High intensity endurance training improves metabolic syndrome in men with type 2 diabetes mellitus

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Abstract
Introduction: Metabolic syndrome (MS) is a defined cluster of cardiometabolic abnormalities that increases an individual’s risk of type 2 diabetes mellitus (T2DM). The purpose of this study was to examine the effect of 12 weeks high intensity exercise training on MS in men with T2DM.

Material and Methods: Sixteen sedentary overweight and obese middle-aged men (aged: 41.18±6.1 years; ±SD) volunteered to participate in this study. The subjects were randomly assigned to training group (n=8) or control group (n=8). The training group performed endurance training 4 days a week for 12 weeks at an intensity corresponding to 75-80% individual heart rate reserve (HRR) for 45 min.

Results: The results showed that waist circumference (WC) as well as triglycerides (TG), blood pressure (BP) and
glucose were decreased in the training group compared to the control group (P<0.05). After 12 weeks, the training group resulted in a significant increase (P<0.05) in the high-density lipoprotein cholesterol (HDL-C) in compared with the control group (P<0.05).

Conclusions: In conclusion, high intensity endurance training improves metabolic syndrome in men with T2DM.

Key words: High intensity endurance exercise, Diabetes, Metabolic syndrome, Insulin resistance

1. Introduction

It is estimated that over 1 billion persons worldwide are overweight, more than 300 million of whom are clinically obese (1). In the United States, >60% of adults are overweight or obese, and the number of obese children and adolescents is dramatically increasing (2). Given its high and increasing prevalence, obesity is considered to be at pandemic levels. This has been attributed to an increasing worldwide adoption of energy-dense diets and sedentary lifestyles, probably as a consequence of urbanization and economic globalization (1). Unfortunately, most health care systems are based on treating diseases caused by specific agents after they occur. What is really needed for the pandemic of obesity, the metabolic syndrome (MS), and type 2 diabetes mellitus (T2DM) is prevention based on changes in lifestyle. However, neither governments nor private insurers have typically provided funds for these approaches.

The concept of MS includes a number of metabolic disturbances linked by insulin resistance, which increase cardiovascular risk (3). Adult-Treatment Panel III (ATP-III) of the National Cholesterol Education Program adopted the increased waist circumference (WC) (≥102 cm in men and ≥88 cm in women), elevated triglycerides (TG) (≥150 mg/dl), reduced HDL-C (≤40 mg/dl in men and ≤50 mg/dl in women), elevated blood pressure (BP) (≥130/85 mm Hg or on treatment for hypertension) and elevated glucose (≥100 mg/dl) as a major component of the clinical diagnostic criteria of the MS (4). It is currently recommended that individuals with MS be targeted for therapeutic lifestyle changes, which
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consist mainly of increases in physical activity and improvements in diet (5).

It is postulated that aerobic exercise improves glycemic control in T2DM primarily through increasing insulin sensitivity (6). A small study utilizing hyperinsulinemic euglycemic clamps has demonstrated an improvement in insulin sensitivity with only 15 days of aerobic exercise (7). The effects of exercise training on the lipid profile of persons with T2DM are not well known.

A meta-analysis examining the effects of aerobic training on lipid profile was performed by Kelley et al. (2007), who found a total of four studies comprising only 220 subjects. Endurance training was found to result in a 5% decrease in low-density lipoprotein cholesterol (LDL-C), but had no impact on high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), or TG (8). Two other meta-analyses attempted to examine the effects of both aerobic and resistance training on lipid parameters in T2DM, but found either no impact (9) or clinically insignificant improvements (10) in HDL-C levels. However, neither of these meta-analyses assessed the risk of bias, which might explain their negative findings. A more sophisticated meta-analysis by Hayashino et al. (2012) addressed both bias and study heterogeneity (11). This study found HDL-C \( (n = 35 \text{ studies}; 2059 \text{ patients}) \) was increased by 0.04 mmol/L, and LDL-C \( (n = 25 \text{ studies}; 1807 \text{ patients}) \) was decreased by 0.16 mmol/L. Although this impact on LDL-C is less than that seen with either statin use or diet intervention, it does suggest that exercise is a valuable adjuvant treatment for dyslipidemias in patients with T2DM (11). The results of the meta-analysis done by Hayashino et al are supported by the results of the 4-year Look AHEAD (Action for Health in Diabetes) trial, which was a multi-center randomized trial of an intensive lifestyle intervention on cardiovascular risk in subjects with T2DM (12,13). The studied intervention included both dietary and physical fitness (primarily aerobic exercise of a similar intensity to brisk walking) interventions. The program demonstrated improvements in both HDL-C, LDL-C, and TC levels, although it is difficult to distinguish how much of the improvements were due solely to the exercise component of the intervention (12,13). The effects of exercise training on MS in T2DM patients are still unclear and there are
conflicting studies; therefore, the purpose of this study was to examine the effect of 12 weeks high intensity exercise training on MS in men with T2DM.

2. Materials and Methods

Subjects
Sixteen men with T2DM with a mean (± SD) body mass index of 31.5 ± 3.9 kg/m², volunteered to participate in a 12 weeks training study. All the subjects were asked to complete a personal health and medical history questionnaire, which served as a screening tool. The subjects were given both verbal and written instructions outlining the experimental procedure, and written informed consent was obtained.

Inclusion criteria
All the subjects had slightly insulin resistance and all of them were complete inactive at least 6 month before the study and they were nonsmokers and free from unstable chronic condition including dementia, retinal hemorrhage and detachment; and they have no history of myocardial infarction, stroke, cancer, dialysis, restraining orthopedic or neuromuscular diseases.

Study design
A two-group, randomized, repeated measures, controlled trial was employed. During their first visit, the subjects were medically screened and had their anthropometric profiles measured. They were given Bouchard questionnaire of physical activity (14) and 3-day diet recall forms to complete. At the second visit, fasting blood samples were collected. Then, the subjects were randomly assigned to control group (n=8) or training group (n=8). The training groups performed endurance training 4 days a week for 12 weeks at an intensity corresponding to 75-80% individual heart rate reserve (HRR) for 45 min and control group were instructed not to change their physical activity and diet. All the measurements were repeated 48h after the last session of training.
Exercise training
The 12 weeks exercise training program included 4 training sessions per week on treadmill. During the 12 weeks intervention, the subjects were trained for 45 min per session at a heart rate corresponding to 75-80% of HRR. Each participant was equipped with a heart rate monitor (Polar, FS3c, Finland) to ensure accuracy of the exercise level.

3. Measurements

Anthropometric and body composition measurements
Height and weight were measured, and body mass index (BMI) was calculated by dividing weight (kg) by height (m²). Waist circumference (WC) was determined by obtaining the minimum circumference (narrowest part of the torso, above the umbilicus) and the maximum hip circumference (HC) while standing with their heels together. The waist to hip ratio (WHR) was calculated by dividing waist by hip circumference (cm).

Biochemical analyses
Fasting blood samples were collected at rest (before training) and after training. All the subjects fasted at least for 12 hours and a fasting blood sample was obtained by venipuncture. Plasma glucose was determined by the enzymatic (GOD-PAP, Glucose Oxidase-Amino Antipyrine) colorimetric method (Pars Azmoun, Tehran, Iran). The intra and inter-assay coefficients of variation for glucose were <1.3% and a sensitivity of 1 mg/dl. The serum insulin level was measured by a radioimmunoassay (RIA) and the insulin resistance index was calculated according to the homeostasis model assessment (HOMA-IR) which correlates well with the euglycemic hyperinsulinemic clamp in people with diabetes (15). Serum TC and TG levels were measured by enzymatic kits (Mann Chemical Company) using an auto analyzer. LDL-C and HDL-C were measured by an Auto analyzer using commercial kits (Pars Azema Company, Teheran, Iran).

Energy intake and energy expenditure controls
All the subjects completed the Bouchard Physical Activity Questionnaire (14) and 3-day diet recall forms and were instructed to maintain their
normal physical activity and dietary habits throughout the study. The nutrient composition was determined by a computer nutritional analysis program (COMP-EAT 4.0 National Analysis System, London, UK) using the McCance and Widdowson Food Composition Tables (16).

The energy expenditure during the exercise was calculated from ACSM equation (17). ACSM guidelines provide formulas to calculate energy expenditure for running speeds when caloric expenditure is calculated based on oxygen consumption (17).

Statistical analysis
Results were expressed as the mean ± SD and distributions of all variables were assessed for normality. Data were analyzed using independent and paired sample t-test. The level of significance in all statistical analyses was set at P<0.05. Data analysis was performed using SPSS software for windows (version 17, SPSS, Inc., Chicago, IL).

4. Results
The mean of carbohydrate, fat, protein, fiber consumption, and calorie intake and energy expenditure of the subjects during 12 weeks are shown in Table 1. Results indicate that the subjects were maintained their normal physical activity and dietary habits throughout the study. As shown in Table 1, the average of energy expenditure induced by exercise training was approximately 510 kcal per each session of training.

<table>
<thead>
<tr>
<th>Table 1.</th>
<th>The composition of the subjects’ diets (carbohydrate, fat, protein and fiber) and calorie intake and energy expenditure during 12 weeks (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate (g/day)</td>
<td>Control 571.58 ± 53.88</td>
</tr>
<tr>
<td>Fat (g/day)</td>
<td>Control 81.99 ± 17.79</td>
</tr>
<tr>
<td>Protein (g/day)</td>
<td>Control 139.7 ± 10.76</td>
</tr>
<tr>
<td>Fiber (g/day)</td>
<td>Control 8.93 ± 1.44</td>
</tr>
<tr>
<td>Energy intake (kcal/day)</td>
<td>Control 3594.51 ± 108.83</td>
</tr>
<tr>
<td>Energy expenditure (kcal/day)</td>
<td>Control 3597.79 ± 110.1</td>
</tr>
<tr>
<td>Energy expenditure (kcal)</td>
<td>Control 510.89 ± 24.5</td>
</tr>
</tbody>
</table>
The energy expenditure in out of the training sessions was calculated by the Bouchard Physical Activity Questionnaire and the energy expenditure during the 45 min exercise was calculated by the ACSM equation for energy expenditure calculation during running on the treadmill. The average of energy expenditure induced by exercise training was approximately 510 kcal per each session of training.

Physical and physiological characteristics of the subjects at baseline and after training are presented in Table 2. Before the intervention, there were no significant differences in any of variables among the two groups. Body weight, BMI, body fat percent and WHR decreased (P<0.05) after 12 weeks high intensity exercise training compared to the control group (Table 2). As shown in Table 2, after 12 weeks training, the high intensity exercise training group demonstrated decreased (P<0.05) in systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting insulin and glucose, HOMA-IR, TC,TG and LDL-C and increased in HDL-C.

**Table 2.** Anthropometric and metabolic characteristics (mean ± SD) of the subjects before and after training

<table>
<thead>
<tr>
<th></th>
<th>Control (mean±SD)</th>
<th>Training (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pretraining</td>
<td>Posttraining</td>
</tr>
<tr>
<td>Body weight (Kg)</td>
<td>90.4 ± 13.9</td>
<td>90.6 ± 14.1</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>32.0 ± 5.3</td>
<td>32.0 ± 5.3</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>106.5 ± 15.2</td>
<td>106.6 ± 15.1</td>
</tr>
<tr>
<td>HC (cm)</td>
<td>106.5 ± 5.8</td>
<td>106.6 ± 6.0</td>
</tr>
<tr>
<td>WHR</td>
<td>0.99 ± 0.08</td>
<td>0.99 ± 0.08</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>126.6 ± 9.6</td>
<td>126.6 ± 9.1</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>82.5 ± 4.2</td>
<td>82.2 ± 3.2</td>
</tr>
<tr>
<td>TC (mg/dl)</td>
<td>169.3 ± 16.5</td>
<td>179.3 ± 44.1</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>170.1 ± 118.4</td>
<td>204.3 ± 122.3</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>99.7 ± 39.7</td>
<td>106.5 ± 41.0</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>41.5 ± 9.1</td>
<td>40.3 ± 8.6</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td>5.5 ± 4.17</td>
<td>5.6 ± 0.45</td>
</tr>
<tr>
<td>Fasting insulin (µU/ml)</td>
<td>11.6 ± 2.73</td>
<td>12.5 ± 2.24</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.8 ± 0.7</td>
<td>3.1 ± 0.62</td>
</tr>
</tbody>
</table>

a P<0.01 for between-group differences.
b P<0.01, pretraining vs. posttraining values.
5. Discussion

The MS _also known as syndrome X, insulin resistance syndrome, deadly quartet or plurimetabolic syndrome_ is a group of clinical and biological abnormalities that confers a greater risk of T2DM. Our results demonstrated that body composition such as body weight, BMI and WHR improved after 12 weeks intervention. Diabetes appears to have an effect on both lean body mass and muscle quality, perhaps due to poor vascular supply and peripheral neuropathy (18). A meta-analysis by Hayashino et al. (2012) demonstrated that structured exercise interventions generally resulted in improvements to both WC and BMI. However, when the different types of exercise were examined separately, significant improvements in BMI and WC were only seen with aerobic and combination (aerobic plus resistance) exercise interventions (19). Overall, there appears to be the most evidence for the benefits of exercise on body composition if the intervention is mixed (aerobic plus resistance training) and if the intervention is combined with other lifestyle interventions such as dietary improvements (20).

Lipoprotein abnormalities play an important role in the causation of diabetic atherosclerosis (21). Dyslipidaemia causes morbidity and mortality in patients with type 2 diabetic mellitus and the most common pattern in type 2 diabetic patients is elevated triglyceride and LDL, and decreased HDL cholesterol concentrations (22). The modifications of LDL lipoprotein increase atherogenicity and available data suggest that LDL is more atherogenic in individuals with type 2 diabetes mellitus (23). The results indicated that TC, TG and LDL-C decreased and HDL-C increased after 12 weeks high intensity endurance training in men with T2DM. The effects of the physical activity on the lipids and lipoprotein profiles are well known. Individuals physically active present higher levels of HDL-C and lower levels of TG, LDL-C and VLDL-C, if compared to inactive individuals (24). Intervention studies demonstrate the unfavorable lipids and lipoprotein profiles improve with physical training (25). These improvements are not dependent on gender, body weight and diet; however, there is a possibility of being dependent on the glucose tolerance degree (24,25). The physical activity has demonstrated to be effective in decreasing the level of VLDL-C in individuals with
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T2DM, however, except for a few, most studies have not demonstrated significant improve on levels of HDL-C and LDL-C in this population maybe due to the low intensity of the exercise employed (26). Although studies on the effect of physical exercises on the lipids and lipoprotein profiles in individuals with MS are scarce, considering the evidences above and the fact that physical exercises increase the ability of the muscular tissue in spending fatty acids and the activity of the enzyme lipoprotein lipase in the muscle (27), it is likely that the physical exercise be effective in improving the lipid and lipoprotein profiles in individuals with MS. Physical activity improve lipid metabolism and increases the conversion of VLDL-C to HDL-C that result activation of lipolysis of fat tissue and decreases insulin and increases glucagon which lead concentration of free fatty acids in plasma. This process effects cholesterol buildup and reduce it (28). The factors influencing HDL-C levels are: Increase utilizing lipids by skeletal muscle as fuel and decrease consumption glycogen (29). Also it is possible physical activity decreases homocysteine which increasing HDL-C. Some study show resistance training improves lipid metabolism by lowering the synthesis of free fatty acids and stimulating lipid oxidation (30).

SBP and DBP decreased after 12 weeks intervention in this study. Epidemiological and clinical studies have demonstrated beneficial effects of the practice of physical exercises on the arterial pressure in individuals of all ages. High level of daily physical activity is associated to lower levels of arterial pressure in rest (31). The regular practice of physical exercises have demonstrated to prevent blood pressure increases associated to age (32) even in individuals with increased risk to develop it (33). Physical activity programs have demonstrated to decrease the systolic and diastolic blood pressure both in hypertensive and normotensive individuals. These benefits of the physical activity on blood pressure make physical activity an important tool on prevention and treatment of the hypertension (34). The decrease in SBP and DBP might due to improvement in aortic stiffness, improvement in vessel wall structure, and activated of parasympathetic tones (35).

At the end, our results showed that fasting insulin and glucose and insulin resistance demonstrated by HOMA-IR reduces after the 12 weeks exercise training. It is postulated that aerobic exercise improves glycemic
control in T2DM primarily through increasing insulin sensitivity (36). A small study utilizing hyperinsulinemic euglycemic clamps has demonstrated an improvement in insulin sensitivity with only 15 days of aerobic exercise (7). Exercise training improves glycemic control by increase in muscle mass (since skeletal muscle is the main glucose sink for the body) and by increasing glucose transporter type 4 (GLUT-4) expression (36). An increase in GLUT-4 expression has been supported by inactivity studies involving muscle biopsies in human subjects (37) and in exercise interventions in rats (38). Overall, it is well established that aerobic exercise improves glycemic control to a moderate extent.

6. Conclusion

In conclusion, the present study suggests that high intensity exercise improves MS in men with T2DM.

7. Acknowledgment

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Conflicts of interest: No conflict of interests amongst authors.

References


