



Effect of aerobic exercise on physical fitness indices and the amount of insulin consumption in boys with type 1 diabetes

Samira Zaheri^{1*}

¹ Department of Exercise Physiology, Faculty of Physical Education and Sport Sciences, University of Guilan, Rasht, Iran

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Abstract

Background: The term diabetes mellitus describes a metabolic disorder of hyperglycemia with disturbances of carbohydrate metabolism resulting from defects in secretion and action of insulin. The aim of this study was to investigate the effects of aerobic exercise on physical fitness indices and the amount of insulin taken in boys with type 1 diabetes

Methods: For this purpose, 64 adolescents boy with diabetes type I were selected and were divided into 2 groups: Aerobic training group (AE) (n = 32) and control group (CO) (n = 32). Aerobic training group did aerobic exercises for 6 weeks (3 days a week), while the control group did not do any exercise. Training program consisted of: a) warm-up (10 minutes); b) the original class (30 minutes); c) cooling (5 minutes). At first both groups performed fitness physical tests that include of flexibility (sit and reach test), muscular endurance test (sit-up test), aerobic capacity test (run 6 minutes' walk), agility test (T-test) and anaerobic capacity (Running-based Anaerobic Sprint Test), also were recorded the amount of insulin consumption as a pre-test and then after six weeks both groups performed the same tests as a post-test.

Result: The results showed that 6 weeks of aerobic training has a significant effect in increasing agility, flexibility, muscular endurance, aerobic power and anaerobic power in boys with type I diabetes ($p < 0.05$). In addition, aerobic exercise group significantly reduced the amount of insulin than the control group ($p < 0.05$).

Conclusion: The result of this study showed that the application of aerobic exercise is effective for improvement of physical fitness indices. This may reduce the amount of insulin in children and adolescents with type 1 diabetes and they are more likely to participate in sports activities.

Keywords: aerobic training, diabetes type 1, insulin, fitness.

* Corresponding Author: zaheri_samira@yahoo.com



Introduction

Type 1 diabetes (T1D) is a potentially life-threatening illness. Type 1 diabetes mellitus (T1DM) is a T-cell-mediated autoimmune disease that begins in many cases three to five years before the onset of clinical symptoms, continues after diagnosis, and can recur after islet transplantation (1). T1D, also called juvenile-onset diabetes mellitus and insulin-dependent diabetes mellitus, is the result of an absolute insulin deficiency, which causes a loss of the insulin-producing beta cells of the pancreas (2). The epidemiology of T1D shows a significant variation in incidence rates across different geographical regions. Countries such as Sweden, Finland, Norway, United Kingdom, and Sardinia exhibit the highest incidence of T1D. On the other hand, China and South America report the lowest incidence of T1D, with rates recorded as $< 1/100000$ patient-years (3,4). Unlike most autoimmune diseases, T1D is more common in males than females. The rate of T1D diagnosis is on the rise in most countries, with a particularly dramatic increase seen in children under the age of 5 (5). Diabetes risk factors encompass both genetic and environmental influences. Within the realm of environmental factors, noteworthy is the impact of maternal vitamin D supplementation during pregnancy, as well as vitamin D supplementation among young children which have shown a reduced risk of T1D development that may be dose-responsive (6,7). Other environmental factors that continue to be explored include nitrosamine compounds, maternal age, pre-eclampsia, and childhood obesity. There is no evidence to suggest that vaccines increase the risk of T1D development (8). Clinical trials focusing on drugs aimed at modulating the immune response and preserving endogenous insulin secretion in patients with new-onset T1D are termed tertiary prevention trials (9). Some of the symptoms of T1D include weight loss, polydipsia, polyphagia, constipation fatigue, cramps, blurred vision, and candidiasis (10).

Diabetes diagnosis is conducted through a fasting plasma glucose test which necessitates an eight-hour fasting period prior to the test. A blood glucose level exceeding 126 mg/dl in two or more tests conducted on separate days confirms a diabetes diagnosis (11). Limited physical fitness stands as a robust indicator of an escalated susceptibility to diabetes development (12). Physical Fitness can be categorized as cardiorespiratory fitness, muscular strength, flexibility, and balance. Comparative analyses reveal that youth afflicted with type 2 diabetes (T2D) exhibit lower fitness levels in contrast to those with type 1 diabetes (T1D), with levels hovering around 25 mL/kg/min. Additionally, adolescents diagnosed with T1D

tend to be more prone to obesity, particularly girls who face a heightened risk of weight gain compared to their male counterparts (13).

In recent times, the prevalence of T1D among adolescents and young individuals has been on the rise. Training has emerged as a valuable tool for managing blood glucose levels. On one hand, one of the optimal approaches to treat T1D is physical activity, especially aerobic exercises. On the other hand, physical fitness factors have also been recommended to improve overall physical performance. In light of these considerations, this study aimed to investigate the effect of aerobic training on various parameters of physical fitness, alongside its potential influence on insulin consumption exclusively among male adolescents diagnosed with T1D.

Material and methods

Subjects

For this study, a total of sixty-four boys between the ages of 14 and 20, all diagnosed with T1D were voluntarily recruited from Guilan City in Iran and were provided with comprehensive instructions about diabetes management and the prescribed training procedures. At first, subjects were informed about the overall study program and the eligibility criteria for participation. The criteria for inclusion encompassed the lack of cardiovascular diseases, renal issues, visual impairments, and cerebral conditions, as well as being non-smokers and non-alcohol consumers. Furthermore, individuals without diabetic complications such as diabetic foot ulcers were also considered eligible. After completing the consent form, height and weight were measured. In addition, a comprehensive medical history was gathered, including information about insulin dosage, through consultations with experts and the examination of medical records from relevant medical centers. Exclusion criteria incorporated patients with other forms of diabetes, thyroid disorders, iron deficiency anemia, blood pressure and coronary arterial diseases, chronic kidney diseases, infection, recent major surgery or illness, individuals under treatment with steroids or lipid-lowering medications, and those with orthopedic conditions leading to movement limitations.

A glucometer is a medical apparatus for determining the approximate concentration of glucose in the blood. To perform the measurement, a small droplet of blood is acquired by gently puncturing the skin using a lancet. This blood droplet is then applied onto a disposable test strip, which the glucometer reads and subsequently employs to compute the blood

glucose concentration. The resulting glucose level is presented by the meter in units of either mg/dl or mmol/l. Capillary blood samples were taken at a room temperature of 20 °C.

There are many types of insulin, with the most common being Neutral Protamine Hagedorn (NPH) and regular insulin. Each type of insulin has a specific duration of action. Variability of NPH insulin's effectiveness might also stem from inadequate resuspension before injection. NPH insulin, being a two-phase solution, requires the insoluble, cloudy part to be thoroughly mixed with the soluble, clear part. This is achieved by gently tipping the insulin vial or cartridge pen multiple times until a uniform suspension is achieved (14). Normal fasting patients received NPH and regular insulin. Regular insulin is a clear, colorless liquid, usually given 30 minutes before a meal. NPH insulin, on the other hand, is an intermediate-acting that begins working within 1 to 3 h and remains active for 16 to 24 h. Insulin is given by injection with single-use syringes with needles. Anthropometric features are shown in Table 1 and the amounts of consumption insulin in the morning and evening are shown in Table 2. Then, subjects were randomly divided into two groups: The aerobic training (AE) (n = 32) and the control (CO) group (n = 32) (Table 1). Exclusion criteria encompassed patients with other types of diabetes, thyroid disorders, iron deficiency anemia, blood pressure and coronary arterial diseases, chronic kidney diseases, infection, recent major surgery or illness, individuals under treatment with steroids or lipid-lowering drugs, and those with orthopedic issues leading to movement limitations.

Throughout the day, the examiner pricks their finger multiple times to obtain a small droplet of blood. This blood droplet is then applied to a plastic strip that is inserted into a glucometer, a handheld device. The glucometer promptly provides information about whether their glucose level is high, low, or right on target.

Testing

Both groups underwent a comprehensive fitness pretest, which encompassed various assessments: an aerobic capacity test (test run in 6-min walk), anaerobic capacity (Running-based Anaerobic Sprint Test), muscular endurance test (sit-up test), flexibility (sit and reach test hand), and agility (T-test). Additionally, the amount of insulin consumption was recorded. For the experimental group, a six-week protocol of aerobic exercise training was implemented, with sessions scheduled three times a week. The intensity of aerobic training was tailored to 60-70% of the participant's maximum heart rate, calculated using the 220-

age equation. The first training session spanned approximately 30 min. As the training progressed, a gradual 5-minute increment in intensity was applied every two weeks. Each training session consisted of a 10-minute warm-up phase, a 30-minute core exercise session, and a 5-minute cooling-down period. The exercise routine within the training included a 15-minute jogging segment, three sets of 1-min walking intervals with 1-minute rests in between, three sets of 1-minute rhythmic exercises accompanied by music, maintaining 60-70% of maximum heart rate, and 1-min rests interspersed between sets. A 3-minute rest was provided between each distinct exercise. During the 6-week training period, the control group did not engage in any regular training regimen. Additionally, participants in both groups refrained from exercising in cases of hypoglycemia or when blood glucose levels exceeded 250 mg/dl during each session(15).

Before each session, the participants' blood sugar levels were assessed. During every session, the subjects were supervised by a medical professional, either a doctor or nurse, who carried first aid supplies and essential medications, including 50% glucose serum vials for cases of sudden drops in blood sugar. The timing of insulin consumption and the most recent meal were monitored using a questionnaire. Throughout the entire 6-week period, the control group was instructed to abstain from engaging in any form of physical activity. Upon completion of the six-week, all of the fitness tests conducted during the pre-test were re-administered in the post-test phase, mirroring the initial procedures. These post-test assessments were conducted in a comprehensive manner, allowing for a thorough comparison of results before and after the intervention.

Aerobic capacity: Six-minute walk test (6MWT)

All patients performed a standardized, self-paced 6MWT in a 20-m-long corridor (16).

Anaerobic capacity: Running-based Anaerobic Sprint Test (RAST)

The participants sprinted at their maximum pace from one end of the track to the opposite end, with officials timing the duration required to complete a single run. Following the sprint, a ten-second rest period was granted before the participants executed a turnaround run back to the starting point. This sequence of sprinting and turnaround was repeated for a total of six cycles (17).

Endurance muscular: sit-up test

For many years, a complete sit-up involving a full 90° hip flexion was the prevailing technique, even though it imposed strain on the lower back due to anterior pelvic tilt. Additionally, it relied on the hip flexor muscles during the latter phase of the test, after the spine had been fully flexed by the abdominal muscles (18).

Flexibility test: Sit-and-reach

Tests in which a fingertips-to-tangent feet distance is measured are probably the most widely used linear measures of flexibility (19).

Agility test: T-Test

The T-test was administered using a version standardized from previous literature. To adapt the measurement units, yards were converted to meters, resulting in a 10 × 10 m course. However, the course procedure, which required participants to touch each cone, lacked standardization in existing literature. As a result, this task was omitted from the test. The instructions followed in this study were derived from Miller et al. (20).

Statistical Analysis

Statistical analysis of this survey was done both via descriptive and inferential methods. We used analysis of variance (ANOVA) to test for any differences in physical activity between groups at baseline (pre-intervention) and follow-up (post-intervention) ($F=17.5$, $P=0.001$). Paired samples t-tests were used to investigate if alterations in physical fitness parameters and insulin consumption had occurred between the baseline and follow-up assessments within the two groups. All calculations were performed using SPSS software, version 21.

Results

The average and standard deviations were incorporated for the following variables: flexibility, muscular endurance, and aerobic power and insulin consumption amount before and after tests. These variables are shown for control and experiment groups in Table 3.

These results indicate a significant increase in the experimental group's post-test scores compared to the pre-test scores in flexibility, muscular endurance, and aerobic power. There

was a significant decrease in insulin consumption after the test. In addition, the amount of flexibility, muscular endurance and aerobic power was significantly higher in the experiment group compared with the control group ($p < 0.05$), and the amount of insulin was significantly lower in the experimental group compared with the control group ($p < 0.05$).

Table1. Baseline Anthropometric Characteristics. Data are mean \pm SD

Group	AE (n=32)	CO (n=32)
Age (yr)	17.31 \pm 2.05	17.22 \pm 2.15
Height (cm)	154.8 \pm 8.68	156.8 \pm 9.21
Weight (gr)	54.3 \pm 7.16	54.3 \pm 9.82
BMI	22.82 \pm 4.08	22.00 \pm 3.15
History (yr)	6.41 \pm 3.03	7.27 \pm 2.90

Table2. The amounts of consumption of insulin. Data are mean \pm SD

Group	time	Vial of insulin	AE	CO
Insulin (unit)	Morning	Clear	4.23 \pm 8.47	2.43 \pm 7.91
		Crystal	9.13 \pm 24.19	5.19 \pm 21.84
	Evening	Clear	8.16 \pm 3.57	7.44 \pm 1.76
		Crystal	17.31 \pm 7.29	18.72 \pm 5.89

Table3. The average and standard deviation of the measured variables in both groups. Data are mean \pm SD. Data are presented as mean \pm SD; * indicates a significant difference ($P < 0.05$) within a group between pre and post-training, † significantly different from the control. Aerobic training group (AE) and Control group (CO).

Group	Aerobic training (AE)		Control (CO)	
	Pre-test	Post-test	Pre-test	Post-test
Agility	14.1 \pm 1.39	13.5 \pm 1.70*†	13.8 \pm 1.52	13.8 \pm 1.16
Anaerobic capacity	23.4 \pm 4.36	24.8 \pm 3.97*†	23.8 \pm 6.29	22.9 \pm 4.70
Flexibility	21.6 \pm 7.26	23.6 \pm 7.21*†	21.1 \pm 5.17	21.0 \pm 4.79
Muscular endurance	21.4 \pm 4.39	23.0 \pm 3.81*†	20.6 \pm 3.83	20.6 \pm 3.24
Aerobic capacity	944.7 \pm 156.96	1076.4 \pm 173.49*†	935.9 \pm 134.06	935.9 \pm 139.89
Insulin consumption	48.18 \pm 15.35	44.36 \pm 15.18*†	47.44 \pm 14.87	47.98 \pm 14.05

Discussion

This study aims to investigate the impact of a 6-week aerobic training program, comprising three sessions per week, on various indices of physical fitness including flexibility, muscular endurance and aerobic power among adolescent boys diagnosed with T1D. According to our results, there were significant increases in the following variables; flexibility, muscular endurance, and aerobic power. Moreover, there was a significant decrease in the amount of insulin consumption after the completion of a 6-week aerobic training program.

Physical fitness, a broad concept encompassing several specific types of fitness including aerobic power, strength, flexibility, and balance is important for persons with diabetes and maintains a strong association with all-cause mortality (21). Despite engaging in similar levels of physical activity, physical fitness parameters among individuals with T1D are generally less favorable. Research suggests that young adults (aged 17–44) with T1D tend to have lower fitness levels compared to their counterparts without diabetes, despite equivalent activity levels (22).

Zachezeweski defines muscle flexibility as "the ability of a muscle to lengthen, allowing one joint (or more than one joint in a series) to move through a range of motion (ROM) (23). Our findings indicate that aerobic training could potentially have an impact on muscle-tendon units, potentially leading to a reduction in stiffness. However, further studies are needed to explore and confirm this possibility. Improvements in maximal oxygen uptake (VO₂max) without accompanying changes in glycemic control were reported by Rowland and Zinman and associates, after 12 weeks of bicycle and treadmill exercise, respectively (24,25). In this study, the implementation of aerobic training directs metabolic pathways toward aerobic processes, enhancing the accessibility and transportation of glucose and oxygen to the muscles in need. This outcome consequently leads to improvements in aerobic power (VO₂ max) and anaerobic power.

Many studies have investigated the effect of exercise on treatment improvement among adolescents and youth with T1D. In a study in 2006, DirecNet group found that prolonged moderate aerobic exercise in youth with T1DM resulted in a consistent reduction in plasma glucose, accompanied by a frequent occurrence of hypoglycemia when pre-exercise glucose concentrations were below 120 mg/dl (26). Guelfi et al. compared the effects of exercise on a bicycle ergometer over a 30-min period with and without brief maximal sprints in seven children with T1D. The exercise session, conducted in the late morning following breakfast

and a pre-breakfast insulin dose when blood glucose levels were at 200 mg/dl, resulted in a 25-mg/dl greater decline in blood glucose when the intermittent sprints were not included. The inclusion of sprints in the exercise regimen led to a more significant rise in counter-regulatory hormone concentrations, potentially mitigating the decline in glucose levels (27). Furthermore, Ramalho et al. evaluated the effect of aerobic versus resistance training on metabolic control in T1D patients and found that neither resistance nor aerobic training improved glycosylated hemoglobin in T1D patients (28). Similar to our finding, Heyman et al. found that aged 13 to 18 with diabetes exhibited a PWC170 ranging from 1.66 to 2.28 w/kg. Although studies have shown that improvements in body composition become noticeable after 3 months of physical activity in T1D adolescent boys (or most boys) (29). In contrast to boys, cardiovascular disease risk factors are more pronounced among T1D adolescent girls, manifested through notable changes in lipid profiles, insulin resistance, and body composition. Herbst et al. studied the cardiovascular risk factors among 251 patients (3-18 years) with T1D, finding that the mean glycosylated hemoglobin (HbA1c) was 7.9%. (30). Through evaluating the intensity and duration of physical activity, it was observed that such activity led to a reduction of approximately 4.2 mmol/mol (0.6%) in HbA1c levels among these patients (22). The gradual reduction in HbA1c level is clinically significant, as the Diabetes Control and Complications Trial (DCCT) reported a 21% to 49% decreased risk for microvascular complications with every 1% decrease in HbA1c (31). Insulin resistance is independently associated with the risk of developing both macro and micro vascular complications in T1D (22). In a study involving 196 adults with T1D, those engaging in moderate exercise once to three times a week experienced significant reductions in HbA1c levels and insulin requirements (32).

The consistent findings across studies on T1D underscore the association between physical activity and decreased insulin requirements, with reductions ranging from 6% to over 15% (22).

In our study, patients showed a significant decrease in insulin which can be attributed to the changes induced by aerobic training in the energy fuel supply mechanism. During the initial stages of exercise, glycogen acts as a major source of glucose, the primary fuel for active muscles. The utilization of non-esterified fatty acids in adipose tissues gradually increases. Concurrently, hormonal and nervous responses are heightened, leading to an augmentation in hepatic glucose production. These processes collectively contribute to a

decline in insulin concentrations. After exercise, there is a transient period during which regulatory hormones such as glucagon, adrenaline, and cortisol remain elevated, causing hyperglycemia. During this phase, insulin sensitivity escalates, and the process of glycogen resynthesis initiates within the muscles.

Several critical factors influence the transformation of glucose into muscular cells, with prominent roles played by AMP-ACTIVATED PROTEIN KINASE (AMPK), Glucose transporter type 4 (GLUT4) proteins, and Nitric oxide (NO).

AMPK, a serine-threonine enzyme, was initially identified as a significant regulator of fatty acid oxidation in heart and skeletal muscle. However, it has since emerged as a key mediator of glucose metabolism as well. AMPK is notably activated during exercise in both cardiac and skeletal muscles, although the precise extent of its involvement in modulating glucose transport during exercise remains a subject of investigation. AMPK facilitates an increase in glucose transport by promoting the translocation of GLUT4 to the sarcolemma in both cardiac and skeletal muscles (33).

In the skeletal muscle of rats rendered diabetic through the injection of a beta cell toxin called streptozotocin, a decline in GLUT4 mRNA levels occurs before the reduction in GLUT4 protein levels. Besides the acute effects of exercise on AMPK-induced GLUT4 trafficking, a positive correlation was observed between acute exercise-induced increase in CaMKII levels and glucose transport in muscle cells (34).

The protein kinase C (PKC) is known as a mediator of the glucose transporter, which is released in response to exercise training. Chen et al found that the consumption of glucose in muscle cells leads to the activation of protein kinase (34).

NO stimulates glucose transport in isolated skeletal muscle, where it is thought to have a role in mediating both insulin and exercise-stimulated glucose uptake (33). NO causes the release of LKB1, which in turn increases the activity of AMPK. A possible explanation for the relationship between PKC and AMPK in the signaling pathway involves the amplification of LKB1 activity, which subsequently enhances AMPK activity. This culminates in the activation of GLUT4 storage vesicles (GSV) whose pivotal role lies in the activation of GLUT4, an essential component of glucose uptake (34).

Conclusion

Aerobic training may improve glucose metabolism by facilitating the movement of glucose transporters to the muscle cell membrane in individuals with T1D. As a result, individuals with diabetes can engage in fitness activities while maintaining stable blood glucose levels. Enhanced fitness parameters, such as strength, enable these individuals to participate in and sustain physical activities for extended durations. This combination of improved glucose regulation and increased fitness levels contributes to their ability to engage in more prolonged and enduring activities.

Declarations

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Conflicts of interest

I have no conflicts of interest.

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