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Research article

ENDURANCE TRAINING AND GLUTATHIONE-DEPENDENT ANTIOXIDANT DEFENSE MECHANISM IN HEART OF THE DIABETIC RATS

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ABSTRACT

Regular physical exercise beneficially influences cardiac antioxidant defenses in normal rats. The aim of this study was to test whether endurance training can strengthen glutathione-dependent antioxidant defense mechanism and decrease lipid peroxidation in heart of the streptozotocin-induced diabetic rats. Redox status of glutathione in blood of diabetic rats in response to training and acute exercise was also examined. Eight weeks of treadmill training increased the endurance in streptozotocin-induced diabetic rats. It did not affect glutathione level in heart tissue at rest and also after exercise. On the other hand, endurance training decreased glutathione peroxidase activity in heart, while glutathione reductase and glutathione S-transferase activities were not affected either by acute exhaustive exercise or endurance training. Reduced and oxidized glutathione levels in blood were not affected by either training or acute exercise. Conjugated dienes levels in heart tissue were increased by acute exhaustive exercise and also 8 weeks treadmill training. Longer duration of exhaustion in trained group may have contributed to the increased conjugated dienes levels in heart after acute exercise. Our results suggest that endurance type exercise may make heart more susceptible to oxidative stress. Therefore it may be wise to combine aerobic exercise with insulin treatment to prevent its adverse effects on antioxidant defense in heart in patients with diabetes mellitus.

KEY WORDS: Streptozotocin, experimental diabetes mellitus, glutathione, oxidative stress, conjugated dienes, heart, blood, rat.

INTRODUCTION

Oxidative stress may occur due to an increase in free radical production and/or a decrease in antioxidant defenses. Autoxidation of glucose and glycated proteins (Wolff et al., 1991), activation of polyol pathway (Grunewald et al., 1993), increased intracellular NADH/NAD^+ ratio (Roy et al., 1997), altered cell glutathione (Yoshida et al., 1995) and ascorbate redox status (Sinclair et al., 1991) as well as perturbations in nitric oxide and prostaglandin metabolism (Tesfamariam, 1994) are the main mechanisms underlying oxidative stress in diabetes.

Oxidative stress generally results in widespread lipid, protein and DNA damage (Halliwell, 1994). Increased lipid peroxidation has been shown by markers in urine (Gallaher et al., 1993), erythrocytes (Garg et al., 1996) and whole blood (Kakkar et al., 1995; Kakkar et al., 1996; Kowluru et al., 1996), and in various tissues such as kidney (Kakkar et al., 1997; Zhang et al., 1997), aorta (Kakkar et al., 1996; Karasu et al., 1997) and heart (Kakkar et al., 1995; Kakkar et al., 1996) in streptozotocin-induced diabetic (SID) rats. Oxidation of low-density lipoprotein cholesterol is believed to be central in the pathogenesis of atherosclerosis and endothelial dysfunction (Curcio and Ceriello, 1992; Tesfamariam, 1994; Witztum, 1994). High glucose levels delay the replication time of endothelial cells through the generation of free

radicals in vitro, suggesting a possible pathophysiological linkage between the high levels of glucose and the development of microvascular complications of diabetes (Curcio and Ceriello, 1992). The issues, diabetes, oxidative stress and exercise, have been recently reviewed (Laaksonen and Sen, 1999; Atalay and Laaksonen, 2002).

Glutathione-dependent antioxidant system plays a fundamental role in cellular defense against reactive free radicals and other oxidant species (Sen and Hänninen, 1994; Sen, 1997; Gul et al., 2000). It consists of reduced glutathione (GSH) and an array of functionally related enzymes, of which γ-glutamyl-cysteine synthetase and glutathione reductase (GRD) are responsible for the synthesis and regeneration of GSH, respectively, whereas glutathione peroxidase (GPX) and glutathione S-transferase (GST) work together with GSH in the decomposition of hydrogen peroxide or other organic hydroperoxides.

Aerobic exercise combined with diet is beneficial in controlling non-insulin-dependent diabetes mellitus and reducing risk factors associated with macrovascular complications such as decreasing the ratio of total to high-density lipoprotein cholesterol in men (Barnard et al., 1994). Although acute exercise induces oxidative stress (Sen, 1995; Khanna et al., 1999; Gul et al., 2001), regular aerobic exercise can strengthen antioxidant defenses (Sen et al., 1992; Ji, 1993; Sen, 1995). Sprint training on a treadmill for 6 weeks increases glutathione peroxidase activity in heart of rats (Atalay et al., 1996). Regular exercise can also reduce acute exercise-induced oxidative stress (Alessio and Goldfarb, 1988; Jenkins et al., 1993; Sen and Packer, 2000).

A limited number of endurance training studies has been carried out in SID rats to determine whether training would prevent the progressive decline in cardiac function (Paulson et al., 1987) or alter the responses of myocardium to ischemia (Riggs et al., 1992). We have recently reported beneficial effects of endurance training on antioxidant defense in skeletal muscle and kidney in SID rats (Gul et al., 2002). To our knowledge, there is no report on the effects of endurance training on GSH metabolism and oxidative stress in heart of the diabetic rats. Heart muscle has a high oxygen uptake at resting conditions, which increases many fold during exhaustive physical exercise. As recently reviewed (Atalay and Sen, 1999), regular physical exercise may beneficially influence cardiac antioxidant defenses and promote overall cardiac function in normal rats. Thus, our aim was to test whether endurance training can strengthen glutathione-dependent antioxidant defense mechanism and decrease resting and exercise-induced oxidative stress in heart of the streptozotocin-induced diabetic rats. Redox status of glutathione in blood of diabetic rats in response to training and acute exercise was also examined.

METHODS

Male outbred Wistar rats (National Laboratory Animal Center, Kuopio, Finland) were maintained at 22 ± 2 ^{o}C with 12:12 h dark: light cycles and had free access to standard rat chow and water. The study (application number 95/19) was approved by the Animal Research Ethics Committee, University of Kuopio. Diabetes was induced by a single intraperitoneal injection of streptozotocin at a dose of 60 mg/kg (prepared in 0.1 M citrate buffer, pH 4.5) to male 12-week old Wistar rats. The state of diabetes was confirmed by glucosuria using glucose test strips (BM-Test-5L, Boehringer Mannheim, Germany) after one week. A dipstick urine test was repeated once a week during the study. Blood glucose levels were also measured at the end of the study in mixed blood collected immediately after decapitation. Blood glucose levels were measured by using a commercial kit (Gluco-quant Glucose/HK, Boehringer Mannheim, Germany) based on hexokinase/G6P-DH enzymatic method.

Rats with sustained diabetes (glucosuria of at least 20 mmol· l^{-1} two weeks after injection of streptozotocin) (n=34) were randomly divided into untrained (n=15) and trained (n=19) groups. Before the exhaustive exercise test, these groups were further divided into groups of rats killed at rest (untrained rest, UR, n=7; and trained rest, TR, n=10) and immediately after exhaustive exercise (Untrained exercise, UE, n= 8; and trained exercise, TE, n=9) at random.

Exercise training of rats

Treadmill exercise training began when the rats are at the age of 14 weeks in the training groups (TR, TE). After familiarizing the rats to the treadmill, training began with gradual increases in training speed and time such that rats were running up to 1.8 km/h, 1.5 h/d, 5 days a week for 8 weeks. The rats tolerated training well, and were able to increase the running distance and intensity according to the training protocol throughout the study. During the 8th week of training program, the UE subgroup was also accustomed to treadmill running 1.0-1.2 km/h, 15 min/day, for 5 days before sample collection. This regimen was used to ensure that untrained rats could also tolerate the acute exhaustive exercise without having a significant training effect.

Exercise to exhaustion

At the end of the training period, half of the rats were randomly selected into the acute exercise

group. The running speed was 1.2 km/h (10% uphill gradient) for the first 10 min, after that, every half an hour the speed was increased gradually to 2.1 km/h until the rats were exhausted. The loss of the righting reflex when the rats were turned on their backs was the criterion of exhaustion.

Sample collection

After the 8-week period of training, the rats were pair matched between groups at the time of sacrifice. The trained rats were killed at rest by decapitation approximately 72 h after the last training session, while rats from the acute exercise groups were sacrificed immediately after exhaustive exercise. Following decapitation blood was collected, and heart was quickly excised, rinsed in ice-cold saline and blotted, cut into small pieces and placed in liquid nitrogen and stored -70° C for later homogenization and biochemical determinations. Blood samples collected for total glutathione (TGSH) and glutathione disulfide (GSSG) analyses were prepared as described before (Sen et al., 1994b). Briefly, for TGSH determination, EDTA-blood was precipitated with perchloric acid and deproteinized supernatant was used. For blood GSSG, the clear supernatant obtained from EDTA-blood treated with 10% 5-sulfosalicylic acid was neutralized and reacted with 2-vinylpyridine. Treated samples were frozen at -70° C until spectrophotometric determination.

Biochemical analyses

Determination of blood total glutathione (TGSH) and glutathione disulfide (GSSG):

Total glutathione in the acidified blood extract was determined by a GSSG reductase recycling method as described previously (Sen et al., 1992). GSSG, from 2-vinylpyridine-treated blood extract, was determined according to Griffith (Griffith, 1980).

Conjugated dienes (CD):

Conjugated diene levels of the tissues were measured as described (Recknagel and Glende, 1984; Nowak et al., 1995) with modifications. Briefly, 150 mg tissue was homogenized on ice with teflon pestle in 3 ml PBS with 0.001 M Na_2EDTA. Then, 2 ml homogenate was mixed with 4.5 ml of chloroform-methanol (1:2 vol/vol), shaken for 60 minutes at room temperature. Shaking was continued for another 30 minutes after adding 1.5 ml of chloroform again. Hydrochloric acid (1.5 ml of 0.003 M) was added and mixed slightly to wash the organic layer. The mixture was centrifuged at 1,500 x g for 10 minutes at 10° C. Then 2 ml of the lower chloroform layer was taken and dried under a flow of nitrogen gas. The residue was reconstituted with 1 ml of cyclohexane and a wavelength scan between 220 and 320 nm was performed to determine its absorbance at 234 nm with a Perkin Elmer spectrophotometer against a cyclohexane blank. The content of CD was expressed as Abs_{234}/g wet weight of the tissue.

Tissue preparation and biochemical analyses of total glutathione and glutathione-related enzymes:

For the determination of TGSH, heart tissue was homogenized on ice in brief bursts by an Ultra-Turax homogenizer (Janke and Kunkel, Germany) in a 1:10 (w/v) dilution of ice-cold 0.5 N perchloric acid. Resultant homogenate was centrifuged at 10,000 *g* for 15 min (4°C), and the supernatant was stored at -70 °C. On the day of measurement, the supernatant was diluted with distilled water and TGSH was measured spectrophotometrically by a GSSG reductase recycling method as described earlier (Sen et al., 1992). The rate of change in absorbance at 412 nm was monitored using a Schimadzu UV-240 double-beam spectrophotometer at room temperature, and tissue concentrations were estimated according to linear regressions from the standard curve.

For the assays of GPX, GRD, and GST, frozen tissues were crushed in liquid nitrogen and homogenized on ice in extraction buffer (50 mM Tris, 0.25 M sucrose, 1 mM EDTA, pH 7.4). The homogenate was centrifuged at 10,000 *g* (4°C) for 15 min. The supernatant was centrifuged again at 105,000 *g* (4°C) for 60 min, and the post microsomal supernatant was stored at -70°C. Activities of tissue GPX, GRD, and GST were determined from the post microsomal supernatant spectrophotometrically as described previously (Sen et al., 1992). Briefly, GPX activity was assayed with cumene hydroperoxide as substrate in potassium phosphate buffer, pH 7.0. GRD activity was assayed by using GSSG as substrate in 50 mM Tris-HCl buffer, pH 8.0, with 1 mM Na_2EDTA in the 1 ml reaction mixture. Both GPX and GRD activity assays based on the absorbance changes at 340 nm due to oxidation/reduction of NADPH/NADP system. GST activity was also assayed at 340 nm with 1,2-dichloro-4-nitrobenzene as substrate. All enzyme activities were measured at 37° C by using the Perkin-Elmer Lambda 2 UV/VIS spectrophotometer also running blanks, not containing the sample only.

Statistical analyses

SPSS for Windows v. 7.5.1 (Chicago, IL) software was used to analyze data. The overall effects of endurance training and acute exhaustive exercise on parameters were tested by two-way analysis of variance (ANOVA). The paired and unpaired *t* tests were used to evaluate body weight changes of the

animals and to compare the distances run by trained and untrained groups, respectively. P<0.05 was considered statistically significant.

RESULTS

Blood glucose

As reported earlier (Gul et al., 2002), blood glucose level of sedentary SID rats at rest, 19.17 ± 3.80 mmol· l^{-1}, was much higher than the values reported (Riggs et al., 1992) in sedentary normal rats, 7.00 ± 1.00 mmol· l^{-1}, and also in the blood of normal resting rats we tested, 8.79 ± 0.65 mmol· l^{-1}. Blood glucose level decreased significantly due to both endurance training (% 17.83, p<0.05 by two way ANOVA), and acute exhaustive exercise (% 45.86, p<0.001 by two way ANOVA) without interaction (Figure 1).

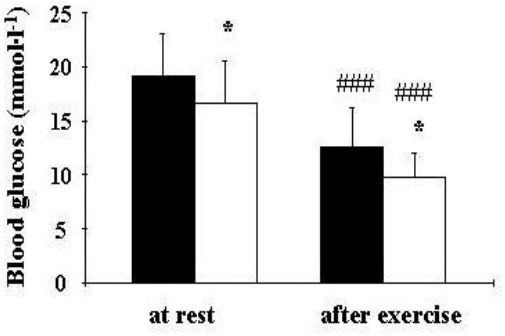

Figure 1. Blood glucose levels in untrained (filled colon) and trained (empty colon) streptozotocin-induced diabetic rats at rest and after acute exhaustive exercise. Values are mean (SD).
* p<0.05, difference due to endurance training, two-way ANOVA. ### p<0.001, difference due to acute exhaustive exercise, two-way ANOVA.

Body weight

As reported earlier (Gul et al., 2002), eight weeks of treadmill training decreased the body weight in SID rats (% 3.8, p<0.05, paired-t test), while body weight did not change in sedentary SID rats during the study (Table 1).

Table 1. Body weights of untrained (UR and UE, n=15) and trained (TR and TE, n=19) streptozotocin-induced diabetic rats. Values are mean (SD), as gram.

	In the beginning	After 8 weeks
UR and UE	302.9 (37.5)	303.7 (34.6)
TR and TE	290.7 (35.7)	279.4 (46.2)*

UR: untrained at rest, UE: Untrained after acute exhaustive exercise, TR: trained at rest, TE: trained after acute exhaustive exercise.* p<0.05 by paired-t test.

Endurance

As reported earlier (Gul et al., 2002), eight-week treadmill training program markedly increased the endurance in SID rats. In the graded exercise protocol to exhaustion, the trained diabetic rats ran on average 46 % further than untrained rats (5.5 ± 1.6 km vs. 3.8 ± 0.6 km, p<0.05, unpaired *t* test, Figure 2).

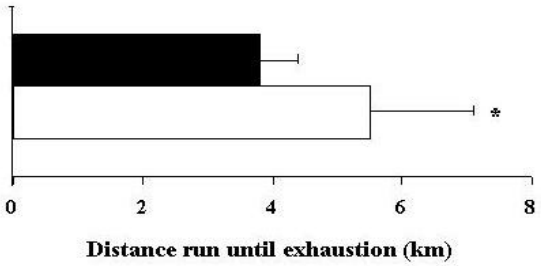

Figure 2. Distances run by trained (empty colon) and untrained (filled colon) streptozotocin-induced diabetic rats in the graded exercise protocol to exhaustion. Values are mean (SD). * p<0.05, unpaired t test.

Blood TGSH and GSSG levels in diabetic rats

Blood TGSH and GSSG levels and also reduced GSH and GSSG/TGSH ratio derived from those values were not affected by either acute exhaustive exercise or endurance training in SID rats (Table 2).

Table 2. Blood glutathione redox status in untrained and trained streptozotocin-induced diabetic rats at rest and after acute exhaustive exercise. Values are mean (SD).

	At rest		After exhaustive exercise	
	Untrained (n=7)	Trained (n=10)	Untrained (n=8)	Trained (n=9)
TGSH (mmol· l^{-1})	.58 (.19)	.50 (.18)	.61 (.22)	.61 (.26)
GSSG (mmol· l^{-1})	.17 (.08)	.13 (.08)	.16 (.08)	.18 (.12)
GSH (mmol· l^{-1})	.40 (.16)	.37 (.15)	.46 (.15)	.51 (.15)
GSSG/TGSH	.31 (.11)	.26 (.11)	.25 (.07)	.26 (.17)

TGSH: Total glutathione, GSSG: oxidized glutathione, GSH: reduced glutathione. GSH and GSSG/TGSH ratio are derived from TGSH and GSSG values.

Table 3. Effects of endurance training and acute exhaustive exercise on heart tissue total glutathione level (µmol· g^{-1} wet weight) and glutathione related enzyme activities (nmol· min^{-1} mg $protein^{-1}$) in untrained and trained streptozotocin-induced diabetic rats. Values are mean (SD).

	At rest		After acute exhaustive exercise	
	Untrained (n=7)	**Trained (n=10)**	**Untrained (n=8)**	**Trained (n=9)**
TGSH	1.69 (.40)	1.68 (.43)	1.61 (.20)	1.69 (.18)
GPX	165.34 (53.64)	107.97 (17.18)*	164.65 (66.34)	104.51 (10.62)*
GRD	33.68 (7.40)	32.48 (8.17)	30.26 (4.33)	29.45 (3.9)
GST	104.68 (40.94)	121.33 (24.87)	117.33 (12.61)	124.02 (17.15)

TGSH=Total glutathione, GPX=Glutathione peroxidase, GRD=Glutathione disulfide reductase, GST=Glutathione S-transferase. *: difference due to endurance training, $p<0.05$, by two-way ANOVA.

Tissue TGSH level and activities of the glutathione-related enzymes in heart tissue of diabetic rats:
Tissue TGSH levels in heart were not affected either by endurance training or acute exhaustive exercise (Table 3). On the other hand, endurance training decreased GPX activity (% 35.61, $p<0.05$, two-way ANOVA) in heart tissue of SID rats (Table 3). However, GRD and GST activities in heart were not affected by either acute exhaustive exercise or endurance training (Table 3).

Conjugated dienes levels in heart tissue of diabetic rats
Conjugated dienes levels in heart tissue were increased by both acute exhaustive exercise (% 35.42, $p<0.01$, two-way ANOVA) and 8 weeks of treadmill training (%20.82, $p<0.05$, two-way ANOVA). (Figure 3).

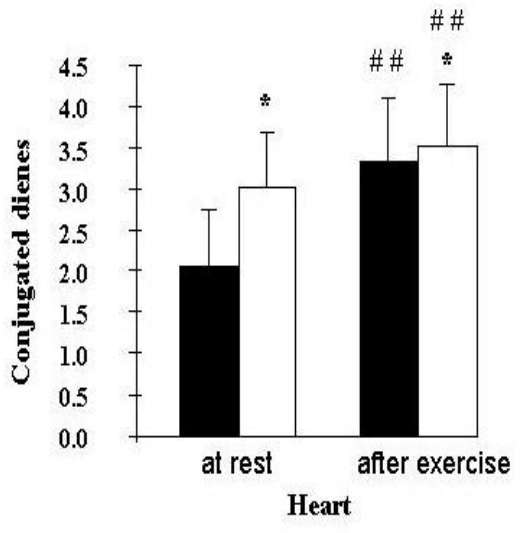

Figure 3. Conjugated dienes levels (Abs234/g wet weight) in heart tissue of untrained (filled colons) and trained (empty colons) streptozotocin-induced diabetic rats at rest and after acute exhaustive exercise. Values are mean (SD).
* $p<0.05$, difference due to endurance training, two-way ANOVA. ## $p<0.01$, difference due to acute exhaustive exercise, two-way ANOVA.

DISCUSSION

We hypothesized that endurance training can strengthen the antioxidant GSH defense mechanism and decrease oxidative stress in the heart tissue of the SID rats. Eight weeks of treadmill training increased the endurance in SID rats. It did not affect glutathione levels in blood and also in heart tissue at rest and after exercise. GRD and GST activities were not affected either by acute exhaustive exercise or endurance training, however, endurance training decreased GPX activity in heart. Acute exhaustive exercise increased the CD levels in heart. In contrast to our hypothesis, CD levels in heart tissue were also increased by 8 week treadmill training.

Endurance
Eight week treadmill training increased the distance run by the trained group compared with the untrained SID rats. Improved endurance due to 8-week treadmill training in SID rats, agrees with the studies carried out in normal rats. It is reported that physical training, either by running on treadmill (Sen et al., 1992; Frankiewicz-Jozko et al., 1996) or swimming (Venditti and Di Meo, 1997) increases endurance in normal rats. It is well known that endurance training increases maximal oxygen consumption ($\dot{V}O_{2\ max}$) (Powers and Howley, 1999; Gul and Hänninen, in press). Radak et al. have recently shown that endurance training increases VO_{2max} in rats (Radak et al., 2002) confirming previous reports (Crisman and Tomanek, 1985). Most of the increase in $\dot{V}O_{2\ max}$ results from the increase in stroke volume and partly comes from the increase in oxygen uptake by skeletal muscle. The increase in endurance to exhaustion in SID rats suggests that the stroke volume is increased probably with increased oxygen uptake in skeletal muscles, despite the compromised glutathione-dependent antioxidant defense mechanism in heart tissue in our study.

Blood TGSH and GSSG levels in diabetic rats
We did not find any alteration in blood GSSG and TGSH levels due to acute exhaustive exercise in

either sedentary or endurance-trained diabetic rats. In contrast to our findings, increased blood GSSG levels have been reported with an unchanged blood TGSH level (Sen et al., 1994a) or an increased plasma reduced GSH level (Lew et al., 1985) in normal rats following acute exhaustive exercise. In addition, although blood TGSH did not change, GSSG level increased in healthy men (Viguie et al., 1993; Sen et al., 1994b) and patients with insulin-dependent diabetes mellitus (Laaksonen et al., 1996) after a single bout of exercise. However, in agreement with our finding, unchanged erythrocyte glutathione (GSH and GSSG) levels were also reported after 40 minutes run in healthy men (Laires et al., 1993).

The reports related to the effects of training on blood glutathione levels are very limited. Ohkuwa et al. (1997) found an increase in the content of reduced glutathione in plasma in young rats after 5 weeks of exercise (Ohkuwa et al., 1997). In athletes running long distance triathlons, GSSG did not significantly change after the race (Margaritis et al., 1997). In our study, blood TGSH and GSSG levels did not change due to training in SID rats. A trivial explanation could be that oxidation of blood GSH may be prevented due to endurance training in untreated SID rats, since training has been shown to increase antioxidant enzymes in the blood in normal rats (Kanter et al., 1985).

Tissue glutathione level and glutathione-related enzymes in heart

There was no change in TGSH levels in heart tissue in SID rats. In contrast to unchanged TGSH level in diabetic rats, decreased TGSH level in heart tissue has been reported in normal rats after exhaustive exercise (Sen et al., 1994a).

Consistent with our observation that GPX and GRD activities did not respond to acute exhaustive exercise in SID rats, unchanged GPX and GRD activity has been reported in heart tissue in normal rats after exercise (Khanna et al., 1999). Stable erythrocyte GPX activity in response to physical activity was also found in men with insulin-dependent diabetes mellitus, while it was up-regulated in healthy control subjects (Atalay et al., 1997). In contrast to our finding of no change in diabetic rats, decreased GST activity in heart has been reported (Khanna et al., 1999). On the other hand, lipid peroxidation by-products, such as 4-hydroxynonenal, is the substrate of GST iso-enzymes (Tjalkens et al., 1999). Increased lipid peroxidation detected as higher CD in our study may partly explain why GST activity was not decreased, despite the depression of GPX activity.

Decreased GPX activity in the heart of SID rats due to training suggests an impairment of glutathione-dependent tissue antioxidant defense mechanism and may make the heart more susceptible to oxidative insult. This was confirmed by increased conjugated dienes levels due to endurance training in our study. However, combination of endurance training and insulin in diabetic patients may prevent the decrease in GPX activity in the heart and kidney. It has been shown that insulin corrects the decreased GPX level in the heart of SID rats (Wohaieb and Godin, 1987).

Lipid peroxidation in heart tissue of diabetic rats

The increase in CD in heart due to acute exercise may reflect increased reactive oxygen species formation, and insufficient antioxidant defense, possibly because of the decreased GPX activity. It should also be kept in mind that the trained group ran longer due to increased endurance capacity, therefore, probably had much higher levels of oxygen consumption during exhaustive exercise. Because reactive oxygen species (ROS) generation during oxidative phosphorylation is presumably a primary source of ROS during exercise (Ji, 1999), the trained group were most likely exposed to much higher levels of ROS than the untrained group during exercise to exhaustion.

Endurance training also increased CD levels in heart in SID rats. In contrast to our finding, decreased lipid peroxidation as measured by TBARS levels in heart tissue has been reported in normal swim-trained (Kihlstrom, 1990) and treadmill-trained rats (Kim et al., 1996). The diabetic state, exercise intensity and duration probably explain the differing results in these training studies. While the 8 week training period strengthens the antioxidant defense and prevents oxidative stress in normal rats, it may have caused overtraining in our SID rats. Overtraining may actually exacerbate the oxidative stress (Tiidus, 1998). Decreased GPX activity due to endurance training may partly be responsible for the increased CD level in heart in diabetic state.

Body weight changes by training in SID rats

Despite the growth period of the rats, body weight did not change in sedentary group, while it slightly decreased by eight weeks of treadmill training in SID rats. After initial dramatic weight loss, experimental diabetes causes reduced body weight gain (Riggs et al., 1992; Young et al., 1992) or weight loss (Saxena et al., 1993) compared to healthy control rats.

Blood glucose level

Both endurance training and acute exhaustive exercise favorably decreased blood glucose level in SID rats. Even though the decrease in blood glucose level due to training was statistically significant, it

was still higher than normal values (16.71±3.81 >10 mmol· l^{-1}). Decrease in blood glucose level due to endurance training has been reported in healthy subjects, and also type 1 diabetic patients as well as SID rats (Wallberg-Henriksson et al., 1982; Mikines et al., 1989; Riggs et al., 1992). This effect has been attributed to increased insulin sensitivity of the tissues, especially skeletal muscle so that glucose can be used more efficiently (Atalay and Hänninen, in press). Furthermore, Chibalin et al. (2000) have reported increased insulin mediated glucose transport activity and GLUT-4 protein expression in epitrochlearis muscle studied 16 h after the last exercise bout in normal rats subjected to swim exercise for 1 and 5 days. They also reported increased expression and function of several proteins in insulin-signal transduction. However, endurance training has also had equivocal effects on glycaemic control in Type 1 diabetic patients (Laaksonen et al., 2000), probably because in contrast to the uncontrolled and untreated diabetic model of rats in the current study, training-induced improvements in insulin sensitivity are balanced by exercise-related hyper- and hypoglycaemia in human patients. Pronounced decrease in blood glucose level due to acute exhaustive exercise may also result from increased insulin sensitivity and increased glucose transport in the untrained group (Richter et al., 1985). However, depletion of the hepatic glycogen stores due to prolonged exercise is more likely in the trained group that had body weight loss (Richter et al., 1992).

CONCLUSION

Eight week treadmill training improved the endurance in SID rats. However, it increased tissue CD levels in heart in SID rats. Although, TGSH level, GRD and GST enzyme activities were not affected, decrease in GPX activity may be responsible for this increased CD levels in heart. Longer duration of exercise till exhaustion in trained group may have contributed to the increased CD levels in heart after acute exercise. Reduced and oxidized glutathione levels in blood were not affected by either training or acute exercise. Our results suggest that intensive endurance type exercise may make heart more susceptible to oxidative stress, therefore, it may be wise to combine aerobic exercise with insulin treatment to prevent its adverse effects on antioxidant defense in heart in patients with diabetes mellitus.

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