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The Effects of Exercise on Antioxidant System and Some Blood Parameters at Experimental Diabetic Rats

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Abstract

The aim of this study is to determine the effects of exercise on antioxidant system (MDA, SOD, GSH) and some blood parameteres (plasma insuline, glucose, ALT, AST) in rats with experimental diabetes induced by streptozotocin (STZ).

In the study, 32 adult Wistar Albino rats were divided into 4 equal groups as control (C), exercise (E), diabetes (D) and diabetes+exercise (DE). Diabetes was induced in D and DE by intraperitoneal injection with a single dose of 60 mg/kg STZ. After the diabetes was induced, swimming exercise was applied to E and DE for 5 days / 30 min a week for 4 weeks. According to the findings obtained; there was a significant decrease in D and DE compared to C. Plasma glucose levels decreased in DE with exercise in the diabetic groups. While ALT levels increased significantly in diabetic groups compared to others, it was found that exercise did not make a difference in diabetics. However, the increase in AST levels was statistically significant only in D. When serum MDA levels were examined, a significant decrease was observed in DE compared to D. While there was a significant decrease in serum SOD levels in the diabetic groups compared to C. The diabetic groups and DE and E were similar to each other. A significant decrease was observed in GSH levels in D. This difference was also detected between diabetic groups.As a result; in the study it was concluded that regular aerobic exercise improved glycemic control, has a lipid peroxidation-reducing effect and may hava a positive effect on strengthening the antioxidant system in diabetes.

Key Words: Antioxidants; Exercise; Diabetes Mellitus; Blood Parameters.

INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolism disease that adversely affects carbonhydrate, fat and protein metabolism due to acute and chronic complications as a result of insufficient insulin secretion and impairment of the response of the relevant tissues to insülin (30). It is known that oxidative stress due to hyperglycemic plays an important role in diabetes and the emergence of diabetic complications (31). The extent of oxidative damage that may occur during physical exercises is also determined by the defense capacity of antioxidants such as SOD, GSH, and CAT. It has been stated that an acute exercise can negatively affect the activities of these enzymes (5, 48). It has been reported that regular aerobic exercise in diabetic patients provides blood glucose regulation, increases the sensitivity of cells to insulin, reduces lipid levels, facilitates weight loss, improves the cardiovascular system and metabolic control (32).

Various experimental diabetes models are created using various experimental animals in order to examine disease prevention and treatment options in diabetes. In these models, experimental

animals such as mice and rats are generally preferred, and chemicals such as alloxan and streptozotocin (STZ), which cause oxidative stress-induced destruction in β cells with low antioxidant capacity, are used to cause diabetes (13). In this context, the effect of exercise on blood parameters such as plasma insulin, glucose, ALT and AST, and SOD and GSH levels, which are the end products of lipid peroxidation, and antioxidant system parameters, were investigated in rats with STZ-induced diabetes.

MATERIAL and METHODS

Subjects

In the study, 32 healty male Wistar Albino rats weighing an avarage of 300 g, 70-80 days old were used. The rats have been provided from the KONUDAM (Experimental Medicine Application and Research Center of Necmettin Erbakan University). The research design was approved by the KONUDAM Ethics Committee for Animal Studies (Ethics Code: 2014-043). The rats were housed in plastic rat cages in the experimental animal unit at 23 ± 2 oC at room temperature and in a 50±10% humidified environment at a 12/12 night/day light cycle and they were fed ad-libitum with a standard rat diet. Rats were provided ad libitum access to water (~ 50 ml/day/rat) to be refreshed daily for four weeks. The animals were divided into four groups as control (C), diabetes (D), exercise (E) and diabetes + exercise (DE), 8 rats in each group.

Induction Of Diabetes

A single dose of streptozotocin (STZ) (60 mg/kg, Sigma S0130-1G) solution was injected intraperitoneally in rats and a diabetes model was created in diabetic groups (D, DE) (3). Group E and DE trained 5 d/week for 4 weeks. The STZ solution was prepared by dissolving 60 mg / kg STZ (Sigma S0130-1G) in 0.1 M citrate buffer (pH 4.5) before application. After STZ injection, checking blood glucose was done after 72 h fast from the tail with blood glucose meters (plusMED). All the animals who obtained blood glucose above 250 mg/dl were contemplated diabetic. After 4 weeks of application, blood samples were taken from the animals by cardiac puncture under anesthesia into anticoagulant for determination.

Swimming Training Protocol

In the study, after the occurrence of diabetes, swimming exercise was applied to the E and DE groups in a tank (180 cm diameter and 80 cm depth) with water at 22-25 °C, 5 days/30 minutes per week for 4 weeks.

Determination Of Hematological Parameters

Plasma samples were kept at -80 C0 until analyzed, insulin, glucose, ALT and AST levels were determined in the "Siemens CentaurXP Immunoassay System" device using commercial kits (Siemens). In serum samples obtained after the research, MDA levels, a lipid peroxidation product, were determined using Oxis (USA) branded commercial kit, and antioxidant parameters such as SOD and GSH levels were determined in the "Biotek ELX 800 ELISA" device using the "Cayman Chemical Company" (USA) brand kit.

Statistical Analyses

Statistical analysis of the obtained findings and determining the importance of the differences between the groups were made using the SPSS 16.0 package program. The significance between groups was determined Duncan's Multiple Range test in analysis of variance (ANOVA). Significant was considered as $P<0.05$.

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RESULTS

In this study, the effects of exercise on some hematological parameters were summarized Table 1 and 2.

Table 1. Plasma insulin, glucose, ALT and AST levels (n=32).

Parameters	Control	Exercise	Diabetes	Diabetes+Exercise	p Value
Insulin (uU/ml)	0,73 ± 0,40 a	0,52 ± 0,14 ab	0,22 ± 0,84 c	0,32 ± 0,17 bc	<0.05
Glucose (mg/dl)	140,50± 30,17 c	167,50± 28,57 bc	411,67 ± 117,74 a	246,50± 93,68 b	<0.05
ALT (U/L)	57,67 ± 8,07 b	59,33± 8,59 b	102,17 ± 26,29 a	82,83± 20,59 a	<0.05
AST (U/L)	88,17 ± 9,28 b	88,50± 8,87 b	144,17 ± 45,70 a	103,00± 21,58 b	<0.05

a, b, c; p<0.05. ALT: Alanine aminotrasdferase, AST: Aspartate aminotransferase

According to the table 1, insulin, plasma glucose in the diabetic groups showed a significant decrease in the D group compared to the C and E groups and in the DE group compared to the C group. In addition, it was determined that the exercise practice decreased glucose level in the DE group compared to the D group.

When Plasma ALT and AST levels were examined, it was found that there was an increase in the D and DE groups compared to the other groups, while a significant increase was found in only AST levels among the diabetic groups.

Table 2. Serum MDA and some antioxidants (SOD, GSH) levels (n=32)

Parameters	Control	Exercise	Diabetes	Diabetes+Exercise	P Value
MDA (nmol/ml)	0,97 ± 0,33 c	1,05 ± 0,24 c	2,79 ± 0,05 a	1,89 ± 0,31 b	<0.05
SOD (U/ml)	0,52± 0,12 a	0,47 ± 0,16 ab	0,30 ± 0,73 c	0,39 ± 0,31 bc	<0.05
GSH (μM)	5,02 ± 1,32 a	4,98 ± 1,90 a	1,07 ± 0,60 c	2,64 ± 0,96 b	<0.05

a, b, c: P<0,05, MDA: malodialdehite, SOD: superoxide dismutase, GSH: Gluatation

In the study, it was observed that serum MDA levels, an indicator of oxidative damage, increased in diabetic groups. When the diabetic groups were compared, it was determined that the exercise applied to the DE group significantly decreased the MDA levels.

It was observed that serum SOD and GSH levels decreased in diabetic groups. However, it was observed that SOD and GSH levels increased in the DE group compared to the D group, depending on the exercise, although this increase in the SOD level was limited to only numerical frames (p>0.05), the increase in GSH level was statistically significant.

DISCUSSION and CONCLUSIONS

An increase in blood glucose levels above 250 mg/dl in rats or other laboratory animals in STZ administrations at doses of 40, 50, 60, 100 mg / kg for single injection is considered as an indicator of the development of experimental diabetes. In the present study, in order to induce experimental diabetes, a single dose of 60 mg/kg STZ was administered to animals by intraperitoneal injection, and animals with blood glucose values higher than 250 mg / dl were considered diabetic (10, 36, 42).

In the study, decrease in plasma insulin levels and increase in glucose levels in diabetic groups (D, DE) were accepted as indicators of destruction in pancreatic β cells.

Plasma insulin levels determined in the study were similar between diabetic groups. This finding was similar to Ahmadi et al. report that the 8-week aerobic exercise they applied in female athletes "did not differ after exercise insulin levels compared to before" (2). Cicioğlu and Onay stated that high intensity exercise lowers insulin values in wrestlers (11).

Differently, it is reported that insulin levels increase after sprint exercise and decrease after endurance exercise, after two different acute exercise methods applied to elite athletes (53).

Similarly, RamzanPour et al. (39) stated that 12-week aerobic swimming exercise in type II diabetic women decreased the plasma insulin level; They

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attribute this decrease to "exercise practice in diabetes reduces insulin resistance".

It was concluded that the reason why the findings obtained in the study differed from some of the mentioned literature reports might be due to the metabolic difference between humans and experimental animals or the differences in the type, intensity and duration of the exercise.

When glucose parameters were examined, it was an expected result to increase serum glucose levels in diabetic groups in. As a matter of fact, the results obtained were in agreement with the literature datas (22, 33, 53). However, Ahmadi et al. (2) reported that glucose levels do not differ after aerobic exercise.

In the study, the decrease in plasma glucose level in the DE group compared to the D group; It was attributed to increased insulin sensitivity due to exercise and increased glucose uptake by muscles due to depletion of glycogen stores.

In addition, it is common for diabetic patients to decrease blood glucose level during exercise (41). It is stated that it may be associated with insufficient hepatic glucose production and / or decreased sympathetic nervous system activation (29). Apart from these factors, it has been noted that some other factors such as the duration and type of exercise, the content of the diet and the time taken may also have an effect on the plasma glucose level (47).

ALT and AST enzyme activities are routine biochemical markers especially used in the evaluation of liver damage (21). In studies investigating the effect of exercise on liver enzyme levels, various exercise programs applied to athletes in different branches and after the competition reported an increase in liver enzyme levels, although some studies reported no change in enzyme levels (7, 21, 28, 40).

In the study, it was determined that plasma ALT and AST levels increased in diabetic groups. This finding was in line with reports that serum aminotransferase levels are generally high in individuals with diabetes (38). On the other hand, Can et al. (9) reported that ALT levels were higher in rats in which they had experimental diabetes. Tanaka et al. (45) detected a cytosolic induced shot in AST activity in diabetic mice. Again, in similar studies, it was reported that ALT and AST values were increased in diabetic rats treated with STZ and liver enzyme activities were affected (23, 52).

In studies examining ALT and AST levels, Valizadeh et al. (49) reported that swimming exercise reduced ALT and AST levels in men with fatty liver and aerobic exercise was effective in this reduction. RamzanPour et al. (39) reported that 12-week aerobic swimming exercise caused a decrease in AST and ALT values in type II diabetic women.

It was observed that the findings regarding plasma ALT and AST levels obtained in the presented study were similar to those studies. In the study, the decrease in plasma ALT and especially AST levels in diabetic groups; It was interpreted that "regular aerobic exercise reduces or may have a protective effect in liver, skeletal muscle and possibly heart cells damage in diabetes".

Oxidative stress induced by hyperglycemia plays an important role in the development of diabetes and diabetes-related complications (14). In diabetes, it has been reported that free radical formation increases and the effectiveness of antioxidant enzymes is reduced as a result of sorbitol pathway activity, metabolic stress, hypoxia and ischemia-reperfusion, especially non-enzymatic glycation (4).

The amount of free radicals generated during exercise varies depending on the type, weight and duration of physical exercise (20). Hara et al. (15) reported that swimming exercise in rats increased lipid peroxidation in the liver and skeletal muscle, and Temiz et al. (46) reported that acute exercise increased lipid peroxidation in rats. Similarly, Semin et al. (43) reported that 60 minutes of running exercise in mice increased lipid peroxidation in skeletal muscle and kidney.

In the study, it was observed that exercise application decreased serum MDA level in the DE group compared to the D group. This finding was attributed to the fact that aerobic exercise in diabetes increased resistance to lipid peroxidation by reducing the production of free oxygen radicals, thus reducing oxidative protein damage and DNA damage.

As a matter of fact, although acute or exhaustion exercise increases free radical production, it has been reported that regular exercise improves antioxidant enzyme activities and decreases free oxygen radical production and MDA levels (12).

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In studies examining the effect of exercise on SOD activity, which is one of the important antioxidants in the body, Powers et al. (34) state that treadmill training increases SOD activity in rats. Burneiko et al. (8) noted that 8 weeks of exercise increased SOD values in liver tissues in rats. Similarly, Qiao et al. (37) reported that anaerobic swimming exercise resulted in increased SOD activity in skeletal muscle and heart tissue in rats, while Lima et al. (26) reported an increase in SOD activity in rats after 6 weeks of aerobic swimming exercise. On the other hand, in some studies using similar animal models, there are also reports that there is not change SOD activity (17, 25).

There are also different reports in studies investigating the effect of exercise on GSH level, which is an important component of the antioxidant defense system and ensures the preservation of membrane integrity in the cell system.

Venditti et al. (50) noted that the 10-week swimming program increased the GSH activity in rats. Similarly, some studies (18, 19) reported that exercise increases GSH levels in different tissues, while others (16, 44) have been reported to decrease it. Indeed, Lima et al. (26) also found that the GSH values decreased in rats after 6 weeks of aerobic swimming exercise. Liu et al. (27) reported that 8-week chronic exercise in rats did not make a difference on heart tissue GSH levels.

It has been reported that the antioxidant system parameter levels are decreased in many studies conducted on people with diabetes and rats with experimental diabetes. Kuyvenhoven and Meinders (24) state that in diabetic patients, GSH values are generally low in parallel with oxidative stress and the amount of free radicals. Adewole et al (1) reported that plasma SOD, CAT, GPx activities were significantly decreased in rats with STZ in which they had experimental diabetes.

In the study, the lowest serum SOD and GSH levels among all groups were determined in group D. The decrease in antioxidant capacity in animals with experimental diabetes with STZ confirms the relationship between diabetes and oxidative stress.

It is stated that exercise improves glycemic control (decreases blood glucose level, increases glucose tolerance), decreases the need for exogenous insulin, increases the number of insulin receptors, and decreases stress and anxiety in diabetic patients (4).

Biçer (6) found that acute swimming exercise decreased erythrocyte GSH and serum SOD values in a study conducted on Spraque Dawley male rats with diabetes induced by STZ; As a result, he states that acute swimming exercise suppresses antioxidant activity.

It was observed that the mean serum SOD and GSH levels determined in the study increased in the diabetic groups in the exercise group DE. However, this increase was observed to be statistically significant only in serum GSH level. This finding was similar to the report of Villa-Caballero et al. (51) That "regular exercise causes an increase in antioxidant activity in diabetics, and thus facilitates the rendering of reactive oxygen species".

In the study; increased levels of antioxidant parameters in diabetic groups; "Regular and continuous aerobic exercise can strengthen antioxidant defenses in diabetic patients". In conclusion of the study, the findings regarding plasma glucose and liver enzymes were interpreted as continuous aerobic exercise improved glycemic control in diabetes and thus reduced damage to liver, skeletal muscle and possibly hearth cell.

In addition, it has has been concluded that long-term aerobic has the effect of reducing lipid peroxidation, exercise performed within the framework of the regular loading principles can have a positive effect in strengthening the antioxidant system and can contribute to maintaining a healty life. In terms of cinfirming this issue, it was concluded that it would be beneficial to conduct studies in which the exercise period is applied longer.

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