

The Effect of Four Weeks Continuous Aerobic Training on Liver Transaminases and Glycemic Markers in Women with Type II Diabetes

Mehrzad Shaabani, Farzaneh Abolfathi, Ali Akbar Alizadeh *

Department of Exercise Physiology,
Shahid Chamran University of Ahvaz
(Islamic Republic of Iran), Ahvaz, Iran.

*Correspondence:

Ali Akbar Alizadeh, Department of
Exercise Physiology, Shahid Chamran
University of Ahvaz (Islamic Republic of
Iran), Ahvaz, Iran.

Tel: (98) 918 143 6507

Email: aliakbar.alizadeh1984@gmail.com

Received: 17 October 2017

Accepted: 15 December 2017

Published in February 2018

Abstract

Objective: Fatty liver disease is one of the most common diseases in women with type II diabetes. While regular exercise can decrease the complication of this disease, it was not clearly identified. The aim of this study was to evaluate the effect of four weeks aerobic training on Liver Transaminases and some glycemic markers in women with type II diabetes.

Materials and Methods: In this study, 20 patients with type II diabetes were participated in two groups (experimental and control group). The experimental group did the continuous aerobic training and running on treadmill with 55 to 80 percent of their maximum heart rate for five times a week during the four weeks. The blood samples were prepared in two pre-test and post-test steps to measure the levels of liver transaminases, glucose and insulin through ELISA method.

Results: Statistical analysis showed that after four weeks of aerobic training, the liver inflammatory markers, glucose and insulin related to the experimental group had no significant difference in comparison with control group ($P>0.05$).

Conclusion: The results indicated that doing the continuous aerobic training five times a week during four weeks with 55 to 80 percent of maximum heart rate, do not diminish liver transaminases, glucose and insulin in women with type II diabetes.

Keywords: Liver transaminases, Continuous aerobic training, Diabetes II type

Introduction

Atherosclerosis, cardiovascular, and liver diseases are resulting from diabetes which affects the quality of life and life expectancy in these patients (1-3). The liver is one of the most important organs of the body and is damaged in diabetic patients (4). The most important liver functions is detoxification of drugs, production of blood clotting factors, glucose storage in the form of glycogen and blood sugar regulation and fat metabolism. In fact, the role of the liver in fat

absorption and defense against germs and toxins should not be ignored (5). Generally, those who are suffering from diabetes type II have higher rates of liver function compared to healthy subjects. Recent studies indicated the integration relationship between diabetes type II and non-alcoholic fatty liver disease (NAFLD). NAFLD is a type of liver disease that is effective in the diagnosis of diabetes type II, and vice versa, and each of these can aggravate the other one (6). Important

biochemical change in NAFLD is an increase in the level of alanine aminotransferase (ALT) and serum aspartate aminotransferase (AST) in blood (7). In patients with diabetes type II, fatty liver disease due to damage to liver cells is very common and in the cases of diabetes along with obesity, the prevalence of this disease is 100% (8). Among liver aminotransferases, ALT is the most specific liver damage indicator and Gamma glutamyl transferase (GGT) is also considered as a sensitive indicator for liver damage (9).

Studies have also shown that changes in ALT, AST and GGT in people are associated with risk of developing cardiovascular diseases, diabetes type II, stroke and high blood pressure (10). The higher level of GGT is associated with the risk of developing insulin resistance and diabetes type II (11). ALT and GGT even in the normal range are associated with diabetes type II. Therefore, it seems that liver function indicators can be involved in the pathogenesis of diabetes. An increase in this indicator is detected in the NAFLD in obese patients with fat accumulation in the liver (12). Physical activity reduces liver lipogenesis enzymes and it has positive impact for type II diabetic patients with fatty liver (13). Regular physical activity can play an important role in the improvement of diabetic complications such as obesity, hypertension, hyperlipidemia, hyperinsulinemia, and increased sensitivity of target tissues to insulin. Aerobic exercises also reduce insulin resistance (14). The visceral fat reduction increase the fatty liver and improve the insulin resistance, moderate level of aerobic exercise is the most efficient method (15). On the other hand, it has been found that the level of liver enzymes in plasma fluctuate under the influence of physical activity. This factor is affected by duration, intensity, and type of exercise (16). It was also found that level of ALT and GGT enzymes reduced linearly with increasing periods of moderate and severe physical exercise (17). However, according to some studies, aerobic exercises do not lead to a reduction in liver pathologic indicators in males and females (18). For

example, Ross et al (13) showed that insulin sensitivity and liver fat level reduction did not change significantly after one week in people with non-alcoholic fatty liver. However, on the effect of aerobic exercise on levels of liver enzymes in patients with diabetes type II, few studies have found inconsistent results (increase, decrease or lack of change) that the effect of exercise on it was unknown and needs further investigation. The objective of this study was to investigate the effect of continuous aerobic exercise for four weeks on liver transaminase levels and some glycemic indicators of diabetes type II.

Materials and Methods

This was a quasi-experimental study. In this study 20 women with diabetes type II (aged 33-53 years, body mass index 25-30 kg per square meter) referred to Diabetes Center of Ahvaz Golestan Hospital in winter 2015 were selected and studied. After explaining the objectives of research and its stages for them and obtaining informed consent and completing the questionnaire (including demographic data, medical and physical activity history), they voluntarily participated in the study and they were randomly assigned to two groups of experimental (n=10) and control (n=10). Evaluation of medical records showed that all patients were treated with blood sugar lowering drugs such as metformin. Inclusion criteria included fasting plasma glucose 140-250 mg/dl, non-smoking, lack of insulin injections, lack of cardiovascular disease, hypertension, respiratory and musculoskeletal disease and no history of recurrent hypoglycemia or sport activity as well as the lack of any regular exercises. Exclusion criteria included absence in exercise sessions and lack of observing medical advices.

A week before the main intervention, they attended in the laboratory to find information on performing test on the device. After dividing the participants into two groups (experimental and control), height, weight and body mass index (dividing weight in

kilograms by the square of height), the ratio of waist to hip circumference (by calculating the waist and hip area), and the percentage of body fat (using a body composition device, Olympia version 3.3, South Korea) of subjects were measured in both pre-test and post-test stages.

Continuous aerobic exercise program included four weeks running on the treadmill, five sessions per week (20 sessions) on daily basis. The experimental group exercise program included warm-up, main stage, and cooling down. Subjects in the warm-up stage walked on treadmill with an intensity of 30-40% of maximum heart rate for 5 minutes. Activity duration was increased from one to four weeks, so that it continued up from 30 minutes in the first week to 60 minutes in the fourth week. Work intensity in walking exercise on a treadmill was considered as a percentage of maximum heart rate of an individual and it was calculated using the equation $220 - \text{age}$ for each subject. Accordingly, in the first and fourth weeks of continuous aerobic exercise, the participants in the activity stage run on treadmill with 55 to 80 percent of their maximum heart rate. The intensity of exercise was controlled by heart rate and in specified intervals with Polar heart rate monitor (Finland). Each subject at the end of each exercise performed cooling down exercise for 5 minutes with 30-40% of maximal heart rate. Table 1 provided continuous aerobic exercise protocol.

Fasting blood samples of all participants were prepared in the pre-test and post-test stages. Then, they were centrifuged at 3500 to 3800 rpm per minute. Samples were placed at -20°C until final analysis. Measuring each of the factors of liver inflammation criteria, glucose and insulin was performed using the special

kits. In this study, serum levels of glucose and liver enzymes were determined by kit (Pars Azmoon Company, Iran) and insulin level was determined using the kit (Cubas) through electrochemiluminescence method.

Statistical analysis

Descriptive statistics was used to determine the mean and standard deviation (SD) of each variable and the Shapiro-Wilks test was used to examine the normal distribution of data. To investigate the intra-group changes, paired T-test was used and to compare inter-group changes, analysis of covariance test was used. All calculations were performed using the SPSS, ver. 17 and level of significance of tests was considered $P < 0.05$.

Results

Mean and standard deviation of anthropometric indicators and body composition are shown in Table 2. The results of this study showed that continuous aerobic exercise after four weeks did not lead to significant changes in body mass index and body weight of patients. In addition, serum liver aminotransferase levels at the end of continuous aerobic exercise protocol did not change significantly (tables 2 and 3). According to the findings of the Table (3), significant changes were not seen in blood glucose and insulin level after implementing exercise protocol. However, intra-group changes showed that levels of (AST and GGT) in the intervention group in pre-test stage reduced significantly compared to post-test stage (P -value:0.01).

Discussion

One of the diseases increased in recent years is nonalcoholic fatty liver disease in obese patients characterized with fat accumulation in the liver. Cross-sectional studies have studied the correlation of this disease with insulin resistance, regardless of BMI, fat distribution and glucose tolerance (19) and it has been found that this disease is one of the metabolic

Table 1. Continuous aerobic exercise protocol

Weeks	Sessions	Moderate (min)	Work intensity (percentage of maximum heart rate)
1	5	30	55-80%
2	5	40	55-80%
3	5	50	55-80%
4	5	60	55-80%

Table 2. Anthropometric indicators of the subjects, before and after the training

Variable	Control Group (Mean \pm SD)		Experimental Group (Mean \pm SD)	
	Pre	Post	Pre	Post
Age	45.25 \pm 6.86	-	47.58 \pm 4.52	-
Height(cm)	157 \pm 5.29	-	156.92 \pm 8.45	-
Weight (kg)	68.84 \pm 0.80	69.48 \pm 1.07	66 \pm 3.35	65.71 \pm 2.99
BMI	26.86 \pm 1.36	27.74 \pm 1.34	27.06 \pm 1.62	27.83 \pm 1.33

Table 3. Hormonal indicators of the subjects, before and after the training program

Variable	Groups	Pre	Post	P-value	P-value
		(Mean \pm SD)	(Mean \pm SD)	(Intra-Group)	(Inter-Group)
Glucose (mg/dl)	Experimental	167/25 \pm 39/32	156/25 \pm 18/16	0/74	0/15
	Control	208 \pm 28/44	214/50 \pm 26/34	0/69	
Insulin (miU/ml)	Experimental	0/77 \pm 0/48	0/43 \pm 0/16	0/07	0/68
	Control	0/62 \pm 0/24	0/48 \pm 0/42	0/51	
Ast (U/I)	Experimental	21/60 \pm 1/20	18/21 \pm 7/70	0/01*	0/96
	Control	17/04 \pm 5/78	17/04 \pm 5/78	0/20	
Alt (U/I)	Experimental	14/4 \pm 2/60	13/57 \pm 4/75	0/16	0/40
	Control	12/42 \pm 4/42	10/85 \pm 3/93	0/81	
Ggt (U/I)	Experimental	17/04 \pm 6/30	21/28 \pm 8/63	0/01*	0/40
	Control	13/85 \pm 3/33	20/71 \pm 6/15	0/08	

*The significance level of $P < 0.05$. T dependent test was used to investigate intra-group changes and analysis of covariance test was used to investigate inter-group changes.

syndromes and it is associated with obesity and diabetes (20). On the other hand, results showed increased levels of AST and GGT are strong markers of liver injury and NAFLD and it is effective in the development of metabolic syndrome and diabetes (21). Many studies suggested the effect of exercise on improvement of glucose metabolism in people with diabetes. However, the clear and specific mechanisms of these effects have not still been recognized. Change in levels of liver inflammatory indicators of liver may be one of these mechanisms. There are few studies regarding the effect of exercise on liver transaminase levels. Therefore, the objective of this study was to investigate the effect of continuous aerobic exercise for four weeks on liver transaminase levels and some glycemic indicators in women with diabetes type II. The results showed that levels of liver inflammatory indicators (AST, ALT and GGT) Glucose and insulin, body weight, body mass index, and body fat percentage did not change significantly after four weeks of continuous aerobic exercise with intensity of 55 to 80% of maximum heart rate. The research findings are consistent with the results of study conducted by Straziki et al (22), while they are inconsistent with findings of study conducted by Suphay et al (23) and

Shahab et al (24). Reduced liver enzymes and reduced weight can be attributed to removing or eliminating of factors increasing these enzymes. Physical activity may reduce liver fat directly through changes in liver fat oxidation and fat synthesis (25). Losing weight can be achieved through resistance exercises and diet planning that can lead to significant improvement in serum ALT and liver histology in patients with NAFLD (22). The average weight loss can improve BMI and serum ALT levels and reduce liver fat refining liver and narcosis inflammations (26). Therefore, the amount of weight loss in this study was not enough to be able to create changes in the concentration of liver inflammatory indicators. Exercise is recognized as a non-medical treatment for many chronic diseases (27). Increasing the duration and intensity of exercise is considered as an important treatment step for patients with NAFLD and chronic liver disease (28,29). Studies showed that performing intensive, continuous, and long-term exercises cause damage to liver cells, resulting in the release of ALT and AST in the blood. The high plasma activity during these exercises can be due to change in muscle membrane permeability, discharge of muscle glycogen, and lipid peroxidation of cell membrane, and

cell damage caused by mechanical processes (30). The exercise program presented in this study included is running on the treadmill five times a week and probably another reason for the lack of significance change in the mentioned indicators is performing continuous and intensive exercises. According to the results of this study, no significant change was found in serum glucose and insulin levels after four weeks of continuous aerobic exercise, which it is consistent with result of study conducted by George et al (31). They justified their finding by small number of subjects and appropriate status of subjects in metabolic control in baseline conditions. Therefore, one of the reasons for lack of significance in glycemic indicators could be attributed to small number of samples in this study. Results also showed that 9 month aerobic exercise on a treadmill three times a week for 140 minutes with 50% to 80% maximum oxygen consumption causes a significant reduction in HbA1c, glucose, and abdominal fat percentage (32). The results of another study showed that aerobic exercise with increasing intensity did not create changes in glucose and insulin levels and insulin resistance. This lack of significant change was due to lack of change in maximum oxygen consumption and body mass index (33). A second reason that could justify lack of change in serum levels of

glycemic indicators in this study is lack of change in body mass index, since according to information found from above-mentioned studies, it could state that change in glucose and insulin level is influenced by reduced body mass. It seems that lack of significant decrease in body mass index of the subjects in the study is one of the possible reasons for lack of significant changes in glycemic indicators. Based on the results of this study, we can say that four weeks of continuous aerobic exercise five times a week has no impact on liver transaminase, glucose, and insulin levels in women with diabetes type II.

Conclusions

Some of the most important factors involved in the different results of this study could include during of diet intervention and exercise program, type of exercise used and calorie content of different types of diet. However, due to limited data, the effects of regular exercise on liver transaminase in diabetic patients is uncertain and it further research with longer time or diet control is required to be conducted in this area.

Acknowledgements

We appreciate sincerely all subjects for their participation in this study.

References

1. Lindro P, Guilherme MP, Wladimir RB, Inaian PT, Ana CG, Gláucio AS, et al. Exercise and spirulina control non-alcoholic hepatic steatosis and lipid profile in diabetic wistar rats. *Leapid in Health Disease* 2011;10(77):1945-50.
2. Delavari A, Mahdavi Hezaveh A, Norouzinejad A, Yarahmady S. Doctor and diabetes (National Programme Diabetes Control and Prevention). Ministry of Health and Medical Education, Department of Health, Center for Disease Control, Department of Endocrinology and Metabolic Disorders. 2th Edition, Seda publication: Tehran, 2004.
3. Amita S, Prabhakar S, Manoj I, Harminder S, Pavan T. Effect of yoga-nidra on blood glucose level in diabetic patients. *Indian J Physiol Pharmacol* 2009;53(1):97-101.
4. Tolman KG, Fonseca V, Tan MH, Dalpiaz A. Narrative review: hepatobiliary disease in type 2 diabetes mellitus. *Annals of Internal Medicine* 2004;141(12):946-56
5. Jamali R, Jamali A. Non-alcoholic fatty liver disease Feyz. *Journal of Kashan University of Medical Sciences* 2012;14(2), 169-81.
6. Williams KH, Shackel NA, Gorrell MD, McLennan SV, Twigg SM. Diabetes and non-alcoholic fatty liver diseases. *Endocr Rev* 2013;34(1):84-129.
7. Nikousokhan Ak. The relationship between fatty liver and diabetes. *Payam Diabete Journal* 2010;12(45):34-41.
8. Villegas R, Xiang YB, Elasy T, Cai Q, Xu W, Li H, et al. Liver enzymes, type 2 diabetes, and metabolic syndrome in middle-aged, urban Chinese men. *Metabolic Syndrome and Related Disorders* 2011;9(4):305-11.

9. Wannamethee SG, Shaper AG, Lennon L. Hepatic Enzymes, the Metabolic Syndrome, and the Risk of Type 2 Diabetes in Older men. *Diabetes Care* 2005; 28:2913-18.
10. Nakanishi N, Nishina K, Li W, Sato M, Suzuki K, Tataru K. Serum gamma glutamyl transferase and development of impaired fasting glucose or type 2 diabetes in middle aged Japanese men. *J Intern Med*. 2003;254:287-95.
11. André P, Balkau B, Born C, Charles MA, Eschwège E, DESIR Study Group. Three-year increase of gamma-glutamyltransferase level and development of type 2 diabetes in middle-aged men and women: the DESIR cohort. *Diabetologia*. 2006;49(11):2599-603.
12. Clark JM, Brancati FL, Diehl AM. The prevalence and etiology of elevated Aminotransferase levels in the United States. *Am J Gastroenterol* 2003;98:960-7.
13. Russ F, Margaret AG, David HB, Lawrence O, Denise MN, Li LJ. Exercise training down-regulates hepatic lipogenic enzymes in meal-fed rats: fructose versus complex-carbohydrate diets. *J Nutr* 1998;128(5):810-7.
14. Rahimi N, Marandi SM, Kargarfard M. The effect of eight weeks aquatic training on lipid profile of patients who suffer from type ii diabetes. *Journal of Isfahan Medical School* 2011;29(148):987-95.
15. Slentz CA1, Bateman LA, Willis LH, Shields AT, Tanner CJ, Piner LW, et al. Effects of aerobic vs. resistance training on visceral and liver fat stores, liver enzymes, and insulin resistance by HOMA in overweight adults from STRRIDE AT/RT. *Am J Physiol Endocrinol Metab*. 2011;301(5):1033-9.
16. Fealy CE, Haus JM, Solomon TP, Pagadala M, Flask CA, McCullough AJ, et al. Short-term exercise reduces markers of hepatocyte apoptosis in nonalcoholic fatty liver disease. *Journal of Applied Physiology*. 2012;113(1):1-6.
17. Debbie A, Sattar N, Davey G. The Associations of Physical Activity and Adiposity with Alanine Aminotransferase and Gamma-Glutamyl transferase. *Am J Epidemiol* 2005;161:1081-8.
18. Devries MC, Samjoo IA, Hamadeh MJ, Tarnopolsky MA. Effect of endurance exercise on hepatic lipid content, enzymes, and adiposity in men and women. *Obesity (Silver Spring)* 2008;16(10):2281-8.
19. Goto T, Onuma T, Takebe K, Kral JG. The influence of fatty liver on insulin clearance and insulin resistance in non-diabetic Japanese subjects. *Int J Obes Relat Metab Disord* 1995;19:841-5.
20. De Fronzo RA, Ferrannini E. Insulin resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia and atherosclerotic cardiovascular disease. *Diabetes Care* 1991;14:173-94.
21. Perry IJ, Wannamethee SG, Walker MK, Thomson AG, Whincup PH, Shaper AG. Prospective study of risk factors for development of non-insulin dependent diabetes in middle aged British men. *BMJ* 1995;310:560-4.
22. Straznicky NE, Lambert EA, Grima MT, Eikelis N, Nestel PJ, Dawood T, et al. The effects of dietary weight loss with or without exercise training on liver enzymes in obese metabolic syndrome subjects. 2012;14(2):139-48.
23. Cassidy S, Thoma C, Hallsworth K, Parikh J, Hollingsworth KG, Taylor R, et al. High intensity intermittent exercise improves cardiac structure and function and reduces liver fat in patients with type 2 diabetes: a randomised controlled trial. *Diabetologia*. 2016;59(1):56-66.
24. El-Kader SM, Al-Jiffri OH, Al-Shreef FM. Liver enzymes and psychological well-being response to aerobic exercise training in patients with chronic hepatitis C. *African health sciences*. 2014;14(2):414-9.
25. Ueno T, Sugawara H, Sujaku K, Hashimoto O, Tsuji R, Tamaki S, et al. Therapeutic effects of restricted diet and exercise in obese patients with fatty liver. *J Hepatol*. 1997;27(1):103-7.
26. Khoshbaten M. Comparison character of clinical and laboratory of nonalcoholic fatty liver disease with healthy people. *J Tabib Shargh Sci*, 2009;13-21. (in Persian)
27. Johnson N, Keating S, George J. Exercise and the liver: implications for therapy in fatty liver disorders. *Semin Liver Dis* 2012;32:65-79.
28. Reynoso E, Lavine J. The role of exercise in treating NAFLD. *Nat Rev Gastroenterol Hepatol* 2012;9:368-70.
29. Mikami T, Sumida S, Ishibashi Y, Ohta S. Endurance exercise training inhibits activity of plasma GOT and liver caspase-3 of rats exposed to stress by induction of heat shock protein 70. *Journal Applied Physiology* 2004; 96(5): 1776-81.
30. Samelman T. Heat shock protein expression is increased in cardiac and skeletal muscles of Fischer 344 rats after endurance training. *Experimental physiology* 2000;85(1):97-102.
31. Jorge M, Oliveira V, Resende N, Paraiso L, Calixto A, Diniz A, et al. The effects of aerobic, resistance and combined exercise on metabolic control, inflammatory markers, adipocytokines and muscle insulin signaling in patients with type 2 diabetes mellitus. *Metabolism clinical and experimental* 2011;60:1244-52.
32. Church TS, Blair SN, Cocreham S, Johannsen N, Johnson W, Kramer K, et al. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: A randomized controlled trial. *J Am Med Assoc*. 2010;304(20):2253-62.

33. Karstoft K, Winding K, Knudsen SH, James NG, Scheel MM, Olesen J, et al. Mechanisms behind the superior effects of interval vs continuous training on glycaemic control in individuals with type 2 diabetes: A randomised controlled trial. *Diabetologia*. 2014;57(10):2081-93.