IgG, IgE) in patients with diabetes type 2.

Methods

This study is a clinical trial which is cross-sectional analytic descriptive type. 60 male patients suffering from type 2 diabetes who based on the criteria for diagnosis of Internal Medicine and Endocrinology, were selected. These patients at the time of study had fasting blood sugar between 150-250 mg/dl and their age ranges was from 30 to 50 years and referred to local clinics and hospital endocrine Ali ibn Abi Talib (aS) Zahedan city.

Non-inclusion criteria was included, patients suffered from other chronic diseases, mental illness, a program of regular exercise in the last three months, having a myocardial infarction record, uncontrolled arrhythmia, third degree heart block, high blood pressure. If during the 8-week study, each group of subjects were exposed to infectious diseases, are excluded.^[22]

In this study of 8-week program of aerobic exercise, we performed 3-hour training session each week that was a group included a stretching and warm-up and cool-down at first then do the training group at the end of each training session. The exercises programmed was running and endurance running, according to the Bruce protocol for 20 minutes on treadmill on the maximum level of 40% of maximum oxygen consumption (VO₂ max).

After taking biography and filling epidemiological questionnaires, hematology and immunology tests were performed on them. 5 ml of peripheral venous blood were taken and serum was separated and kept at -80°C in freezer until testing. After eight weeks of training, again 5 ml of peripheral venous blood were taken. Immunoglobulins G, A, M, E and IL-17 serum of patients before and after exercise, were measured by ELISA method and the results were analyzed using statistical tests by SPSS software.

Descriptive statistics for classification and data set and determine the central tendency (mean and standard deviation diffusion index) was used. To determine the normal distribution of data Kolmogorov-Smirnov test (KS) was used to compare pre-test and post-test and the within-group paired T-test was used.

Table 1: Anthropometric characteristics of the subjects such as age, height, weight and BMI.

BMI	Age	Weight	Height
24 ± 3	40 ± 10	76 ± 7	175 ± 8

Table 2: Comparison of mean and standard deviation of immunoglobulins and IL-17 before and after exercise on diabetic patients (case group).

Variables	Before exercise	After exercise	p-value
IgA	1.79+0.63	2.36+0.86	0
IgM	1.20+1.07	1.58+0.71	0.04
IgG	13.77+3.56	15.23+3.53	0
IL-17	1.22+0.20	1.23+0.28	0.94

Table 3: Compare the mean and standard deviation of immunoglobulins IL-17 before and after exercise on diabetic patients (control group).

Variables	Before exercise	After exercise	p-value
IgA	1.83+0.66	1.96+0.55	0.21
IgM	1.36+0.38	1.15+0.51	0.44
IgG	13.53+3.50	14.05+2.88	0.26
IL-17	1.21+0.20	1.20+0.28	0.77

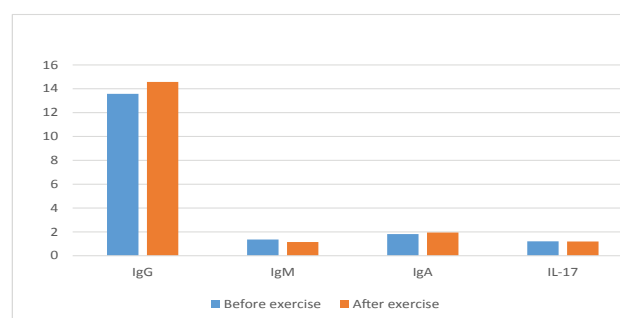


Figure 1: Changes in immunoglobulins and IL-17 levels before and after training in case group can be seen.

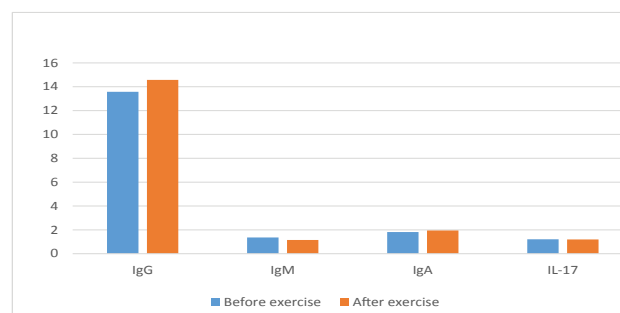


Figure 2: Changes in immunoglobulins and IL-17 levels before and after training in control group can be seen.

Results

The result of general and anthropometric characteristics of the patients are shown in Table 1. Kolmogorov-Smirnov test results showed normalization of data. The results of paired T test between case and control groups are shown in Tables 2 and 3. Thus these results showed that the serum immunoglobulin levels of patients after 8 weeks of aerobic exercise significantly changed but the serum levels of IL-17 was not significantly changed. Changes in amount of Igs and IL-17 levels in patients with diabetes in case and control groups are shown in Figures 1 and 2.

Discussion

Exercise plays a vital role in preventing and controlling type 2 diabetes. [23] So sports programs should be more appropriate in clinical care systems especially for patients who are at risk of type 2 diabetes. Although the regular physical activity may play a role in the prevention, complications and treatment of diabetes, but more people of at risk of type 2 diabetes are inactive in doing exercise. Meanwhile, despite the importance of physical activity in improving diabetes, there is still too much debate on the role of physical activity on preventing and controlling type 2 diabetes. One of the physical activity kind is aerobic exercises. It seems that aerobic exercises training promote the effectiveness of medical treatment in Type 2 diabetes mellitus. [8]

As mentioned in introduction, type 2 diabetes causes high blood sugar and hormonal changes and these affect changes and weakness in the immune system function. So physical exercise causes changes in the diabetic patient's immune system.

The results our study showed that serum levels of immunoglobulin G, A, M and E in type two diabetic patients was significantly increased after 8 weeks of aerobic exercise training. According to these results, we can say that strength training improves the diabetic patient's immune system and reduces the risk of infection. The results also showed significant difference in amount of immunoglobulins between case and control groups. Andrew et al. investigated on the fifteen active men who had physical activities for sixty minutes with seventy-five percent of $VO_2\text{-max}$'s. Their results showed that the levels of IgA, IgG, IgG2 and IgG3 were significantly increased that is similar to our findings. [24] Furthermore, Khazaei et al. and Jalili et al. showed changes of immunoglobulins levels after exercise is directly related to the duration and intensity of activity. Their results showed that exercise duration has a greater impact on changes immunoglobulins. Based on the results of this research, an intense anaerobic exercise (Wingate test) caused did not change in levels of serum immunoglobulins and only IgG was significant decreased. The researchers also found that activity in the conditions of fasting and fasting for 30 days caused significant changes in the immune system. In this study, IgM and IgA, were significant increased whereas IgE significantly reduced. Thus our results are partially consistent with these studies. [25-27]

In another part of our study IL-17 levels in diabetic patients after eight weeks of aerobic training in case and control groups did not significantly change. As mentioned earlier, IL-17 is a proinflammatory cytokine produced by different types of cells including lymphocytes and microglia cells expressed. Reduced levels of inflammatory and proinflammatory cytokines such as IL-17, will increase insulin sensitivity and improve diabetes disease. Similar to these findings, Barbara Strasser and Dominik Pesta found that glycogen during resistance training has been increased expression of GLUT-4 glycogen synthase adiponectin and decreased TNF- α and these led to improved insulin sensitivity. [28]

Furthermore the Effect of different training mode on Interleukin-6 (IL-6) and C-reactive protein (CRP) in type 2 diabetes patients has been studied by Kwi Baek Kim. [29] He showed significant decreases in the

post training values of weight, % Fat, BMI, IL-6 and CRP ($p < 0.05$) were observed in the circuit training group (CTG) compared to pre-training. However, there were no differences in the physical characteristic and blood inflammatory factors between the groups (aerobic training group ATG & CTG) aerobic training group (ATG, $n = 8$). Based on measured THR (target heart rate) for maximum oxygen consumption rate, the circuit training group (CTG) exercised at 60% intensity, 60 min/day, 5 sets, 3 days/week for 12 weeks. Our results with the results of Tofighee et al. are consistence. These researchers found that IL-17 after an intense training anaerobic did not change significantly [17] but with the research of IL-33, IL-6 levels after an intense aerobic workout session (Brus test) was consistent. [25]

Conclusion

Our results of this study showed that 8 weeks aerobic exercise considerably improved the diabetic patient's serum immunoglobulins. No significant changes in IL-17 level in this study were due to the low-intensity exercise sessions. However, the effects of aerobic and different types of exercise on various variables of immune systems function and inflammatory markers need to be investigated further.

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Conflict of Interest

The authors disclose that they have no conflicts of interest.

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