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Changes in some of the indicators of liver inflammation and cardiovascular risk factors during a term of synthetic aerobic exercise of diabetic women

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ABSTRACT

People with type II diabetes have more liver function abnormalities than non-diabetics. Recent studies have shown the mutual relationship between metabolic conditions of type II diabetes and non-alcoholic fatty liver disease. Therefore, this study explores the effects of synthetic aerobic exercises on the indicators of liver inflammation (AST & ALT) and some of the cardiovascular risk factors of serum of the middle-aged women with diabetes (HDL, LDL, & triglyceride) who live in Behbahan city. Methodology: In this study, 30 participants were selected randomly from among women with type II diabetes with BMI>25, aged 45-60, and divided into control and experimental groups. The participants of the practicing group practiced 12 weeks (three days a week with the intensity of 55-70 % maximum heart rate (MHR) and 35-50 minutes per session). The results were analyzed with SPSS and dependent t-test was used to compare the average score of each group in pretest, and independent t-test was used to compare the averages of the different variables between two groups. Results: According to the results, 12 weeks of aerobic exercise have significant effect (p<0/05) on the level of alanine transaminase and aspartate transaminase of participant's serum. In addition, the results have shown that 12 weeks of aerobic exercise have significant effect (p<0/05) on high-density lipoprotein, low-density lipoprotein, and triglyceride of the participants. Conclusion: It can be concluded that synthetic aerobic exercise can be effective in the conditions of patients with type II diabetes with reducing some indicators of liver inflammation and improving the lipid profile of serum of the participants.

Keywords: diabetes, synthetic aerobic exercises, aminotransferase, lipids

INTRODUCTION

Many diseases like atherosclerosis, cardiovascular disease, and liver diseases result from diabetes that affects the quality of life and life expectancy [1]. The vital phenomenon and the risk of metabolic defect, including type II diabetes and cardiovascular disease, has been considerably increasing among the middle-aged and young [2]. More than 150 million people in the world and nearly three million people in Iran are suffering from diabetes and, according to the prediction of World Health Organization, this will be increased to 300 million adults by 2025 [3]. Despite these statistics, the reduction of blood sugar with standard treatment and consumption of chemical drugs has been not effective for preventing the side effects like liver disorders, cardiovascular diseases, eye diseases, neuropathy, and kidney failure [6]. Normally, the metabolism of fat that we consume in our food chain, takes place in the liver, and the fatty liver syndrome occurs when the liver cells start to accumulate the fat droplets (mainly triglyceride) [7]. Obesity and dyslipidemia have been associated with diabetes. In addition, fat accumulation in liver without inflammation is common in people with obesity and diabetes and those who suffer from other components of metabolic syndrome. Five enzymes that are commonly measured in liver diseases and are used to detect these diseases include: alanine aminotransferase (ALT), aspartate aminotransaminase (AST), Gamma glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH). Liver diseases are the main factor for increasing the activity of transaminase in serum [7]. AST enzyme has more activity than ALT in most types of diseases [7]. Ageing is related to the liver cell's function and the occurrence of chronic liver diseases. Liver function test is measured through various biological indicators (proteins). These proteins show different aspects of liver's normal function [8]; for example, the normal levels of ALT or AST show that the liver cells are normal [9].

It has been found that exercising has an integral role in managing and controlling type II diabetes. Traditionally, aerobic and endurance exercises have been recommended to elderly people with type II diabetes which, with reducing weight, can result in improved glucose tolerance and increased cardiovascular fitness [12]. Women have a lower quality of life compared to men; therefore, educational programs and appropriate intervention in order to improve the quality of these patients' lives has been considered as a basic necessity [13]. Given the importance of women's health in society and the effects of repeated practice and exercise on their liver, there are still many questions that require more study [14].

With ageing in human subjects, liver biopsy is usually not done because ageing reduces the regenerative capacity of liver cells significantly [15]. Moreover, considering the fact that in addition to liver cells, AST and ALP enzymes are also found in some other body tissues, the possible effects of regular exercise on the quality of human life [16], especially in ageing people, have been one of the major concerns of researchers [17]. Therefore, the purpose of the present study is to explore the effect of 12-week synthetic aerobic exercise on the indicators of liver inflammation and some cardiovascular risk factors of middle-aged women with diabetes.

MATERIALS AND METHODS

The present study is quasi-experimental and its purpose is applied. The participants of the study are women with type II diabetes, aged 45-60, who went to clinic No. 1 of Behbahan city. The sample was selected from among 250 files that were qualified (without cardiovascular, pulmonary, and skeletal diseases, treatment with defined tablets, specified blood glucose range BMI > 25), and finally 30 participants were randomly selected according to the purpose of the study and divided into control and experimental groups. After being informed about the research conditions, the participants were invited to interview in order to take initial measurements and run the required tests. Medical records and the kind of the drug that they use were determined (treatment was done through tablet). First, height and weight of the volunteers were measured and then their body mass index (BMI) was calculated using BMI-w/m^2 formula [17]. Kaiser physical activity questionnaire was used in order to ensure whether the participants were athlete or not, and it was revealed that the participants hadn't have regular exercise during the last six months. Before receiving testimonial from the participants, they were informed about the nature of conducting the research, the possible dangers, and the points they should keep in mind in order to participate in this study. After selecting the qualified samples, the 30 participants were randomly divided into two groups according to the table of random numbers (15 people in control group & 15 people in experimental group). To observe research ethics, in addition to getting consent from all participants, at first it was explained to them that the results of the study will be published for only research purposes and without mentioning their name. Moreover, their participation was completely optional, and they could withdraw at any stage of the research.

Table 1. The procedure of practice [resting heart rate 60% × (resting heart rate – maximum heart rate) = heart rate during practice]

Week	Warm-up time (minute)	Walking time (minute)	Duration of aerobic activity (minute)	Activity intensity (MHR)	Cooling down time (minute)
1	5	15	10	55-60%	5
6	5	15	15	60-65%	5
12	5	15	25	65-70%	5

The procedures of synthetic aerobic exercises:

The practice schedule with the intensity of 55-70 % maximum heart rate was held three days a week for 12 weeks, and the intensity was organized so that the practice began with 55% intensity of maximum heart rate and ended in the last week with 70 % intensity of maximum heart rate. Correspondingly, the duration of sessions changed from 35 minutes in the first session to 50 minutes in the last session. The schedule for each practicing session includes: five minutes warm-up, 25-40 minutes selected aerobic activity including 15 minutes fast walking (according to the required intensity of the practicing protocol), 10-25 minutes practice of aerobics, coordinated movements of the hands and feet, and finally five minutes cooling down. The implementation of the practicing schedule was according to the America diabetes association agenda that included warming up, running on a flat surface, team aerobic exercise, and cooling down [18].

Collecting Data

The test of aerobic endurance measurement (Rockport test): Rockport walk test is a test for estimating the range of human aerobic ability or the maximum consumption of oxygen VO 2 max in men and women in the range of 20 to 69 years. In this test, the participants are asked to walk 1 mile as fast as possible. This test is easy to perform and is suitable even for sedentary people or the elderly. The required equipment's: stopwatch (timer), one-mile road, and heart rate monitor. Procedure: during a one-mile (1/6 km) path, individuals' pulses are controlled with a monitor and the path is divided to 400 meters sectors, but the paths which are not divided to different sectors are also suitable. The participant should wear suitable clothes and comfortable shoes and, before beginning the test, make light stretching movements. The participant is trained how to walk during giving the test; that is, he should walk as fast as possible during a mile. The participants' pulses are taken as soon as they finish walking a mile. Preferably, it is better to attach a monitor to the participant so that it can show the heart rate. To estimate the participant's aerobic ability, the following formula can be used:

Vo_{2max} = 132/853 – 0/769 (weight) – 0/387 (age) + 6/115 (gender factor) –
3/2649 (time) – 0/1465 (pulse)

The estimation of Vo_{2max} according to ml/kg, is minute. In this formula, body weight is in pounds, age is in year, gender factor (men = 1 & women = 0), the completion time for one mile is in minute. After taking this test, the heart rate (HR) is in beat every minute which is included in the formula. Standard deviation (SD) of result in Rockport test is estimated up to 2 ml/kg min that shows a good reliability and validity for such a simple test [19].

Blood measuring

Measurement of blood parameters took place before the beginning of practicing schedule and after the end of the 12^{th} week. Before the participants go to the laboratory, the main and essential points regarding the nutrition and physical activity of the disease were announced to the participants so that they observe them carefully. All participants in the two groups of the study went to the laboratory at the same time of the day, between 8-10 a.m., while they didn't eat anything for 12 hours and didn't do strenuous physical activity 24 hours before the experiment. In the laboratory, 56 ml of venous blood from each participant's elbow was taken and poured in a test tube which contained anticoagulant, and then to separate the serum, the test tubes were placed in a centrifuge. After removing the test tubes from the centrifuge, they were moved to biochemistry and hormone sections in order to measure the density of ALT, AST, HDL, LDL, and triglyceride. According to the required instructions and using the automatic biochemistry analyzer and automatic gamma counter analyzer, this density is used to measure the dependent variables. In order to separate the serum, the blood samples were centrifuged for 10 minutes with a speed of 2000 rpm.

According to the previous planned schedule and observing the required points, the participants came to the specialized laboratory of Dr. Amini Behbahani in order to give blood sample for the pretest. Then, their body weight, resting heart rate, the maximum oxygen consumption, and height were measured and recorded in the personal information form. The participants were divided into control and experimental groups. The experimental group participated in the selected aerobic exercise program for 12 weeks. During the exercise protocol, one person withdrew from the experimental group in the middle of the practice and one person from the control group didn't participate in the post test. Therefore, the number of participants in each group was 14.

Statistical analysis

Descriptive statistics were used to show the raw information, estimate central tendency and dispersion, and draw tables and charts. Then, the Kolmogorov-Smirnov test was used to explore the normal distribution of data, and their normality was ensured. Considering the study purpose, inferential statistics (*t*-test) was used to test the hypotheses. After receiving the laboratory results, statistical methods using SPSS were used to analyze the results. Dependent *t*-test was used to compare the average score of each group in pretest and posttest, and finally independent *t*-test was used to compare the different variables' averages of the two groups. Bar charts were drawn to show the data and their differences in pretests and posttests.

Initial Test

The purposes of the initial tests were to control intensity, determine the suitability of practice with the selected group, and also become aware of the possible events or accidents. In order to determine whether the participants have the ability to do the activity with the required intensity and time, four participants were asked to do the practice with the determined intensity during an intended time for the first week (MHR = 55%). After this stage and becoming ensure of the accuracy of the protocol, the program was done with 15 experimental subjects.

RESULTS

According to the results, the participants of the control and experimental groups have no significant difference regarding the demographic characteristics, age, height, and weight (Table 2). The results show that 12 weeks of aerobic exercise can make a significant difference in the participants' high-density lipoprotein and low-density lipoprotein levels (Table 3).

According to the data in Table 3, because the significance level for alanine transaminase enzyme is equal to 0/035, 12 weeks of selected aerobic exercise have significant effect on the alanine transaminase levels of the participants' serums. In addition, the significance level for aspartate transaminase enzyme was 0/024; therefore, 12 weeks of selected aerobic exercise have also significant effect on the aspartate transaminase levels of the participants' serums. Moreover, the results have indicated that 12 weeks of synthetic aerobic exercise made significant difference on the serum amount of the blood triglyceride (Table 4).

Table2: Description of participants' age, weight, and height in the experimental and control groups

Characteristic	Group	Standard deviation ± Average	Minimum	Maximum
Age (year)	Experimental	53/25 ± 4/726	45	60
	Control	54 ± 5/736	45	60
Height (cm)	Experimental	159/6 ± 5/743	149	168
	Control	157/58 ± 4/420	148	164
Weight (kg)	Experimental	74/96 ± 8/996	65/5	84
	Control	72/37 ± 7/854	65	80/5

Table 3: Statistical analysis of the participants' aspartate transaminase enzyme (u/l) and alanine transaminase enzyme (u/l) in the experimental and control groups

Variable	Group	Test	Standard deviation ± Average	Significance level
ALT	Experimental	pre	22/71 ± 10/97	0/024
		post	22/03 ± 9/057	
	Control	pre	21/58 ± 7/744	
		post	27/25 ± 7/821	
AST	Experimental	pre	27/64 ± 16/73	0/035
		post	26/82 ± 14/95	
	Control	pre	26/5 ± 11/805	
		post	32/58 ± 10/93	

Table4: Statistical analysis of the participants' serum's lipids in the experimental and control groups

Variable	Group	Average difference	Significance level
LDL	Experimental	7/65	0/035
	Control		
HDL	Experimental	- 12/63	0/048
	Control		

Variable	Group	Average difference	Significance level
Triglyceride	Experimental	- 55/16	0/024
	Control		

DISCUSSION

For years, metabolic syndrome has remained a growing problem in the world, and this epidemic has become a pandemic [12]. Thus, having a longer life is of essential importance, and the immediate support of community against chronic diseases is a heavy duty [21]. When there is no balance between consumption and reception of energy, metabolic diseases develop [21]. Low levels of physical activity and lack of physical activity in lifestyle affect on organs such as the liver, heart, muscle and fat tissue as well as the relationship between these organs and create a defective cycle [22]; therefore, exercise and physical activity avoids such a cycle. It can be concluded that exercise and physical activity not only improve metabolism and functional capacity of tissues but also have a combined effect on the body's overall system. Physical activity and its role in society has been always a matter of discussion and investigators have always paid attention to it. High levels of inactivity play an essential role in spreading diseases like obesity, type II diabetes, and NAFLD. Finding ways to target the consequences of inactivity is one of the challenges of our generation. From the historical point of view, aerobic exercise intervention is used for understanding the impact of exercise on metabolic health and wellbeing. However, there should be more emphasis on physical activity level and the reduction of inactivity. Even without weight loss or a change in diet, small and achievable changes in physical activity habits have benefits for controlling the overall metabolic and especially for liver and hearth health [23].

In this study, it can be suggested that synthetic aerobic exercise for 12 weeks had a significant effect on aspartate amino transaminase enzyme. Although AST level of the experimental group had low reduction after aerobic exercise, it had significant difference compared to control group in which this level in post test was higher than pretest. Since type II diabetes has a direct relationship with NAFLD and has a direct impact on liver, fat in liver cells deposits over time. At first, the transformation of fat in the liver can be seen. Then, it changes to NAFLD, and finally leads to liver cirrhosis. As said before, the importance of the measurement of this enzyme is in the evaluation of myocardial infarction and disorders of liver cells. Since this enzyme is in hepatocyte mitochondria, its increase in blood serum is an indicator of serious liver diseases, and it is used for the diagnosis of liver cirrhosis.

Normally, fatty acids are transferred to liver through intestinal blood flow, and they change there and exit from liver in the form of phospholipid; this process is regulated by insulin. In the case of insulin resistance, fat accumulates in the liver, fat production also increases, and secretion of phospholipids reduces. This accumulation results in inflammation, insulin resistance, and liver cell death. Perseghin (2007) has found that higher levels of physical activity have a direct relationship with fat in the liver. Generally, physical activity oxidation increases total body fat in adipose tissue, muscle tissue and liver tissue that results in decreased circulating fatty acids [24]. Systematic physical activity results in capillary proliferation in skeletal muscle which in turn results in more effective reception of fatty acids in muscle cells. Within muscle cell, mitochondria density increases and more fatty acid enters the mitochondria. In addition, when mitochondrial enzyme content and the number of fatty acids attached to protein increase, oxidation of fatty acids increases. A significant increase in VLDL during and after physical activity can be seen and VLDL is removed by skeletal muscles that accelerate the cleaning up of fatty acids obtained from liver [25]. Moreover, physical activity reduces abdominal fat and visceral fat; both of them are the main sources of fatty acid that are released in plasma and they are accessible to liver. The findings of this study revealed that 12 weeks of aerobic exercise could reduce the AST enzyme; these results were in line with the findings of Mir (1391), Valizadeh (1390), Davoodi (1391), Noori (1391), Strazniki (2009) and in contrast with the findings of Mirdar (1398), Bashiri (1389), and Rezaei (1390). In this study, physical activity had high intensity and was done without considering the opportunity for recovery that could cause damage to some organs. Loza (2010) explored active lifestyle of the participants who were elderly; the findings were not consistent with the present study.

After analyzing the results, it was found that 12 weeks of synthetic aerobic exercise have significant effect on ALT liver enzyme. Physical activity resulted in the reduction of this enzyme in the experimental group while this enzyme increased in the control group.

Widely distribution of this enzyme is seen in the body tissues, and its highest density is related to liver tissue. The clinical importance of measuring this enzyme is restricted to evaluation of liver disorders and its amount is higher than AST at the beginning of hepatic lesion. Accumulation of fat in liver cells increases when fat production is high and their secretion from liver is disrupted, and this happens when the entrance fat to liver increases and secretion of phospholipid reduces. Physical activity increases the density of mitochondria in skeletal muscle that increases the oxidation capacity of fatty acid. Circulation of skeletal muscle capillaries increases the delivery of fatty acid to muscle. Increased carnitine transferase facilitates the transport of fatty acids into mitochondrial space and regulates the increase of fatty acid connected to the transfer protein of myocytes fatty acid [26]. Therefore, physical activity changes the fatty liver content and liver fat intake path [27].

The results of the study regarding ALT enzyme are consistent with the findings of Valizadeh (1390), Davoodi (1391), Noori (1391), Mir (1391), Strazniki (2009), and Slenter (2011). But, it seems that because of difference in age and the type of intervention, the results were different from the findings of Mirdar (1389), Rezaei (1390), Mariana Loza (2010), and Dories (2008). Dr. Bashir used endurance exercises in his studies, and this is may be the reason for the inconsistency of the result of his study with the present study.

The results of the present study indicated that synthetic aerobic exercise increased the amount of high-density lipoprotein in the blood. These findings were consistent with the findings of Blumenthal (2011) and Abedi (1390) but were in contrast with the findings of Firouzeh (1389), James A. (2011), Neiman et al. (2002). Some researchers have found that people adhering to diet and aerobic exercise for 60-90 minutes, 5-7 days a week, can increase VO2 and HDL level. Increased capillary density in aerobic exercises has more potential for removing and using fatty acids in people which results in increasing the density performance of HDL.

In Akaqueen studies, with high intensity of exercise, one group had significant improvement in increasing HDL and particle size, but this improvement remained only for 15 days after stopping the exercise. They concluded that lack of physical activity has a negative effect on lipoprotein metabolism, and moderate exercise moderates this. Three minutes moderate exercise each day like jogging (slow walking) has sustainable beneficial effect on HDL metabolism. Therefore, regular aerobic exercise increases HDL cholesterol levels.

High-density lipoprotein exits from the liver and the small intestine in order to collect cholesterol and binds with cholesterol and stores it in its center.

$$\text{lysolecithin + cholesterol ester} \longrightarrow \text{lecithin + cholesterol}$$

Lecithin cholesterol acyl transferase catalyzes this process. Exercise causes the increase and activity of this enzyme, and, in this way, it feeds and increases high-density lipoprotein particles. In addition, the increase of energy to more than 1200 kilocalorie per week results in increasing the amount of high-density lipoprotein [31].

The findings of the present study suggested that synthetic aerobic exercise created a significant increase in low-density lipoprotein; generally, these results are in line with the findings of Firouzeh (1389), Abedi (1390), Neiman et al. (2002) but in contrast with the findings of Blumenthal (2011). Although one of the most important lipid risk factors is to create arterial low density lipoprotein, when practicing a slight reduction in low density lipoprotein occurs that is susceptible to oxidation of low-density lipoprotein focus and finally leads to an increase in high-density lipoprotein. Moreover, people with normal lipid profile who exercise can reduce low-density lipoprotein [31]. But, in general, oxidation of low-density lipoprotein depends on the lipid composition and plasma antioxidant status [18]. Normally, in case of high levels of low-density lipoprotein and if cells do not need them, there is a lack of low-density lipoprotein receptors on cell surfaces. But when exercising, low-density lipoprotein enters the cells using endocytosis method and is decomposed by parser enzymes so that its compounds can be used by cells.

The results of the present study showed that aerobic exercise reduced the amount of serum triglyceride. Generally, this finding is consistent with the findings of Blumenthal (2011), Firouzeh (1389), and Neiman et al. (2002) but contrasted with the findings of Abedi (1390). Physical activity is effective in reducing triglycerides and raising high-density lipoprotein. These changes in lipids and blood lipoproteins are probably by changing their size [30]. It is suggested that individual's DNA status or paired chromosomes has a significant relationship with total cholesterol, low-density lipoprotein and triglycerides [31]. It is proven that a reduction in the amount of triglycerides remains stable for three days after exercising [29]. Studies have shown that those walking more than 6000 steps a day have 3mg dl higher high-density lipoprotein and 10 mg dl lower triglycerides compared to those walking less than 2000 steps a day. Moreover, exercises like jogging and swimming that consume 300 kilocalories energy in each practicing session that lead to 10 mg dl reduction in triglycerides and 5 mg dl increase in the amount of blood high-density lipoprotein [29]. Lipids in the body decompose in the form of triglycerides and fatty acids and enter blood [28]. Then lipoprotein transfer fatty acid which is used as substrate at the time of activity. Fatty acid is primarily stimulated by high-density lipoprotein which itself is stimulated by catecholamines. After this circulation, fatty acid enters active muscles and is used. Doing physical activities may lead to an increase in the amount of lipoprotein lipase in muscle capillaries, and this, in turn, results in the reduction of the amount of plasma triglycerides. In addition, the reduction of the amount of triglycerides in physical activity depends on individual's weight and occurs after reducing weight. An increase in high density lipoprotein also leads to reducing the density of triglycerides. This reduction occurs according to the accumulation of triglycerides and is related to intravascular transfers [31].

However, there are evident differences regarding the study factors that can be attributed to duration of practice, the age range of participants, and different intensities of practice.

CONCLUSION

The present study that explored regular physical activity for 12 weeks indicated that synthetic aerobic exercise had significant effect on participants' levels of alanine and aspartate transferase serum (p<0/05) which was the result of practicing intervention in experimental group. The findings of the study suggest that aerobic exercise can reduce high-density lipoprotein, low-density lipoprotein, and triglyceride levels of patients with type II diabetes (p<0/05). The reduction of AST and ALT which is the indicator of damaged liver cell is a sign for the relative improvement of liver in patients with type II diabetes. Generally, it can be stated that synthetic aerobic exercise can improve the condition of patients with type II diabetes by reducing some of the liver inflammation indicators and improving lipid profile.

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