INFLUENCE OF AN ORALLY EFFECTIVE SUPEROXIDE DISMUTASE (GLISODIN®) ON STRENUOUS EXERCISE-INDUCED CHANGES OF BLOOD ANTIOXIDANT ENZYMES AND PLASMA LACTATE

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Abstract

Strenuous exercise abruptly increases oxygen consumption aggravating oxidative stress by generation of free radicals. In healthy individuals, the antioxidant system defends tissues against free radical attack and superoxide dismutase (SOD) is one of the major antioxidant enzymes. Recently an effective oral preparation of SOD was developed and we evaluated its influence on exercise-related change of blood antioxidants and lactate. Forty-four healthy volunteers participated in this study and a daily dose of 1500 IU oral SOD (Glisodin®) was administered to each participant for 4 weeks. Before and after the 4 week SOD treatment, they performed the same quantity of acute cycling or treadmill exercise. Shortly before and after the exercise serum total antioxidant status (TAS), erythrocytic SOD, whole blood glutathione peroxidase (GPx), serum glutathione reductase (GR), and plasma lactate (Lac) of each participant were measured. Based on the degree of initial exercise-induced lactate increase, subjects were classified into severe exercise group (n=27) and moderate exercise group (n=17). After 4 week adminitration of oral SOD, baseline TAS and GR were significantly decreased ($p<0.01$) while SOD, GPx and Lac showed no significant change. In severe exercise group, significant exercise-induced increases in TAS, SOD, GR and Lac were observed before SOD treatment ($p<0.01$). After 4 week SOD administration, this group showed significantly decreased amount of exercise-induced increases in TAS, SOD ($p<0.05$) and Lac ($p<0.01$). These results suggest that exhausting exercise is responsible for a significant increase in blood TAS, SOD, GR and Lac and a 4-week administration of the newly developed oral SOD induces a significant change in oxidative status and a significant decrease in exercise-induced lactate release.

Introduction

Generation of reactive oxygen species (ROS) is a normal process in the life of aerobic organisms. Under physiological conditions, ROS are mostly removed by the cellular antioxidant systems. During exercise, whole body oxygen consumption increases up to 20-fold, with an even more dramatic muscular oxygen expenditure. A rise in oxygen consumption will enhance the electron transfer through the respiratory chain and thereby increase free oxygen radical production, since 1-3% of the total oxygen consumed is transformed to free radicals. As the antioxidant reserve capacity in most tissues is rather marginal, strenuous physical exercise presents a challenge to the antioxidant systems. However a review of current literature revealed no consistent data regarding activity of antioxidant enzymes during strenuous exercise.

Dietary antioxidant supplements are marketed to and used by athletes as means to counteract the oxidative stress of exercise. Recently an effective oral preparation of superoxide dismutase (SOD), one member of the family of major antioxidant enzymes was developed. This novel nutritional formula (Glisodin®) contains a plant (*Cucumis melo LC*) SOD extract and is chemically combined with a gliadin biopolymer system, which allows efficient oral delivery of antioxidant enzymes overcoming the limitation by the gastrointestinal digestive processes.

The aim of the present study is to evaluate the effect of an oral preparation of SOD on strenuous exercise-induced changes of blood antioxidant enzymes and plasma lactate.

Materials and Methods

Samples

Forty-four healthy volunteers including 27 male and 17 female subjects participated in this study. The age distribution ranged from 26 to 54 years with a median of 35. After the purposes of the protocol were explained, oral and written informed consent was obtained.

Before starting administration of oral SOD, each participant performed strenuous cycling or treadmill exercise up to 200 kcal consumption within 20 minutes or 300 kcal consumption within 30 minutes according to one's physical strength. Shortly before and after the exercise, blood was drawn and the antioxidant profiles and plasma lactate level were measured by the methods described below. Then a daily dose of 1,500 IU oral SOD was administered in 3 divided portions to each participant for four consecutive weeks. During these weeks they were recommended not to take any other antioxidants or nutritional supplements.

After the 4-week administration of oral SOD, they performed the same quantity of cycling or treadmill exercise and the same blood tests before and after the exercise were done. With these pre- and post oral SOD administration data, effect of oral SOD on basal level and strenuous exercise-induced changes of blood antioxidants and plasma lactate were analyzed. Paired Student t-test was done to compare the values before and after oral SOD administration and the values before and after exercise.

Measurement of blood antioxidants and plasma lactate

Serum levels of total antioxidant status (TAS), erythrocytic SOD activity, whole blood GPx activity and serum GR activity were measured using a commercially available kit (Randox Laboratories, Crumlin, UK).

Heparinized plasma was separated from the cells within 15 minuets and plasma lactate level was measured by Vitros 950 chemistry analyzer (Johnson & Johnson Clinical Diagnostics, Inc., Rochester, NY).

Results

We took the value of 4.5 mmol/L for the exercise-induced increase in plasma lactate concentration (ΔEx Lac) as a cut off value indicating a heavy physical exercise. Therefore subjects could be classified into severe (ΔEx Lac≥4.5 mmol/L) and moderate exercise group (ΔEx Lac<4.5 mmol/L). Overall blood antioxidants and lactate concentrations [mean (SD)] according to the exercise group and the presence of SOD treatment or acute exercise were listed in Table 1.

Table. 1 Effect of exercise and 4 week administration of oral SOD on blood antioxidants and lactate concentrations [mean (SD)]

Oral SOD administration	Exercise	Analytes	All subjects (n=44)	Severe exercise group[a] (n=27)	Moderate exercise group (n=17)
Before	Before	TAS (mmol/L)	1.57 (0.19)	1.56 (0.18	1.57 (0.21)
		SOD (U/g Hb)	1323.5 (227.6)	1378.3 (243.5)	1236.4 (172.5)
		GPx (U/g Hb)	48.8 (13.0)	47.2 (13.7)	51.3 (11.9)
		GR (U/L)	54.1 (9.1)	51.3 (7.3)	58.5 (10.0)
		Lac (mmol/L)	1.2 (0.4)	1.2 (0.4)	1.1 (0.5)
	After	TAS (mmol/L)	1.68 (0.19)	1.68 (0.19)	1.68 (0.19)
		SOD (U/g Hb)	1377.8 (266.1)	1476.6 (279.6)	1220.9 (143.8)
		GPx (U/g Hb)	49.3 (13.2)	48.7 (13.9)	50.2 (12.4)
		GR (U/L)	57.4 (9.3)	56.7 (7.8)	58.5 (11.4)
		Lac (mmol/L)	7.8 (4.4)	10.5 (3.4)	3.6 (1.3)
After	Before	TAS (mmol/L)	1.52 (0.19)	1.53 (0.20)	1.49 (0.18)
		SOD (U/g Hb)	1308.7 (294.0)	1288.5 (241.1)	1340.8 (368.8)
		GPx (U/g Hb)	51.3 (12.9)	53.2 (14.4)	48.2 (9.5)
		GR (U/L)	51.2 (8.8)	49.9 (6.8)	53.2 (11.1)
		Lac (mmol/L)	1.2 (0.4)	1.3 (0.4)	1.2 (0.4)
	After	TAS (mmol/L)	1.57 (0.19)	1.60 (0.20)	1.51 (0.16)
		SOD (U/g Hb)	1335.4 (372.4)	1301.6 (285.5)	1389.1 (485.1)
		GPx (U/g Hb)	51.0 (12.4)	53.5 (14.3)	46.9 (7.3)
		GR (U/L)	55.0 (11.4)	53.8 (8.4)	56.8 (15.1)
		Lac (mmol/L)	6.1 (3.0)	6.7 (3.3)	5.1 (2.2)

[a] According to the exercise-induced plasma lactate change (ΔEx Lac) before oral SOD administration, subjects were classified into severe exercise group (ΔEx Lac≥4.5 mmol/L) and moderate exercise group (ΔEx Lac<4.5 mmol/L).

Effect of oral SOD treatment on blood antioxidants and lactate change (Table 2)

Both TAS (-0.05±0.11 mmol/L, $p < 0.01$) and GR were significantly reduced (-3.0± 6.8 U/L, $p<0.01$) after 4 week administration of oral SOD, while no significant change was observed in pre-exercise SOD, GPx and plasma lactate level.

Table. 2 Effect of 4 week administration of oral SOD on blood antioxidants and lactate change (n=44)

Analytes	ΔSOD[a]	p[a]
TAS (mmol/L)	-0.05 (0.11)	<0.01
SOD (U/g Hb)	-14.8 (292.2)	NS
GPx (U/g Hb)	2.5 (8.7)	NS
GR (U/L)	-3.0 (6.8)	<0.01
Lac (mmol/L)	0.1 (0.5)	NS

[a] ΔSOD is SOD related change of each analyte [mean (SD)] which means values after SOD administration minus values before SOD administration.
[b] Paired Student t-test was done to compare values before and after oral SOD administration; NS, not significant.

Effect of exercise on blood antioxidants and lactate change (Table 3)

When considering only the population exhibiting ΔEx Lac greater than 4.5 mmol/L (severe exercise group), a significant ($p<0.01$) increase in TAS (0.12±0.09 mmol/L), SOD (98.2±156.7 U/g Hb) and GR (9.3±3.4) was observed before SOD treatment. However, after 4 week oral SOD administration only TAS showed significant exercise-induced increase (0.07±0.06 mmol/L, $p<0.01$) in this group. Although lactate was also significantly increased after exercise, most exercise induced changes of blood antioxidants were not significant in moderate exercise group (ΔEx Lac < 4.5 mmol/L) except increase in TAS (0.1±0.10 mmol/L, $p<0.01$) and decrease in GR (-0.1±8.5 U/L, $p<0.01$) before SOD treatment.

Table. 3 Effect of exercise on blood antioxidants and lactate change

Group[b]	Analytes	Before SOD		After SOD	
		ΔEx[a]	p[c]	ΔEx[a]	p
Severe exercise group[a] (n=27)	TAS (mmol/L)	0.12 (0.09)	<0.01	0.07 (0.06)	<0.01
	SOD (U/g Hb)	98.2 (156.7)	<0.01	13.1 (218.2)	NS
	GPx (U/g Hb)	1.5 (4.9)	NS	0.3 (3.4)	NS
	GR (U/L)	5.4 (5.8)	<0.01	3.9 (6.8)	NS
	Lac (mmol/L)	9.3 (3.4)	<0.01	5.4 (3.3)	<0.01
Moderate exercise group (n=17)	TAS (mmol/L)	0.11 (0.10)	<0.01	0.03 (0.08)	NS
	SOD (U/g Hb)	-15.5 (132.2)	NS	48.3 (320.9)	NS
	GPx (U/g Hb)	1.1 (3.4)	NS	-1.3 (5.0)	NS
	GR (U/L)	-0.1 (8.5)	<0.01	3.6 (9.6)	NS
	Lac (mmol/L)	2.5 (1.2)	<0.01	3.9 (2.2)	<0.01

[a] ΔEx is exercise-induced change of each analyte [mean (SD)] which means post-exercise value minus pre-exercise value
[b] According to the exercise-induced plasma lactate change (ΔEx Lac) before oral SOD administration, subjects were classified into severe exercise group (ΔEx Lac≥4.5 mmol/L) and moderate exercise group (ΔEx Lac<4.5 mmol/L).
[c] Paired Student t-test was done to compare analyte concentration before and after exercise

Effect of oral SOD on exercise induced changes of blood antioxidants and lactate (Table 4)

In severe exercise group, oral SOD was responsible for a significant decrease in the exercise-related lactate increase (-3.9± 4.1 mmol/L, $p<0.01$). Interestingly, in moderate exercise group, a significant increase in exercise-induced lactate release was found (1.4±1.7 mmol/L, $p<0.01$). Regarding the oxidative status, the changes induced by the exercise were lessened by oral SOD for TAS (-0.05±0.10, $p<0.05$) and SOD (-85.2±195.5, $p<0.05$) in severe exercise group, while such change was deepened by oral SOD for TAS (0.08±0.08, <0.01) in moderate exercise group.

Table. 4 Effect of 4 week administration of oral SOD on exercise-induced change of blood antioxidants and lactate

Group[b]	Analytes	ΔsodΔEx[a]	p[c]
Severe exercise group (n=27)	TAS (mmol/L)	-0.05 (0.10)	<0.05
	SOD (U/g Hb)	-85.2 (195.5)	<0.05
	GPx (U/g Hb)	-1.2 (5.4)	NS
	GR (U/L)	-1.5 (8.3)	NS
	Lac (mmol/L)	-3.9 (4.1)	<0.01
Moderate exercise group (n=17)	TAS (mmol/L)	0.08 (0.08)	<0.01
	SOD (U/g Hb)	63.9 (294.1)	NS
	GPx (U/g Hb)	-0.2 (6.42)	NS
	GR (U/L)	3.7 (8.2)	NS
	Lac (mmol/L)	1.4 (1.7)	<0.01

[a] ΔsodΔEx[mean (SD)] of each analyte is exercise-induced change (ΔEx) after oral SOD administration minus Δ Ex before oral SOD administration.
[b] According to the exercise-induced plasma lactate change ΔEx Lac) before oral SOD administration, subjects were classified into severe exercise group (ΔEx Lac≥4.5 mmol/L) and moderate exercise group (ΔEx Lac<4.5 mmol/L).
[c] Paired Student t-test was done to compare ΔEx before and after oral SOD administration; NS, not significant.

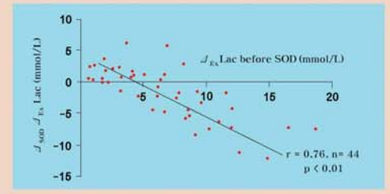

Fig. 1 Effect of 4-week oral SOD administration on exercise-induced increase in plasma lactate. Significant relationship between the magnitude of the reducing effect of SOD on exercise-induced lactate release (ΔsodΔEx Lac) and the extent of the exercise-induced lactate release before SOD administration (ΔEx Lac before SOD) was observed, indicating that the higher is the initial exercise-induced lactate release, the stronger is the effect of oral SOD.

Conclusion

Four weeks oral SOD (glisodin®) treatment induces:
- a significant change in oxidative status
- a significant decrease in exercise-related lactate increase
Exhausting exercise is responsible for a significant increase in TAS, SOD, GR.