AENSI Journals

Advances in Environmental Biology

ISSN-1995-0756 EISSN-1998-1066

Journal home page: http://www.aensiweb.com/aeb.html

The Impact of Aerobic Selected Exercises on some of the Inflammatory Cardio-vascular Factors in type II Diabetics

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ARTICLE INFO

Article history:
Received 28 February 2014
Received in revised form 19 April 2014
Accepted 23 April 2014
Available online 25 May 2014

Key words:
Aerobic exercise, Cardio-vascular parameters, Diabetes type II

ABSTRACT

Introduction: Different studies about the role of inflammatory markers on emergence of type Ii diabetes show different findings and coronary diseases are the main factor of death in diabetics. **Goal**: Determining one selected aerobic exercise on the rate of some cardio-vascular parameters in type II diabetics **Methodology**: In the present study, 24 women suffering from type II diabetes with age average of 42.5 qualified to participate in the exercises program were randomly divided to two distinct and identical groups of exercise and control (each 12 persons).the subjects passed 8 weeks of exercise with three sessions on each week with intensity of 65 to 75%maximum heart rate. Blood sampling procedures before and after exercise program was done and the research variables were measured by Elisa method. The data normality was determined by Komolgrov-Smirnov method and the data analysis was done by descriptive analysis, dependent and independent T test. **Findings**: In the level IL-6(p=0.030) TNF- α, (p=0.004),hsCRP(p=0.006) significant difference was seen in average difference in pre-test and post-test. **Conclusion**: The findings indicate that regular aerobic exercise and blood sugar and insulin sensitivity control in diabetes cause reduce common cardio-vascular diseases and it is always looked at as a anti-inflammatory factor .Performing a regular aerobic exercise while observing the intensity and the principle of overload in exercise cause reduce inflammatory factors in emergence, prevention and control of cardio-vascular diseases and reduce the atherosclerosis risk.

To Cite This Article: Seyyed Mahmoud Hejazi, Ladan Hosseini Abrishami, Marzieh Ashkanifar, The Impact of Aerobic Selected Exercises on some of the Inflammatory Cardio-vascular Factors in type II Diabetics. ***Adv. Environ. Biol., 8(9),*** *357-362, 2014*

INTRODUCTION

Today diabetes is spreading throughout the world. It is one of the most common chronic diseases that not only brings about inability and low quality of life, but also imposes huge costs to the patients, their families and the society [1].

By increase in the cases of the disease, it is expected to remain as one of the main causes of pathogenesis and mortality. Cardiac disease specially coronary diseases is a main cause of death in diabetics [2]. In comparison with non-diabetics, the diabetics have a higher rate of cardiac coronary disease, coronary ischemia, more risk of MI and asymptomatic myocardial ischemia. Hence, diabetes is known equal as coronary cardiac disease and sugar control that starts just after diagnosing diabetes, does reduce the cardio-vascular complications [3,4]. The most common cause of cardio-vascular disease in a diabetic person is the rigidity of coronary arteries or arthrosclerosis caused by accumulation of cholesterol in the vessels responsible to take food and oxygen to the heart. Accordingly, the cardiac and diabetics specialists recommend that like the patients with heart attack history, the diabetics should try to take away the risk factors of heart diseases as they are more vulnerable to heart attack. The rate of mortality due to cardiac diseases among the diabetics is higher than other people. Not only The rate of heart attack risk but also the risk of heart failure is high in diabetics [5].

The pathological similarity of resistance to insulin with the inflammatory condition of arthrosclerosis has also been defined in the recent years and the cause is known as pre-inflammatory cytokines [6]. The hypothesis of relationship between inflammatory factors and diabetes was first proposed by Pickup and Crook. They believed that diabetes type II can be a response of the inflammatory cytokines manifestations of the body. [7]. One of the major inflammatory factors is the high-sensitivity –C reactive protein (hs-CRP) which is the most significant and the most sensitive marker and predictor of diabetes and cardiovascular diseases [8,9] In a number of temporary studies , increase in the levels of C reactive protein has been seen in diabetes type II.

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Different findings have also been found in studying the role of this factor in predicting diabetes type II. HuFb studies showed the independent role of inflammatory factors in predicting emergence of diabetes type II but this role disappeared in Festa A study after being balanced by BMI [10,11]. Different factors can influence this marker [12,13].

It has been stated that diabetes type II is characterized with deficiency and destruction of pancreas ß cells and resistance to insulin. This means that fatness and deficiency in insulin secretion are the most significant risk factors. A vast reduction in ß cells efficiency will lead to glucose intolerance in diabetes type II. These changes are probably caused by an increase in inflammatory cytokines such as IL-6,TNF-α and IL-1[14]. It has also been revealed that adipose tissue is responsible for releasing proinflammatory cytokines like IL-6 and TNF-α[15].

Interleukin-6 plays a basic role in destroying beta cells .Beside increasing apoptosis, it controls insulin production and release which in itself increases diabetes type II[16,17]. On the other hand, CRP is under Interleukin-6 induction and Tumor necrosis factor alpha. It is produced in liver and it is a risk factor that has to be diagnosed before the start of the disease [18].

Tumor necrosis factor alpha by itself, causes intravascular thrombosis mainly caused by diminishing the natural anticoagulant property of endothelium .This cytokine makes endothelial cells to express tissue factor. This substance is drastically anticoagulant. Activating neutrophils intensifies the endothelial changes and vascular blockage .The capability of this substance in necrotizing tumors that is also its appellation is mainly because of blood vessels thrombosis [19].

Studies have shown that most women are afraid of cancer before reaching their menopause and try to control the symptoms of the disease. While the risk of diabetes and heart diseases are common in women. Dr. SharonneHayes, women cardiac diseases advisor believes that most women are ignorant of the risk factors and symptoms of cardiac diseases. Studies have shown that the risk of diabetic coma in women is 50 % higher than in men. Not considering the condition of menopause, the diabetic women suffer 6 to 7 times more from peripheral vessels than non-diabetic women. Intermittent limping accompanied with 3 to 4 times the risk of coronary disease, stroke, or heart failure in diabetic women. When being affected by MI ,the diabetic women are more vulnerable to death and there is normally less treatments for these group of patients [20]. Findings show that physical activities mostly aerobic ones can have positive effects on hypertension, lipid components ,insulin resistance, fatness and blood clotting [21]. Thus regular physical activity can be considered as a therapeutically program the main advantage of which is to help preserve the health and prevent a number of future diseases [22]. This study tries to determine the amount of biomarkers and risk factors related to diabetes and cardiovascular diseases diagnosis in diabetic women in order to make them informed in which stage of the disease they are and what they should do to prevent the disease.

METHODS AND MATERIALS

This is a semi-experimental applied study. The middle-aged women suffering from diabetes type II and some inflammatory cardio-vascular parameters (IL-6, TNF-α and hs CRP) were studied. After calling for participation in the research, 80 middle-aged women suffering from diabetes type II announced their agreement to take part in the research. After screening ,interview and medical records and type of medication they had,24 type II diabetic women with age range of 42.5 whose blood sugar ranged between 130 to 200 mlg/dcl and did not have any history of regular physical activity for at least 6 months before the study, were selected and divided into two groups: exercise group (12 persons) with BMI average of 29.60 and control group [12] with BMI average of 29.30 with the goal of increasing the intensity of the activity from 65% maximum heart rate in the first week to 75% maximum heart rate in the last week, the exercise group performed activities in the gym observing the principles of adaptation with exercise and the principle of overload to aerobic exercises for 8 weeks, three days per week. The MHR(maximum heart rate) was calculated by the equation (220-age).

The aerobic exercise sessions were done in 60 minutes. Primarily 15 stretch and flexibility movements for warming up and then 20 to 30 minutes main exercise of running with increasing intensity on treadmill with 65 to 75% MHR. The subjects had the active rest in the form of "Intensity reduction" during the exercise if required and they had 10 to 15 minutes for cooling up. According to the overload principle and based on exercise protocol, at the beginning of the weeks the time of exercises increased and the time for cooling up decreased. Throughout the exercise, the heart rates of the subjects were measured several times by polar stethoscope F1mt made in Finland to control the exercise intensity.

The stages of blood sampling was 14 hours before the first exercise session and after the last session of exercise and finally for extracting plasma after two stages of blood sampling, the samples were centrifuged and plasma was transferred and preserved in a standard freezer with a definite temperature .The standard kit of Bender-med made in Austria was used for chemical analysis and testing hsCRP, IL-6 and TNF-α in Elisa method by Elisa reader made in the United States.

For primary analysis of the data and drawing the tables of frequency, percentages, averages and SD, the SPSS software version 18 was used and Kolmogrov-Smirnov test (K-S test) was used to determine the

normality of the variables. In order to compare pre-test and post-test within each group paired-samples T test was used and independent t test was used between the two groups in level of significance of P,0.05 for the research hypotheses.

Results:

The data were classified according to average and standard deviation in either groups of control and exercise. The Kolmogorov-Smirnov test showed normal distribution of data in all stages of post-test and pre-test. Descriptive statistics results of the difference of inflammatory cardiovascular risk markers in either groups between the pre-test and post-test are given in table 1.

Table1: Descriptive data for inflammatory factors difference between pre test and post test

Difference between pretest and posttest *mean±sd*	Control Group	Aerobic Training Group
hsCRP(mg/l)	0.10±0.19	-0.39±0.36
TNF-α(pg/ml)	0.11±0.66	-0.61±0.49
IL-6(pg/ml)	0.05±0.38	-0.33±0.43

The mean difference between the pre-test and post-test in the inflammatory marker hsCRP in exercise group was -0.39 while it was 0.10 in the control group , TNF-α levels were -0.61 and 0.11 in exercise group and control group, respectively, and the levels of IL-6 in exercise group were -0.33 and 0.05 in the control group According to the data in table 2, all three factors (hsCRP , TNF-α, and IL-6) were significantly lowered in the aerobic exercise group in comparison with the control group. As table 3 and the results of independent t-test indicate, a significant difference was observed in the levels of hsCRP ($p = 0.006$), TNF-α ($p = 0.004$), and interleukin-6 ($p = 0.030$) in the mean difference of pre-test and post-test of control and exercise group after 8 weeks of aerobic exercise training.

Table2: Dependent t test results on control and exercise group

	Group	Pretest	Post test	T	P-Value
hsCRP(mg/l)	Control	2.60±0.36	2.70±0.40	1.946	0.078
	Training	2.70±0.27	2.31±0.41	-3.713	0.003
TNF-α(pg/ml)	Control	26.12±3.14	26.01±2.97	-0.574	0.577
	Training	25.41±2.96	26.02±3.00	4.324	0.001
IL-6(pg/ml)	Control	3.05±0.64	2.99±0.70	-0.462	0.653
	Training	2.97±0.57	2.64±0.73	-2.673	0.022
Significance was set at P<0.05.					

Table3: Independent t test results on control and exercise group

	Levene's Test for Equality of Variances		T- test for Equality of Means		
	F	Sig	Means Difference	T	P-Value
hsCRP(mg/l)	2.219	0.151	-0.500	-3.030	0.006
TNF-α(pg/ml)	0.001	0.981	-0.721	-3.20	0.004
IL-6(pg/ml)	0.087	0.771	-0.385	-2.313	0.030
Significance was set at P<0.05.					

Discussion:

The findings of the research show that regular aerobic exercises while observing intensity and duration of the exercises as well as the overload principle improves the endothelial function and reduce the interlukin-6,High-sensitivity-C Reactive Protein and Tumor necrosis factor alpha. These findings are confirmed by previous reports stating that regular physical activity and cardiac-respiratory fitness are accompanied with lower inflammatory cardiovascular parameters [23].

In type II diabetics, the inflammatory biomarker levels and the parameters related to endothelial function significantly increase. Imperfect insulin function prevents glucose metabolism and makes it stored as lipid (lipid tissue) which is the cause for increase in blood density and systolic and diastolic hypertension in diabetics. Following an increase in blood density in the diabetics, CRP level and other inflammatory cytokines specially TNF-α and IL-6 also increase .Regular aerobic activities are accompanied with useful changes in developing muscular mass, effective glucose storage and increase in glucose in blood circulation and improvement in resistance to insulin and this clearly reveals the influence of athletic activities on useful adaptations. The relation between lower levels of inflammation and physical activity makes one of heart protecting mechanisms. The common concept in pathophysiological inflammation in connection with atherosclerosis is the production of cytokines with inflammation in response to oxidized LDL stimulus and macrophages accompanied with

atherosclerosis plaques .It has been stated that regular exercises reduces oxidized LDL as well as Interlukin-6 and TNF-α.The potential mechanism of physical activities and hsCRP changing levels is that by regular physical activities, the lower density base of plasma interleukin can be defined. One of the most significant interleukins responsible for reducing hsCRP levels in people after having sport activity is inflammatory cytokine IL-6 which shows CRP synthesis stimulation in liver released from lipid cells in lipid mass. Thus regular exercises can probably affect IL-6 level and reduce hsCRP levels in exercise group.

Interleukin-6 is one of the cytokines which has been widely studied for its changes after physical activity .A number of studies have shown that IL-6 increase is something beyond a tissue damage and it is probably a physiological response to physical activity [24] and its increase in the muscles while doing physical activities has been proved .This increase in the body is the result of liver production or macrophages. In the present study, IL-6 in exercise group showed a drastic reduction. Considering the role of this cytokine in balancing metabolism, this decrease can be known as a kind of adaption in burning lipid tissue to glucose .A process that can lead to preserving the glycogen storage.

In a study, Woods (2000) investigated the role of six months aerobic exercise on immunity function and changes of some cytokines .He concluded that after 6 months light exercise on treadmill interleukin reduced a little but showed no significant change [25].

Studies have shown that the amount of releasing cytokines like Interleukin-6 and Tumor necrosis factor alpha in fat people increases and this increase is related to some aspects of the syndrome of resistance to insulin followed by diabetes. Immobility followed by overweight exposes the person to the risk of metabolic syndromes like diabetes type II ,hypertension and disorder in distributing blood lipid ,it can act effectively in developing atherosclerosis procedures by forming lipid inflammatory defected profiles [26]. Regular and long sport activities has known advantages that reduce the prevalence of cardio-vascular problems in healthy and ill people. Meanwhile, an intensive activity causes increase in the amounts of pre-inflammatory cytokines which in themselves lead to increase in gene expression and serum amounts of leukocytes sticky molecules and enhances the monocyte reaction of endothelial cell[27]. Regular physical activity can have protective effects against cardio-vascular diseases. Physical activity directly affect cardio-vascular organ by increase in blood and plasma volume ,reduction in blood viscosity , increase in stroke volume and increase in VO_{2max}[28]. Nevertheless, lower amount of inflammation due to adaptation with sport activity may be related with antioxidant property of the activity. There are evidences of the made studies that indicate aerobic and strength exercise considerably decrease oxidant stress by increasing antioxidant capacity of the body [29]. Regular physical activities controls cytokines release from lipid tissue by decreasing sympatic stimulation [30]. The present study showed a significant difference in relation with performing aerobic exercises in TNF-α serum level of type II patients.

Previous studies such as the study made by Nei(2011) showed similar results with this research. After a 6 – month exercise program .He experienced a significant decrease in the rate of this parameter in old -aged diabetics .One of the reasons for this significant decrease ,he believed, was because of muscular dystrophy due to old age and a regular physical activity can reduce TNF-α gene expression and finally decrease this process [31].

Luiza (2012)observed the effect of three different types of exercise on insulin resistance ,inflammatory markers and cytokines in diabetics. The aerobic exercise program included 12 weeks exercise (3 weeks per week each session 60 minutes).At the end of the program, decrease in hs-CRP and IL-6in all three exercise group was evident but it was more considerable in aerobic group. While this change was not significant in spite of decrease in level of TNF- α [32]. Sallam (2010) in studying the effect of physical activity with moderate intensity on CRP plasma levels and TNF_ α and endothelial function in diabetic mice found a reduction in CRP level but this decrease was not significant in sixth week but in the sixth week CRP showed a considerable decrease as compared with control group [33].

Kondo (2005) studied the relationship between hs-CRP and aerobic exercise and insulin resistance in middle-aged men .The findings showed that hs-CRP had a significant reduction (34(.On the other hand, Zoppini (2006) studied the effect of moderate intensity exercise on inflammatory markers of type II diabetics. The exercise program consisted of 6 months aerobic exercise, 2 times per week. The findings showed that physical activity with moderate intensity has not made any change in hs-CRP and TNF-α.

Balducci(2010)studied the effects of different exercise programs on hs-CRP and some other inflammatory markers on type II diabetics with metabolic syndrome. The findings showed that hs-CRP in all three exercise groups had a significant reduction. This study showed that sport activities in type II diabetics with metabolic syndrome is accompanied with considerable reduction in hs-CRp and other inflammatory markers [35]. Jebeli(2012)in his study on type II men diabetics got similar results [36]. Malin(2012) studied the simultaneous use of metformin and aerobic exercise on cardio-vascular risk factors in diabetics. The subjects were divided into four groups: Pharmacological (P), Metformin (M), Pharmacological and exercise (EP) and metformin and exercise (EM).The results showed hs-CRP and IL-6 decrease only in M and EP groups. Of course due to lack of sufficient background and novelty of the issue, more studies with different statistical community and different intensity and duration of exercise is required. [37]. Generally speaking , existence of some differences in the

present research with previous studies can be because of different statistical community, age group ,intensity, duration and type of exercise, diet, the base level of inflammatory marker and life style of the people. It is probable that performing one course of regular aerobic physical activity while observing the intensity and duration and the principle of overload may reduce some inflammatory factors and decrease cardio-vascular diseases and decrease the risk of atherosclerosis in type II diabetic women.

Conclusion:

Considering the findings of previous studies and the present one, regular aerobic activity accompanied with blood sugar and insulin sensitivity control in diabetics reduce the diseases related including common cardiovascular diseases in these patients and it is always known as an anti-inflammatory factor. Generally, it is probable that performing a period of regular physical activity while observing intensity, duration and the principle of overload can decrease some inflammatory factors and reduce the risk of type II diabetic women to be caught by cardiovascular and atherosclerosis diseases. Thus regular exercises can have a valuable role in preventing diseases such as diabetes, atherosclerosis and inflammatory diseases. Therefore the people who are more physically active and have a better fitness hold lower levels of inflammatory markers. Moreover, further studies and investigations to support these findings seem essential.

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