Regular Physical Activity Increases Glutathione Peroxidase Activity in Adolescents With Down Syndrome

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Objective: The present study was designed to determine the influence of a 12-week exercise program on the activity of erythrocyte glutathione peroxidase (GPX) in adolescents with Down syndrome.

Design: An interventional study with before-after comparison.

Setting: Sport Medicine School, University of Cadiz (Andalusia, Spain).

Patients: Thirty-one male adolescents (16.3 ± 1.1) with Down syndrome. None of them suffered acute medical problems at that moment and had not taken part in any physical activity program in the last 6 months.

Intervention: A 12-week training program with 3 days per week, consisting of warm up (15 min) followed by a main part (20 to 35 min) at a work intensity of 60% to 75% of peak heart rate (HRmax = 194.5–[0.56 × age]) and by a cool-down period (10 min).

Main Outcome Measurement: Erythrocyte activity of GPX.

Results: Preexercise and postexercise GPX activity in adolescents with Down syndrome were 24.8 ± 3.1 [23.1 to 26.5] U/g hemoglobin and 29.3 ± 2.9 [28.1 to 30.5] U/g hemoglobin, respectively. When compared with baseline values it was increased significantly (24.8 ± 3.1 vs. 29.3 ± 2.9; $P = 0.011$).

Conclusion: Regular exercise increased significantly GPX activity. Further studies are required to assess the behavior of other antioxidant enzymes to highlight potential benefits of regular exercise in redox metabolism.

Key Words: exercise, antioxidant enzyme, erythrocyte, trisomy

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In recent years it has been claimed that the trisomic cells are more sensitive to oxidative stress. This fact is of particular interest because oxidative stress has been proposed as a pathogenic mechanism of atherosclerosis, cell aging and neurodegeneration in individuals with Down syndrome.[1]

In general population it has been recently published that regular exercise may increase antioxidant system.[2] However, far less information is available on handicapped populations such as Down syndrome.

For the reasons already mentioned the present study was designed to assess the influence of a 12-week training program on erythrocyte glutathione peroxidase (GPX) activity in adolescents with Down syndrome to determine its capacity to attenuate their increased oxidative damage.

MATERIALS AND METHODS

Thirty-one sedentary male adolescents with Down syndrome (16.3 ± 1.1 y) performed a 12-week training program, 3 sessions/week, consisting of warm up (15 min) followed by a main part [20 to 35 min (increasing 5 min each 3 wk)] at a work intensity of 60% to 75% of peak heart rate (HRmax = 194.5–[0.56 age]) and by a cool-down period (10 min). Written informed consent was obtained from all their parents.

Fasting blood samples were drawn from the vein in the antecubital fossa in a sitting position, 72-hour before the beginning of the program and after its ending. Lysed erythrocytes were prepared by putting cells through 3 freeze-thaw cycles in dry ice and by the addition of 5 volumes of ice-cold distilled water. After centrifugation, supernatant was frozen at −20°C until enzyme activity determination.

The activity of GPX (E.C. 1.11.1.9), was determined in the supernatant of erythrocyte hemolysates. The conversion of NADPH to NADP was evaluated using UV absorbance at 340 nm.[3] In this respect, it should be mentioned that enzyme activities were related to cell hemoglobin content and expressed as U/g hemoglobin.

Results were expressed as mean ± SD and 95% confidence intervals. The statistical analysis of data was performed using Student *t* test for paired data. The significance of the changes observed was ascertained at $P < 0.05$.

RESULTS

GPX activity in male adolescents with Down syndrome was 24.8 ± 3.1 [23.1 to 26.5] U/g hemoglobin. After a 12-week training program, GPX activity was 29.3 ± 2.9 [28.1to 30.5] U/g hemoglobin. Consequently, it

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was increased significantly (24.8 ± 3.1 vs. 29.3 ± 2.9; $P = 0.011$).

DISCUSSION

It is generally accepted that antioxidant enzyme superoxide dismutase (SOD) catalyzes the dismutation of superoxide anion (O_2^-) to H_2O_2 and then, in a second step, glutathione peroxidase (GPX) and catalase (CAT) convert hydrogen peroxide (H_2O_2) to water. Consequently, the activity of the first-step (SOD) and second-step (GPX, CAT) antioxidant enzymes, expressed as the quotient SOD/GPX + CAT, must be balanced to prevent cell damage by oxidative stress.[4]

The gene for SOD lies in humans on chromosome 21 and consequently it is conceivable that its activity is increased, whereas the above-mentioned quotient got disbalanced in individuals with Down syndrome. A pathogenesis termed "SOD-catalyzed hydroxyl radical formation" is proposed by Kowald et al[5] to explain this and states the excess of un-neutralized hydrogen peroxide is converted to the highly damaging hydroxyl radical that may finally lead to increase oxidative damage in this population.

As was hypothesized regular exercise increased significantly erythrocyte GPX activity in adolescents with Down syndrome. It should be pointed out that the influence of exercise on antioxidant enzyme activity in individuals with Down syndrome has received little attention in the literature. In this respect, Monteiro et al[6] reported a 16-week program increased SOD activity in 16 young male adults with Down syndrome. However, we have recently found regular physical activity did not increase significantly SOD activity.[7]

In any case, it has been recently published that regular exercise may enhance the blood antioxidant system in general and GPX activity in particular both in human[2] and experimental[8] research. On the contrary, acute exercise does not affect the activity of serum GPX in healthy young people.[9]

Another observation one can make when reviewing the literature is that the size of the present series (n = 31) was very similar to the highest number of participants with Down syndrome included in previous studies.[1,10]

It may be concluded regular exercise increased significantly GPX activity and consequently it may contribute to balance the quotient SOD/GPX + CAT in Down syndrome subjects. Further studies are required to assess the behavior of other antioxidant enzymes included in this quotient to highlight potential benefits of regular exercise in redox metabolism.

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REFERENCES

1. Pastore A, Tozzi G, Gaeta LM, et al. Glutathione metabolism and antioxidant enzymes in children with Down syndrome. *J Pediatr*. 2003;142:583–585.
2. Elosua R, Molina L, Fito M, et al. Response of oxidative stress biomarkers to a 16-week physical activity program, and to acute physical activity, in healthy young men and women. *Atherosclerosis*. 2003;167:327–334.
3. Flohe L, Gunzler WA. Assays of glutathione peroxidase. *Meth Enzymol*. 1984;105:114–121.
4. Crosti N, Bajer J, Gentile M, et al. Catalase and glutathione peroxidase activity in cells with trisomy 21. *Clin Genet*. 1989; 36:107–116.
5. Kowald A, Klipp E. Alternative pathways might mediate toxicity of high concentrations of superoxide dismutase. *Ann NY Acad Sci*. 2004;1069:370–374.
6. Monteiro CP, Varela A, Pinto M, et al. Effect of an aerobic training on magnesium, trace elements and antioxidant systems in a down syndrome population. *Magnesium Res*. 1997;10:65–71.
7. Ordonez FJ, Rosety-Rodriguez M, Rosety M. Regular exercise did not modify significantly superoxide dismutase activity in adolescents with down syndrome. *Br J Sports Med*. 2006. In press.
8. Oztasan N, Taysi S, Gumustekin K, et al. Endurance training attenuates exercise-induced oxidative stress in erythrocytes in rat. *Eur J Appl Physiol*. 2004;91:622–627.
9. Rush JW, Sandiford S. Plasma glutathione peroxidase in healthy young adults: influence of gender and physical activity. *Clin Biochem*. 2003;36:345–351.
10. Muchova J, Sustrova M, Garaiova I, et al. Influence of age on activities of antioxidant enzymes and lipid peroxidation products in erythrocytes and neutrophils of down syndrome patients. *Free Radic Biol Med*. 2001;31:499–508.