Effects of Exercise Training and Selenium on MCT1 and MCT4 Protein Levels in Skeletal Muscles of Diabetic Goto-Kakizaki Rats

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The purpose of this study was to determine the possible additive effects of endurance exercise training (EXER) and selenium (SELE) on the improvements of glucose and lactate transport capacities in diabetic Goto-kakizaki rats. Animals either remained sedentary control (SED) or performed EXER or received SELE [5μmol kg body wt (-1) day (-1)], or underwent both EXER and SELE (COMBI), which lasted for 6 wk. Compared with sedentary control, EXER alone or the SELE alone group, or the combined treatment group had significant reduction in glucose response measured at 90 min and 120 min during an intraperitoneal glucose tolerance test (IPGTT) and body weight after 6week treatment. EXER alone, or combined group individually had significantly higher glycogen contents in liver compared with SED or SELE groups. EXER alone increased glycogen content in soleus and plantaris compared with SED, and this parameter was increased to greatest extent in the combined treatment groups compared with SED or SELE groups. EXER alone, SELE alone or COMBI, caused significant decreases in the plasma lactates, serum glucose, insulin, total cholesterol and HOMA-IR along with a significant increase in high-density lipoprotein cholesterol compared with SED. In addition, EXER or COMBI individually had significantly lower serum triacylglycerol compared with SED or SELE. With respect to protein expression related to glucose and lactate transport capacities, EXER alone, SELE alone, or COMBI increased in MCT1 and MCT4 protein level in soleus and plantaris. Furthermore, EXER alone, SELE alone or COMBI caused significant increases in mt MCT1 protein level in soleus and plantaris. The findings of the current study suggest that endurance exercise training and selenium treatment may provide therapeutic values to type II diabetic patients with peripheral insulin resistance and hyperlactatecemia by improving glucose and lactate transport capacities, leading to improvements in plasma lactate, serum glucose, insulin and lipid profiles (TC, TG, HDL).

Key words : Exercise training, selenium, MCT1, MCT4, Goto-Kakizaki rats, glycogen, intraperitoneal glucose tolerance test (IPGTT)

Introduction

Type II diabetes is characterized by peripheral insulin resistance and sometimes severe metabolic disturbances such as hyperlactatecemia [2]. This serious condition caused by the build up of lactic acid in the blood induces the body to become excessively acidic. If large amount of lactate builds up within a muscle tissue, glycolysis is inhibited and the muscle fiber is fatigued. To help maintain intracellular acid-base homeostasis and lactate metabolic control in insulin resistance state, monocarboxylate such as pyruvate and lactate are well transported across cellular and organelle membranes by a family of mono-carboxylate transporters (MCTs) [6,14,15]. MCT1 is ubiquitously expressed in many tissues and highly correlated with muscle fiber oxidative capacity whereas MCT4 is present in tissues with high glycolytic capacities such as fast-twitch skeletal muscle [5,16].

The diabetes and lactate transport are closely related. Numerous studies have shown that STZ-induced diabetic rat has been found to decrease skeletal muscle lactate transport [23]. MCT1 and MCT4 in skeletal muscles and in the heart are reported to be reduced in STZ-induced diabetic rats [22]. The impairment of lactate exchange could contribute to hyperlactatemia. Moreover, resting blood lactate is reported to be elevated in streptozotosin (STZ)-induced diabetic rats [9,18,23]. Thus, specific defects in the lactate homeostasis and exchange contribute to hyperlactatecemia in diabetic rats.

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Interventions that improve insulin resistance of skeletal muscle lactate transport include diet, exercise, and pharmaceutical and nutriceutical compounds. Selenium (SELE) is recognized as one of the trace elements which remove free radicals, reduce insulin resistance and improve glucose tolerance [20]. In contrast, the deficiency of SELE impaired glucose tolerance and associated with gestational hyperglycemia [2]. However, the precise cellular mechanisms responsible for the stimulatory effect of SELE on lactate transport capacity have not been determined. Another effective intervention that improves lactate transport in insulin-resistant states is exercise training (EXER). Few studies have reported favorable metabolic adaptations in skeletal muscle of the insulin-resistant diabetic rats in response to treadmill training, including significant enhancements of lactate transport, MCT1 and MCT4 protein expression [9,15,22].

However, the potential interactions between exercise training and selenium treatment have not yet been investigated in an animal model of insulin resistance. In this context, the purpose of the present experimental study was to test the hypothesis that exercise training and chronic treatment with the selenium, in combination, could improve MCT1 and MCT4 in skeletal muscle of Goto-Kakisaki (GK) rats [11] which are animal model of Type II diabetes without obesity, to a greater extent than either intervention used individually.

Materials and Methods

Animals and treatments

All experimental procedures were approved by the Committee on Animal Research at Korea National Sport University. Eight-wk-old male Goto-Kakisaki (GK) rats which are highly inbred strain of wistar rats that spontaneously develop Type II diabetes without obesity (n=40, 280.30±20.35 g) were obtained from Charles River JAPAN (Charles River Japan, Inc, Yokohama) and cared for according to the Guiding Principles for the Care and Use of Animals, based on the Helsinki Declaration of 1964 and were studied from 46 weeks of age (n=26, 336.05±4.13 g) to 52 weeks of age (n=26, 365.16±38.23 g).

They were maintained at a 12:12 hr dark-light cycle, housed at 22±2°C with 50% relative humidity, and had free access to fed standard chow diet (Purina Mills Inc.) *ad libitum*. The body weight of animals measured at the start of the study and after training period of each group. The GK rats were randomly assigned to one of the following groups: a sedentary control group, selenium-treated group, an exercise-trained group, or a combined selenium-treated and exercise-trained group. Animals in the selenium-treated groups received 5 mol/kg body wt of the purified sodium selenite (Sigma-Aldrich, St. Louis, MO, USA), dissolved in 100 mM Tris buffer (pH 7.4), by intraperitoneal injection every morning for 6 wk, and the sedentary control animals received same dose of 100 mM Tris buffer (pH 7.4).

Animals in exercise-trained group ran 30 minutes a day at 21 m/min for 5 day/week, at 0% grade for 6 weeks. Prior to the treadmill exercise training, the Goto-Kakisaki rats were allowed a minimum 2 week familiarization period to the new environment, consisting of running for 10 min/day on the treadmill (11 m/min). The combined-treatment animals performed the treadmill training protocol exactly as described above while also receiving daily treatment with selenium.

Intraperitoneal glucose tolerance test

Twenty-four hours after the final exercise training bout or selenium treatment, The rats were intraperitoneally administered a glucose solution [1 g/kg body wt saline (0.9% NaCl)]. Blood was drawn from a cut at the tip of the tail at 0, 30, 60, 90, 120 min after administration for measurements for plasma glucose. The glucose levels in the blood from each of groups was detected with the sensitive strip method using a blood glucose monitoring system (I-sens Co., Korea). The homeostasis model assessment (HOMA-IR, μlu/ml×mmol/L/22.5) were calculated. This latter variable is defined as index of insulin resistance, the reduction of this value reflecting an increase in all body insulin sensitivity.

Tissue preparation

whole soleus and plantaris muscle were excised from hind limbs without damage by severing tendons and excess connective tissue and quickly frozen in liquid nitrogen and stored at - 80°C until biochemical assays were performed. Muscles with different metabolic properties were selected to study glycogen content, monocarboxylate transporter 1, 4 (MCTs) expression.

Glycogen content determination

Muscle and liver glycogen content was assayed as pre-

viously described [1]. Briefly, soleus, plantaris muscles and liver samples were placed in 2 NHCl and incubated at 100°C for 2 hr. After neutralization with 0.66 N NaOH, the liberated glucose units were assayed fluorometrically and glycogen content was expressed as micromoles of glucosyl units liberated per gram wet muscle and liver weight (μ mol·g^{-1} w·w.).

Isolation of mitochondria

Mitochondria were extracted muscles by use of mitochondria extraction kit (IMGENEX Corporation, San Diego, USA) as follows. 1g of each sample was homogenized in 5 ml homogenizing buffer and centrifuged at 3,000 rpm for 10 min at 4°C and then removed the supernatant. The resulting supernatant was again centrifuged at 12,000 rpm for 30 min at 4°C. The pellet was mixed with 5ml suspension buffer and then centrifuged at 12,000 rpm for 10 min at 4°C. The resulting pellet was mixed with 5 ml for 30 min at 4°C. The supernatant (mitochondria fraction) was obtained.

Western blot analysis

For Western blot analysis, Proteins (80 g/lane) were separated by using a 10% gel concentration of SDS/PAGE under denaturing condition and then transferred to nitrocellulose membranes (Immuno-Blot, PVDF membrane, Bio-Rad, CA, USA) for 2 hr at a constant voltage of 40 volts. The membranes were blocked with 2% skim milk in PBS-T (150 mM NaCl, 10 mM Tris-HCl, 0.05% Tween 20, pH 8.0) overnight at 4°C. Primary polyclonal anti-GAPDH (Santa Cruz Biotechnology, sc-20357, CA, USA) were used in a 1:1,000 concentration for whole muscle. anti-MCT1 (Santa Cruz Biotechnology, sc-14917, CA, USA), and anti-MCT4 (Chemicon, AB 3314P, Danvers, USA) were used in a 1:500 concentration for whole muscle and 1:1,000 concentration for mitochondria fraction in PBS-T, and 1-2% skim milk for 2 h at room temperature followed by three 10-minute washes with TBS-T. The membranes were washed with washing buffer and then incubated with secondary antibodies, horseradish peroxidase-conjugated donky anti-goat (Santa Cruz Biotechnology, sc-2004, CA, USA) for MCT1, mt MCT1, GAPDH (1:5,000), and horseradish peroxidase-conjugated goat anti-rabbit (Santa Cruz Biotechnology, sc-2020, CA, USA) for MCT4 (1:5,000). The immunoreactivity on the membrane was detected by treatment with an enhanced chemiluminescence Western blot analysis system (Santa Cruz, Biotechnology, CA, USA) following the manufacturer's instruction. The density of the developed bands was scanned by ChemiDoc XRS system (Bio-Rad, CA, USA).

Biochemical analysis

Whole blood was extracted immediately after twenty-four hours after the final exercise training or selenium treatment by inserting an 18-guage needle connected to a 10 ml syringe into the heart and then withdrawing the syringe plunger. After the extraction, blood samples were centrifuged at 15,000 rpm, at 4°C for 10 minutes and the supernatants were transferred into new tubes and stored at - 80°C until total cholesterol (cholesterol reagent kit, Bayer, Pittsburgh, USA), triglyceride (triglyceride reagents, Bayer, Pittsburgh, USA), high-density lipoprotein-cholesterol (Direct HDL-cholesterol kit, Bayer, Pittsburgh, USA), low density lipoprotein-cholesterol (LDL-cholesterol kit, Bayer, Pittsburgh, USA), lactate (lactate kit, Roche, USA), glucose (glucose hexokinase kit, Bayer, Pittsburgh, USA) and insulin (insulin RIA kit, Linco Research Inc, Missouri, USA) were analyzed.

Statistical analysis

The data were analyzed by using SPSS (version 10.0). All values were expressed as means±SE. A two way ANOVA for repeated measures was used to evaluate statistically significance of IPGTT measured. Student Newman-Keuls post hoc test was the post hoc analysis used to detect difference over time. When comparing groups, statistical significance was determined by using one-way ANOVA. If a statistically significant difference was observed, Student Newman-Keuls post hoc test was used. The differences were considered statistically significant at $p<0.05$.

Results

Body weight, plasma lactate, serum glucose, insulin, and lipids

The exercise-trained (EXER) alone, selenium (SELE) treatment alone and combined treatment group had significantly lower final body weights compared with the sedentary control group (Table 1). The plasma level of lactate and the serum levels of glucose, insulin, and lipids in the various groups are shown in table 1. The exercise-trained, selenium treatment and combined treatment groups had

Table 1. Effect of exercise training and selenium treatment on body weight, plasma lactate, serum glucose, insulin, and lipid profiles in the diabetic Goto-kakizaki rat

Group	Initial body Wt, g	Final body Wt, g	Change in Wt/day, g/da	LA mmol/l	Glucose mmol/l	Insulin μU/ml	HOMA -IR	TC mg/dl	TG mg/dl	HDL mg/dl
Sedentary	340.00±65.10	422.50±79.40	1.96±0.34	2.24±0.26	8.73±0.10	19.90±2.00	7.72±0.76	81.50±11.56	78.83±12.43	40.83±1.75
Exercise trained	332.37±37.45	345.00±45.68	0.30±0.19[a]	1.30±0.09[a]	6.98±0.22[a]	12.96±1.84[a]	3.82±0.37[c]	53.20±6.67[a]	50.33±7.28[af]	49.00±2.22[c]
SEL-treated	339.25±26.86	346.50±31.39	0.17±0.10[a]	1.32±0.19[a]	6.91±0.63[a]	14.21±2.58[a]	4.36±0.71[c]	67.00±3.95[a]	68.16±3.50	44.50±0.99[d]
Combined	332.60±39.11	346.64±64.50	0.33±0.60[a]	1.20±0.34[c]	6.86±0.39[b]	11.66±1.12[b]	3.50±0.29[c]	49.62±3.33[b]	47.26±6.37[af]	49.33±0.61[c]

Values are means±SE for 6 animals/group, [a]$p<0.05$ vs sedentary group. [b]$p<0.01$ vs sedentary group. [c]$p<0.001$ vs sedentary group. [d]$p<0.05$ vs sedentary group. [e]$p<0.05$ vs exercise group, [f]$p<0.05$ vs SELE-treated group

significantly lower plasma lactates, serum glucose, insulin, total cholesterol, and HOMA-IR along with a significant increase in high-density lipoprotein cholesterol compared with sedentary controls. Exercise trained or the combined groups individually had significantly lower serum triglyceride compared with the sedentary control group or selenium treatment group.

IPGTT responses

The glucose response during the IPGTT in the experimental groups are shown in Fig. 1. Compared with the sedentary control group, exercise training alone, SELE treatment alone, or the two interventions in combination resulted in a lowering of the glucose response at 90 min and 120 min. Table 1 shows HOMA-IR. HOMA-IR was significantly higher in the sedentary control group compared with he exercise-trained alone, selenium treatment alone and combined treatment group.

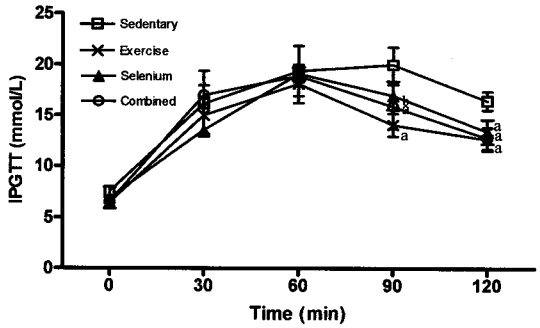

Fig. 1. Glucose responses during an intraperitoneal glucose tolerance test (IPGTT) in diabetic Goto-Kakizaki rats after chronic treatment with exercise training (EXER), selenium (SELE), or selenium combined with exercise training (COMBI). Values are means±SE for 6 animals/group. [a]$p<0.05$, [b]$p<0.01$, [c]$p<0.001$. sedentary control group

Glycogen content

The contents of glycogen in the four groups (Fig. 2) were determined in liver , soleus, and plantaris muscles. The exercise-trained or the combined groups individually had significantly greater glycogen contents compared with the sedentary controls (57.7%, 66.2%, respectively) or SELE-treatment group (38.7% and 46.2%, respectively) in the liver. Compared with the sedentary controls, glycogen content was increased by exercise training alone or in the combined groups in the soleus (28.2% and 36.9%, respectively) and plantaris (22.7% and 38.5%, respectively). In addition, the two interventions in combination alone had significantly greater glycogen content compared with the SELE-treatment group in the soleus (24.1%) and the plantaris (25.0%).

MCT1 and MCT4 protein

MCT1, MCT4, and mt MCT1 protein levels (Fig. 3) were determined in the soleus and plantaris muscles. The exercise-trained alone, selenium treatment alone or combined treatment group, caused significant increases in MCT1 protein level in soleus (40.3%, 31.2% and 58.8%, respectively, vs. sedentary control) and plantaris (32.9%, 28.6% and 25.1%, respectively, vs. sedentary control). Moreover, The exercise-trained alone, selenium treatment alone or combined treatment group, caused significant increases in mt MCT1 protein level in soleus (26.7%, 37.1% and 31.0%, respectively, vs. sedentary control) and plantaris (25.2%, 31.7% and 45.0%, respectively, vs. sedentary control). The exercise-trained alone, SELE-treatment alone or combined treatment group, caused significant increases in MCT4 protein level in soleus (31.6%, 28.3% and 42.5%, respectively, vs. sedentary control) and plantaris (21.7%, 29.7% and 38.2%, respectively, vs. sedentary control).

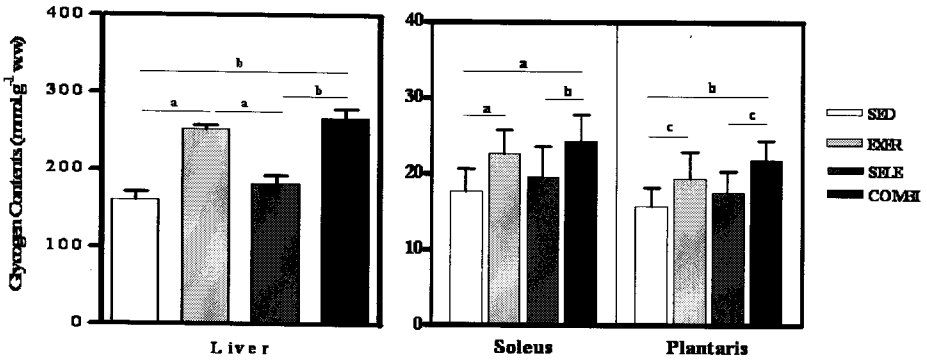

Fig. 2. Effects of chronic treatment with exercise training (EXER), selenium (SELE), or selenium combined with exercise training (COMBI) on glycogen contents of the liver, soleus and plantaris muscles. Values are means ±SE of 6 animals/group. $^{a}p<0.05$, $^{b}p<0.01$, $^{c}p<0.001$.

Discussion

In the present study, we found that blood lactate, glucose, insulin, and lipid concentrations were increased in sedentary diabetic rats at rest (Table 1). This conforms several previous studies [9,12,17,19]. An additional evidence for this study is that liver and muscle glycogen contents are much lower in sedentary diabetic animals (Fig. 2). Those results are in accordance with previous studies [7,10].

Thus, the elevated circulating those metabolic parameters and the reduction of muscle glycogen content may be mechanistically linked to a reduction in skeletal muscle glucose and lactate transport capacity, possibly via inhibition of lactate utilization, glucose and lactate transport, insulin signaling, glycogen synthase activity, and carbohydrate or lipid oxidation [8,18]. Furthermore, the body weights of the animals in each of the four groups were markedly changed during the course of this study. In particular, sedentary diabetic rats gained weight at much higher rate, as has been shown previously [25].

We have also confirmed the previous findings by others that marked reductions in metabolic parameters (blood lactate, glucose, insulin, TC, TG) can be elicited by either exercise training alone [9,18,26] or chronic supplementation of the antioxidant selenium alone [21,27] in diabetic rats. More importantly, the combination of exercise training and selenium results in a further diminution in circulating metabolic parameters and HOMA-IR along with a significant increase in high-density lipoprotein cholesterol (Table 1).

It is clear from the present findings that the selenium treatment alone induces insulin-like effects in lowering metabolic parameters along with increase in HDL-C in se-

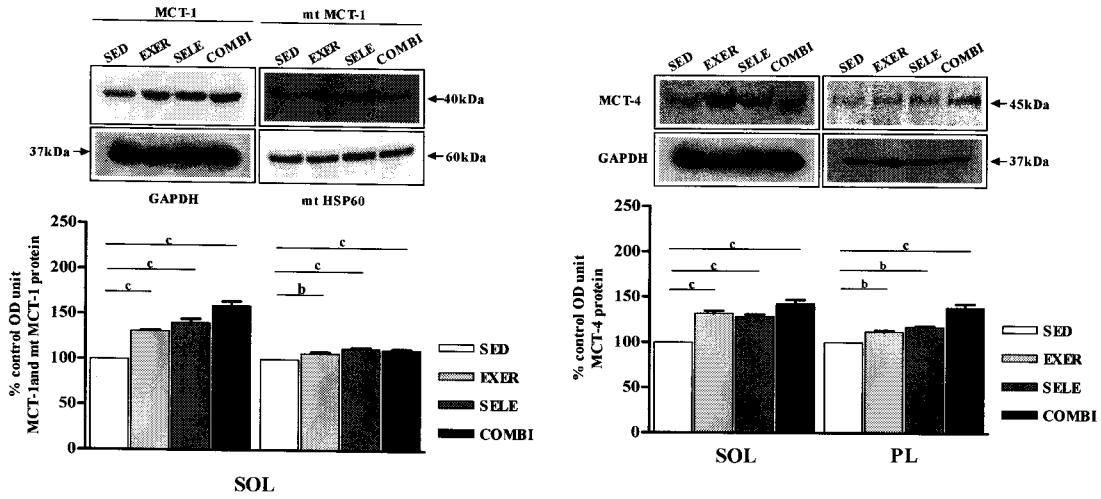

Fig. 3. Effects of chronic treatment with exercise training (EXER), selenium (SELE), or selenium combined with exercise training (COMBI) on whole muscle and mitochondria level of MCT1 protein in the soleus muscle and whole muscle MCT4 protein in the soleus and plantaris muscles. Values are means±SE of 6 animals/group. $^{a}p<0.05$, $^{b}p<0.01$, $^{c}p<0.001$.

lenium treated diabetic GK rats. In addition, liver and muscle glycogen contents are much increased in selenium treated diabetic GK rat compared with sedentary diabetic rats (Fig. 2). This increased glycogen content, along with the hypoglycemic effect induced by the chronic selenium treatment, could be attributed to increased insulin-like actions on the influx of glucose into the muscle which then uses it for glycogenesis. This conforms several previous studies [3,11].

The diabetes and lactate metabolism are closely related. there is increasing evidence that elevated lactate level has been shown to decrease skeletal muscle lactate transport capacity by down regulating their known mono-carboxylate transporters in insulin resistance states [18]. The underlying mechanism of the elevated lactate level is that this may be due to increases in circulating glucose levels in combination with the concomitant impairments of total and mitochondrial MCT protein levels in diabetic animals. Although not a main subject of inquiry in this study, we found that the exercise training or selenium treatment individually, caused significant decreases in the plasma lactate level compared with sedentary controls. This suggested that there was a positive effect of the exercise training alone, or selenium treatment alone on lactate homeostasis in this model of type II diabetes. This conforms several previous studies [9,18].

Our results provide important new information regarding the potential role of lactate transport capacity (MCT1 and MCT4 protein expression) in the multi-factorial etiology of insulin resistance and address the potential utility of exercise training or antioxidant selenium treatment, individually, or in combination, to increase lactate transport capacity in skeletal muscle insulin resistance. First, we found that exercise trained GK rats are significantly increased in total and mitochondrial MCT1, and total MCT4 protein levels in the soleus or plantaris muscles, compared with the sedentary GK rat (Fig. 3). Those results are in accordance with previous studies [9].

Therefore, it is clear that exercise training provided a substantial prophylactic effect on total and mitochondrial MCT1, and total MCT4 protein levels in insulin resistant skeletal muscle. This study has shown that total and mitochondrial MCT1, and total MCT4 protein levels in muscles are regulated both by the ambient metabolic milieu (glucose, insulin, lactate) and by exercise training. A number of studies have already shown that exercise training or altered metabolic demand by muscle regulates MCT expression [9,18]. It is well known that exercise training markedly improves substrate metabolism, many of which are linked to insulin resistance in this model. This prove that insulin necessarily regulates MCTs expression.

This study also suggest that increased concentrations of lactate in the sedentary diabetic animals contributed to the down-regulation of total and mitochondrial MCT1, and total MCT4. The present studies demonstrate that the metabolic milieu can alter total and mitochondrial MCT1, and total MCT4 in skeletal muscle. Therefore, it appears that exercise training can override these metabolic effects that contribute to the up-regulation of total and mitochondrial MCT1, and total MCT4 in the sedentary diabetic animals

Second, we also found that selenium treated GK rats are significantly increased in total and mitochondrial MCT1, and total MCT4 protein levels in the soleus or plantaris muscles, compared with the sedentary GK rat (Fig. 3). However, we can not explain whether selenium treatment induces up-regulation of total and mitochondrial MCT1, and total MCT4 in the sedentary diabetic animals. Nevertheless, Whatever the mechanism involved, or as a mentioned previously, it is clear that selenium treatment provided a substantial insulin-like effects on total and mitochondrial MCT1, and total MCT4 protein levels in insulin resistant skeletal muscle. Further research is needed to identify the mechanisms underlying the beneficial effects on selenium treatment in ameliorating the skeletal muscle insulin resistance of the diabetic GK rat. The results of the present study indicate that improvement in lactate transport in soleus or plantaris muscle is regulated either by the supplemented selenium through insulin-like action on ambient metabolic milieu (glucose, insulin, lactate) or by increased contractile activity (exercise training).

Second, it is noteworthy that the combination of exercise training and selenium treatment favorably alters several lactate transport parameters (MCT1, mt MCT1 and MCT4) suggesting that these treatments in combination cause a greater degree of improvements in several lactate transport parameters in sedentary diabetic GK rat. It could be hypothesized that selenium treatment enhances homeostasis and transport capacity of glucose or lactate, and oxidative metabolism in the sedentary diabetic GK rat, which in turn led to an exercise-induced improvements in homeostasis and transport capacity of glucose or lactate, and oxidative metabolism similar to that reported in diabetic rats that

have undergone exercise training [24,26].

In conclusion, we have confirmed that endurance exercise training and chronic administration of the antioxidant selenium individually improve glucose tolerance and induce insulin-like actions on down-regulation of glucose, TC, TG level and prophylactic effect in the markedly insulin- resistant, diabetic GK rats. Moreover, we have provided new evidence that the combination of these interventions is associated with greater improvements in skeletal muscle insulin-like action than either intervention individually.

Although the enhancement of insulin-like action following exercise training or selenium treatment was associated with up-regulation of total and mitochondrial MCT1, and total MCT4 protein expression and both exercise training and antioxidant treatment induced increases in insulin-like action that were associated with decreased metabolic parameters and circulating levels, it is clear that the interactive effects of the two interventions could be attributed to additive effects on total and mitochondrial MCT1, and total MCT4 protein levels. Further research is needed to identify the mechanisms underlying the beneficial interaction between exercise training and selenium in ameliorating the skeletal muscle insulin resistance of the diabetic GK rat.

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초록 : 지구성 운동과 셀레니움 투여가 당뇨 Goto-kakizaki 쥐의 골격근의 MCT1과 MCT4단백질 발현수준에 미치는 효과

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이 연구는 지구성 운동과 셀레니움 투여가 Goto-Kakizaki 쥐의 젖산수송 능력에 독립적으로 혹은 상호작용하여 영향을 미치는가를 구명하는데 그 목적이 있다. 실험동물들의 집단은 비교집단(n=10, SED), 지구성 운동집단(n=10, EXER), 셀레니움 투여집단(n=10, SELE)과 지구성 운동과 셀레니움 투여 병행 집단(n=10, COMBI)으로 분류하여 6주간 실험을 실시하였다. 6주간 실험 처치 후 체중은 비교집단에 비해 지구성 운동집단, 셀레니움 투여집단과 지구성 운동과 셀레니움 투여 병행 집단이 현저하게 감소하였으며 당 부하검사를 실시한 결과에서도 비교집단에 비해 지구성 운동집단, 셀레니움 투여집단과 지구성 운동과 셀레니움 투여 병행 집단이 90분과 120분 사이에서 혈당 수준이 유의한 낮은 것으로 나타났다. 간 글리코겐 수준은 비교집단과 셀레니움 투여집단에 비해 지구성 운동집단과 지구성 운동과 셀레니움 투여 병행 집단이 유의하게 높은 것으로 나타났다. 가자미근과 족저근의 글리코겐 수준도 비교집단과 셀레니움 투여집단에 비해 지구성 운동집단과 지구성 운동과 셀레니움 투여 병행 집단이 현저하게 높은 것으로 나타났다. 혈액 생화학 성분의 경우, 지구성 운동집단, 셀레니움 투여집단과 지구성 운동과 셀레니움 투여 병행 집단이 비교집단에 비해 고밀도 지단백 수준 증가와 함께 혈장 젖산, 혈청 중성지방, 인슐린, 총 콜레스테롤과 HOMA-IR 수준이 현저하게 감소한 것으로 나타났다. 특히 혈청 중성지방 수준은 지구성 운동집단과 지구성 운동과 셀레니움 투여 병행 집단이 셀레니움 투여집단에 비해 유의하게 낮은 것으로 나타났다. 이 연구에 가장 중요한 결과는 혈당과 젖산 수송과 관련된 단백질 발현 수준이 6주간의 실험처치 후에 지구성 운동집단, 셀레니움 투여집단과 지구성 운동과 셀레니움 투여 병행 집단이 비교집단에 비해 가자미근의 MCT1과 미토콘드리아 MCT1 단백질 발현수준이 현저하게 증가하였다는 결과와 함께 가자미근과 족저근의 MCT4 단백질 발현 수준도 지구성 운동집단, 셀레니움 투여집단과 지구성 운동과 셀레니움 투여 병행 집단이 비교집단에 비해 현저하게 증가하였다는 결과이다. 이러한 결과를 근거로 볼 때 지구성 운동과 셀레니움 투여는 독립적으로 혹은 상호작용하여 혈당과 젖산수송 능력을 개선시키는데 도움이 된다는 것을 알 수 있으며 특히 인슐린 저항 특성과 함께 고젖산혈증을 나타내는 제 II형 당뇨 환자들의 당뇨 처치를 위한 방법으로 활용할 만한 가치가 있는 것으로 생각된다.