The Effect of 12 Weeks of Selective Aerobic Exercise on Insulin Resistance and Hepatic Enzymes in Middle-Aged Type II Diabetic Women

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Abstract

Purpose: Hepato-diabetes as a serious complication has been studied by numerous researchers the world over and it has long been their dream to prevent hepatic tissue loss in diabetic cases. Regular physical activity and exercise have recently been suggested in this regard. There are not many studies on the effect of exercise on hepatic enzyme levels simultaneously with insulin resistance factor. This study aims to determine the effect of selective aerobic exercise for 12 weeks on insulin resistance and hepatic enzymes in middle-aged type II diabetic women.

Materials and Methods: the present study is applied semi-empirical. The participants included diabetic women who are members of Iranian diabetes society in Mashhad out of whom 30 were randomly selected for the goals of the study and were divided into two groups of experiment and control, each 15. They all took the pre-test and after 12 weeks of exercise (three sessions a week) by the experimental group, both took the post-test. Smirnov’s Kolmogorov statistical test was used to determine the normality of data and data analysis and independent t-test was used to test the hypotheses.

Conclusion: selective aerobic exercise created a significant change in insulin resistance and hepatic enzymes (AST and ALT) after 12 weeks (p<0.05). According to the findings of this study it can be said that aerobic exercise have positive effects on diabetes indices and would prevent the adverse effects of diabetes on live and reducing hepatic pathology indices.

Keywords: Type II diabetes, Aerobic exercise, Insulin resistance, AST, ALT.

Introduction

Many diseases like atherosclerosis, cardiovascular diseases and hepatic diseases are due to diabetes and will affect the quality of life and life expectancy of the patients (Lindro et al., 2011). Liver is a vital organ whose main functions in the body include detoxification of drugs, disposing of excess bi-products of red blood cell destruction and regeneration in form of bile, production of blood coagulant agents, storing glucose in form of glycogen as well as regulating sugar and fat metabolism. Indeed, the role of liver in absorption of fat and defending against microbes and toxins from foods should not be overlooked (Jamali, 2010). First noted glycogen accumulation in the nucleus of cells and suggested episodes of diabetes, tuberculosis, septicemia, hepatitis and self-immune diseases whose excessive accumulation will leave irreversible damage on liver tissue.

Those who contract type II diabetes, have higher rate of liver function compared with otherwise healthy individuals. Recent studies are indicative of a mutual correlation between type II diabetes and non-alcoholic fatty liver disease. NAFLD or non-alcoholic fatty liver disease is prognostic of type II diabetes and vice versa and each of these could lead to further exacerbation of the other (Williams et al, 2013). The most important biochemical change in NAFLD is an increase in AIT and AST levels of blood. They are kinds of protein that responsible for accelerating chemical reactions in liver. A rise in AIT level is a rather more specific symptom of NAFLD (Nikousokhan, 2010). Type II diabetes is indicative of insulin resistance and shows that normal insulin
levels of the body are not enough for insulin response to fat and liver cells and due to this lack of insulin reaction, pancreas consistently produces insulin so it results in high blood insulin and hyperglycemia. If this situation continues, the kidneys will suffer and the liver will become fatty. Insulin resistance also effects liver that results glycogenolysis and also increases hepatic glucose production. Abnormal accumulation of triglyceride and lipogens in insulin-sensitive tissue like liver are primary signs of insulin resistance and are detectable sooner that elevated blood sugar level (Harris and Benedict, 1991).

In case of high levels of insulin, the liver will turn the excess glucose into fat to prevent hyperglycemia. High concentration of triglyceride will intensify insulin resistance and create a futile chain reaction (Halls worth et al., 2011). Findings suggest that physical activity will reduce liver lipogens enzymes. Decrease of fatty acids with long chains result in synthesis reduction of triglyceride and this antilipogens effect of physical activity is greatly positive for type II diabetics with a fatty liver (Russ et al., 1998). Aerobic exercise reduces triglyceride and serum cholesterol and improves the situation of liver. Usually type II diabetics patient with a fatty liver are overweight and loss of weight, because liver tissue ALT levels improve (Davoodi et al., 2012).

Regular physical activity can play a crucial role in improving diabetes complications like obesity, hypertension, hyperlipidemia, hyperinsulinemia and increased sensitivity of target tissue to insulin. Aerobic exercises can decrease insulin resistance and hemoglobin glycolysis (Rahimi et al., 2011). However, according to some studies, aerobic exercise did not lead to a decrease in hepatic pathologic indices of men and women (Devries et al., 2008). But Russ (1998) observed a rise in insulin sensitivity and a fall in liver fat level after a week in cases with non-alcoholic fatty liver. In another study 12-month lifestyle intervention with high mobility did not alter the level of hepatic enzymes of obese people (Losa, 2005).

In light of contradictions observed in the studies and lack of research concerning hepatic pathologic factors in diabetic cases, this study followed the question does the regular aerobic exercise effect on the levels of ALT and AST enzymes and also on hemostasis indices of insulin resistance in type II diabetic cases.

Materials and Methods

The present study is quasi-experimental. The statistical population included type II diabetic women between the age of 45 and 55 that refer to Iran diabetes clinic in Mashhad, out of which 30 qualified cases were randomly selected and put into two groups of experimental and control, each with 15 cases. (Entrance qualification: without cardiac, vascular, pulmonary or skeletal disease history, medical treatment with specified pills, specific glycemic range, BMI≥25). Subjects recourse for initial measurements and essential tests. Medical history, drugs taken and glycemic ranges were determined. It was made sure that they did not have regular sport exercises in the past six months.

An aerobic routine with 55 to 70% maximum heart rate (that was continuously monitored) was given to them for three sessions a week for 12 weeks with increasing duration and intensity. In the first week, exercises started at 55% maximum heart rate and in the last week they finished at 70%. Accordingly, the duration of sessions started at 35, ending in 50 minutes in last week. Exercise schedule in every session was as follows:

1. Five minutes warm up
2. 20 to 25 minutes selective aerobic exercise that included 15 minutes jogging (according to the essential intensity by exercise protocol), 10 to 25 minutes aerobic moves i.e. coordinated arm and leg movements.
3. Five minutes cool down

This routine was based on American Diabetics Society instructions (Segal, 2001). Measurement of blood components was done prior to exercise routines on week one and at the end of treatment. Before the participants went to the laboratory, they were provided with information on major and essential nutritional and physical activity facts so that they can abide by them carefully. All participants in control and experimental groups were referred to the laboratory in similar times during the day (8 to 10 am) while 12 hours on fast and had no intense physical activity during the previous 24 hours. The density of glucose and insulin on fast, ALT and AST were measured using automatic biochemical analyzer and automatic gamma counter analyzer in the study. Glycaemia on fast was measured via glucose enzyme oxidase using Cubas Auto Analyzer (Parsazmoon Co. Iran) and in order to measure serum insulin by chemoschitophotometry, Demeditec lab equipment by German producer model DBC, Dim plus, Demeditec was used. Insulin resistance was calculated via insulin-resistance hemostasis HAMO-R (or insulin-resistance index) using glucose and insulin density on fast by the following formula:

$$\text{HAMO-R} = \frac{\text{fast glucose} (\text{mg/dl}) \times \text{fast insulin} (\mu\text{ml})}{415}$$

Upon receiving lab results, SPSS software was used to analyze the findings of statistical procedures. Smirinov’s Kolmogorov statistical test was used to determine the normality and the normal distribution of data. Then a dependent t-test was incorporated to compare the mean-scores of both groups in pre-test and post-test.
and then an independent t-test was used to compare the means of different variables. Significant level was (0.05).

**Results**

The collected data from 12 weeks of selective aerobic exercise in experimental group was analyzed. The results of statistical tests indicated that both groups are homogeneous in terms of age, weight and BMI (Table 1). Following the exercise program in experimental group, a significance decrease in weight and BMI was witnessed (p=0.049).

Insulin resistance had a significant fall in experimental group compared to control group (p=0.037) and also physical activity lead to a slump in plasma insulin levels of ALT enzyme (p=0.035) and AST enzyme (p=0.024) in experimental group (Table 2).

| Table 1: Description of age, height, weight and BMI variables in both groups (SD± average) |
|---|---|---|---|
| Group | Age (years) | Height (cm) | Weight (km) | BMI (kg/m2) |
| Experimental | 50.25±4.725 | 159.6±5.743 | 74.96±8.99 | 29.25±2.912 |
| Control | 51±5.736 | 157.58±4.420 | 72.37±7.845 | 29.33±2.149 |

| Table 2: level of ALT and AST enzyme in plasma and insulin-resistance in both groups |
|---|---|---|---|---|
| Item | Group | Test | The mean ± SD | The mean difference | Levene significance test | T- statistics | Sig |
| Insulin resistance (mg/dl.miu/ml) | Experimental | Pre | 6.16±2.63 | -1.64±1.83 | 0.556 | -2.174 | -0.037 |
| | Post | | 4.64±1.758 | | | | |
| | Control | Pre | 5.23±2.648 | -0.209±1.917 | | | |
| | Post | | 5.02±1.674 | | | | |
| ALT (u/l) | Experimental | Pre | 27.64±16.73 | -0.82±9.23 | 0.921 | -2.18 | 0.035 |
| | Post | | 26.82±14.95 | | | | |
| | Control | Pre | 26.5±11.05 | 6.08±8.92 | | | |
| | Post | | 32.58±10.93 | | | | |
| AST (u/l) | Experimental | Pre | 22.58±10.97 | 0.32±6.57 | | | |
| | Post | | 22.03±9.057 | | | | |
| | Control | Pre | 21.58±7.844 | 5.66±55 | 0.50 | -2.35 | 0.024 |
| | Post | | 27.25±7.218 | | | | |

**Discussion and Conclusion**

Results of this study show that 12 weeks of selective aerobic exercise has had a significant effect on type II diabetic cases. As is known, insulin action deficiency (resistance to insulin) and insulin secretion are signs of type II diabetes. This resistance is due to a reduction in insulin’s ability to leave its effects on target tissue, especially liver and kidney. When insulin stimulation for the transfer of glucose into the muscles decreases (insulin resistance) the result is a lack of ability to maintain blood glucose density within normal range. One factor responsible for this resistance can be a message deficiency through kinesis that will lead to a decrease in (glut4) plasma tissue. Lack of coordination between oxidative capacity of mitochondria and glycolysis capacity may be an important element in increasing insulin resistance because mitochondria contents and activities and oxidative capacity can be lowered in cases with type II diabetes (Peterson et al., 2004; Hawley and Lessard, 2007).

It seems that physical activity will increase insulin receptors in muscle tissue that will boost glucose delivery to the muscles and also boost the transfer of GLUT4 to muscle cell membrane and insulin-independent glucose absorption (Agosti et al., 2009). Physical activity also increases the number and density of mitochondria in skeletal muscles (Toledo et al., 2007) that will lead to an increase in oxidative capacity and a fall in insulin resistance (Rowell et al., 1996). These findings were consistent with those of, Russ et al (2011), Mariana et al (2011), Dubé et a (2008), Goodpaster et al (2003) and Slentz et al (2011), but were in contrast with those of Johnson et al (2009) and Hamedinia et al (2011) that is maybe due to short period of exercise protocol (4, 5 weeks verses 12 weeks). Physical activity resulted in a decline in levels of ALT enzyme in experimental group.
while in control group it actually elevated. A huge dispersion of this enzyme is seen in body tissues with the highest density in liver tissue. But the clinical significance of measuring it is limited to assessing hepatic pathologies and its levels are higher than AST in early hepatic damages. Excess deposit of fat in liver cells happens when fat production accelerates and liver excretion of fats is disrupted. At this time, incoming liver fat increases and phospholipid secretion decreases. Physical activity will improve mitochondria density in skeletal bones that will in turn boost the oxidation capacity of fatty acids. Capillary network of skeletal bones will better transfer fatty acid to the muscle and a rise in carnitine transferase will facilitate the transfer of fatty acid to mitochondrial space and will regulate the upward trend of fatty acid attached to the protein responsible mitosis fatty acid (Goodpaster et al., 2003). Hence, physical activity will change the hepatic fatty content and the consumption of hepatic fat (Boulé et al., 2001).

The results of this study regarding ALT enzyme are consistent with those of Valizadeh et al (2011), Davoodi et al (2012), Nuri et al (2012), Mir et al (2012), Stramieky et al (2012) and Slentz et al (2011), but were in sharp contrast with the findings of Rezaei et al (2011), Mariana et al (2011) and Devries et al (2008) that seems is due to age difference and the type of physical intervention. Bashiri (2009) used endurance exercises and the apparent inconsistency may be because of this. According to the results of this study, selective aerobic exercise for 12 weeks has significant effects on AST levels. Although AST levels of experimental group showed small reductions after exercise, significant difference exists with elevated post-exercise levels observed in control group.

Since type II diabetes is directly related to NAFLD and increases liver fat, this fat is deposited in the liver through time. At first, fat permutation is seen in the liver which is followed by NAFLD and then chang to hepatic Cirrhosis. As was said before, the significance of measuring this enzyme is in assessing myocardial infarction and liver cell disorders. Since this enzyme exists mostly in hepatocyte mitochondria, its increase in blood serum is indicative of acute hepatic disease which is used to diagnose an alcoholic liver.

It is known that fatty acids are normally transferred to the liver through intestinal blood stream and are changed there to exit the liver in form of phospholipid and the whole procedure is regulated by insulin. When insulin resistance exists, fats are deposited in the liver and fat production is accelerated combined with a decrease in phospholipid secretion. This accumulation will finally result in inflammation, insulin resistance and liver cell death. Persgin 2007 has showed in a study that higher levels of physical activity are directly correlated with lower levels of fat in the liver. In general, physical activity increases fat oxidation in fatty tissue, muscle tissue and liver that will lead to a fall in circulating fatty acid levels (Ormsbee et al., 2007).

Systematic physical activity increase capillary multiplication in skeletal muscles that cause the more effective transfer of fatty acid to muscle cells. The mitochondrial density inside cells increases and more fatty acid enters mitochondria. On the other hand, enzyme contents of mitochondria and fatty acids attached to proteins rise then increase the fatty acid oxidation. There was a significant growth in VLDL levels during and after physical exercise and this VLDL is taken up by skeletal muscles that will boost the filtration of fatty acids from liver. Physical activity will also help reduce the abdominal and intestinal fat, both of which are sources of fatty acids that are released into plasma and are absorbable by the liver (Church et al., 2007). In the findings of this study, 12 weeks of aerobic exercise has led to a decrease in ASL enzyme levels and this is consistent with the findings of Valizadeh et al (2011), Davoodi et al (2012), Nuri et al (2012), Mir et al (2012), Stramieky et al (2012) and in contrast with those of, Rezaei et al (2011) and Bashiri et al (2009). In these studies, high intensity physical activity was done without cool down that damaged some organs. Losa (2010) analyzed high-mobility lifestyle intervention on participants with high age average and her findings were inconsistent with the present research.

Selective aerobic exercise for 12 weeks caused significant effects on insulin resistance and hepatic enzymes (ASL and ATL). Experimental group post-test level decreased compared to their pre-test level while the levels of control group had huge rise that is a result of intervention in the experimental group. After aerobic exercise, BMI in the experimental group changed significantly in comparison with control group. It can be said that based on the findings, in type II diabetic cases, aerobic exercise may decrease insulin resistance. Also subsequent insulin resistance and blood glucose decrease the level of hepatic enzymes in serum that shows liver cell damage, decrease. This is a sign of improvement in the liver situation in type II diabetic patient. Thus, physical activity can be used as effective drug-free intervention for improvement and prevention from the destructive effects of this disease.

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