Relation between anabolic androgenic steroid administration, aerobic physical training and glycogen supercompensation

Tatiana S. Cunha[1], Ana Paula Tanno[1], Maria José C.S. Moura[2] and Fernanda Klein Marcondes[1]

ABSTRACT

Glycogen supercompensation is one of the adaptations induced by physical training. To potentiate this phenomenon, many athletes use supraphysiological doses of anabolic androgenic steroids (AAS). The purpose of this study was to evaluate the effects of nandrolone and aerobic physical exercise in rats, on body weight, plasmatic triglycerides levels, blood glucose and glycogen content. Male Wistar rats were randomly divided into 4 groups: Sedentary + vehicle (SV), Trained + vehicle (TV), Sedentary + AAS (SAAS) and Trained + AAS (TAAS) (n = 7-14/group). They received i.m. injections of nandrolone or vehicle for 9 weeks, and during the same period trained rats were submitted to aerobic exercise. Data were analyzed by two-way ANOVA and Tukey tests ($p < 0.05$). The groups SAAS, TV and TAAS presented lower body weight than the SV group (SAAS: 339 ± 10 = TV: 342 ± 14 = TAAS: 332 ± 6 < SV: 398 ± 9 g). Physical training significantly reduced plasmatic concentration of triglycerides [(TV: 46 ± 4 = TAAS: 44 ± 3) < (SV: 104 ± 1 = SAAS: 101 ± 6 mg/dL)] and of hepatic glycogen [(TV: 3,38 ± 0,57 = TAAS: 2,62 ± 0,34) < (SV: 4,95 ± 0,11 = SAAS: 4,43 ± 0,23 mg/100 mg)] and increased the cardiac glycogen concentration [(TV: 0,38 ± 0,04 = TAAS: 0,42 ± 0,03) > (SV: 0,2 ± 0,02 = SAAS: 0,21 ± 0,02 mg/100 mg)]. Blood glucose and soleus glycogen reserves remained unaltered. The use of supraphysiological doses of nandrolone did not potentiate any of the effects obtained in response to aerobic physical training.

Key words: Nandrolone. Aerobic exercise. Skeletal muscle.

INTRODUCTION

As physical exercise is a condition resulting in fast mobilization and distribution of energy substrates, it represents a serious challenge to the bioenergetic pathways of the active muscle[1]. Thus, the type of substrate and speed it is used at to produce adenosine triphosphate (ATP), depend on the intensity and duration of the physical exercise performed.

It is known that regular physical training induces a series of physiological adaptations that may lead to enhanced athletic performance[2]. One of the well known and studied adaptations is the glycogen supercompensation mechanism that increases the muscular and hepatic glycogen concentrations[3,4]. This prolongs muscular work during physical exercise, delays fatigue and consequently improves the athletic performance[3-5]. Although its mechanisms are not yet fully understood, this phenomenon is related to the activation of glycogen synthetase, the increase in synthesis and translocation of glucose transporters to the cell membrane surfaces, and to the increase in insulin secretion and muscular sensitivity to this hormone[3,6]. It should be pointed out that peak glycogen supercompensation occurs 24 hours after exercise, concomitantly with the increase in insulinemia and glucose uptake without, however, changing blood glucose levels[3].

To potentiate the physiological effects obtained in response to physical training, many athletes make use of ergogenic resources[4]. According to the International Olympic Committee statistics, from 2000, the anabolic androgenic steroids (AAS) are the most commonly used group of ergogenic substances in the doping process[7]. AAS are natural or synthetic testosterone-like compounds that act on one single type of receptor[8] to modulate both the anabolic and the androgenic effects in an undissociated manner[9]. The classical therapeutic indication of AAS is associated with hypogonadism, but they are also used to treat protein metabolism deficiency, because they stimulate protein synthesis[10]. Based on this action, AAS are widely used by athletes that practice physical activities, for the main purpose of increasing muscular mass[11]. However, this effect is still open to question in the scientific literature[12-14].

It has also been suggested that the enhanced athletic performance as a result of AAS use, could be related to the increase in energy reserves, mainly by diminishing glycogen phosphorylase enzyme activity and increasing glycogen synthetase I activity[5]. By inverse action, the castration of male rats results in decreased glycogen reserves, and hormone replacement with physiological doses of testosterone reverses this condition, by stimulating glycogenesis and inhibiting glycogenolysis[15].

Considering the frequent use of AAS in work-out gyms, the potential health risks and the existent controversies about its effects on enhanced athletic performance, the aim of the present study was to evaluate the effects of nandrolone and aerobic physical training in rats, on body weight, on plasmatic concentrations of triglycerides and blood glucose, and on muscular and hepatic glycogen reserves.

MATERIAL AND METHODS

Animals

Male Wistar rats, two months old, Specific Pathogen Free (SPF), provided by the Unicamp multidisciplinary biological investigation center ("Centro Multidisciplinar de Investigação Biologica da Unicamp – CEMIB") were used in this study. The animals were kept at the Piracicaba Dentistry School vivarium, housed in collective cages in a temperature-controlled room (22 ± 2°C) with 12 h/12 h light/dark cycle, and received filtered drinking water and commercial rodent chow ad libitium throughout the entire period. All the

1. Department of Physiological Sciences, Piracicaba Dentistry School, Campinas State University, Piracicaba, SP.
2. Laboratory of Physiology, Life Sciences Center, Pontifical Catholic University of Campinas, Campinas, SP.

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Correspondence to: Fernanda Klein Marcondes, Departamento de Ciências Fisiológicas, FOP/Unicamp. Av. Limeira, 901, Vila Areião – 13414-903 – Piracicaba, SP. Phone/Fax: +55-19-3412-5212. E-mail: fklein@fop.unicamp.br

procedures used were approved by the Committee for Ethics in Animal Research of the State University of Campinas (CEEA – Unicamp/protocol number 391-1), in accordance with the rules of the Brazilian College of Animal Experimentation (COBEA).

Treatment

The animals were randomly divided into four experimental groups (n = 7-14/group): sedentary + vehicle-treated (SV); Trained + vehicle-treated (TV); Sedentary + AAS-treated (SAAS); and Trained AAS-treated (TAAS). The animals in the vehicle and AAS groups received intramuscular injections of vehicle (propyleneglycol – 0,2 mL) or nandrolone decanoate (Deca Durabolin®, Organon – 5 mg/kg body wt) respectively, twice a week, between 7:30 a.m. and 8 a.m. In spite of the difficulty of establishing equivalence between the therapeutic dose and the one used in workout gyms, mainly considering the illegal preparations used by athletes, it is estimated that the abusive doses range from 10 to 100 times higher than the therapeutic dose[16]. In the present study, the AAS dose used was approximately 65 times higher than the indicated therapeutic one[17].

Physical training

The animals from trained groups were collectively submitted to swimming sessions in a glass tank (100 x 50 x 50 cm), containing water to a depth of 38 cm at 30ºC[18]. The training program consisted of daily swimming sessions, five days a week[19], between 2 p.m. and 4 p.m., totaling 42 sessions, as shown in table 1.

TABLE 1
Swimming physical training protocol

Training week	Duration of sessions (min)
1	10, 20, 30, 40, 50
2	50, 50, 60, 60, 60
3	60, 60, 70, 70, 70
4	70, 70, 70, 70, 70
5	70, 70, 70, 70, 70
6	70, 70, 90, 90, 90
7	90, 90, 90, 90, 90
8	90, 90, 120, 120, 120
9	120, 120

Material collection and biochemical analyses

At the end of the nine week training period, the animals were kept at rest for 14 hours after the last exercise session. As the technique used for determining muscle and hepatic glycogen concentrations[20,21] recommends that the animals should have free access to food in the period preceding dosages, they were not kept fasting until they were sacrificed. The trained or sedentary animals were anesthetized by halothane inhalation[22]. Median laparotomy and puncture of the left renal vein was performed to collect blood[23] tubes under vacuum, containing EDTA (B&D® No. 367653), for obtaining plasma afterwards. The animal was kept anesthetized and a longitudinal incision was made at sternal level. The thoracic cavity was opened, the diaphragm ruptured and the animal killed by respiratory arrest (pneumothorax). Liver, cardiac and soleus muscle samples were carefully collected and weighed to determine the glycogen concentration by the sulphuric phenol method[20,21]. The tissue glycogen concentrations are expressed in mg/100 mg tissue. The glucose and triglyceride plasmatic concentrations were determined by the enzymatic-colorimetric method, using commercially available kits (Laborlab, No. 02200 and No. 02700, respectively)[24]. Sample reading was done by optic spectrophotometer, with the appliance temperature kept at 25ºC and wave length of 505 nm. The plasmatic glucose and triglyceride concentrations are expressed in mg/dL.

Statistical analysis

Data were submitted to two-way Analysis of Variance, followed by the Tukey test for multiple comparisons of means. Values of p lower than 0.05 were indicative of statistical significance (GraphPad Prism 4.01®).

RESULTS

The results with reference to the analysis performed in sedentary rats or in those submitted to 42 swimming sessions, treated with vehicle of AAS are presented below. The data are presented as means ± standard error of mean (SEM).

Figure 1 present the data referring to the animal body weights. There were no statistical differences in the initial body weight among the four groups: sedentary vehicle (288 ± 7 g), sedentary AAS (266 ± 8 g), trained vehicle (271 ± 11 g) and trained AAS (278 ± 7 g); ($p > 0.05$). At the end of the experimental period, the animals from the four experimental groups presented with a mean body weight significantly higher than that of the first week ($p < 0.05$). In the ninth week, the body weight of the sedentary AAS animals (339 ± 10 g), trained vehicle (342 ± 14 g) and trained AAS (332 ± 6 g) was significantly lower than that of the sedentary animals treated with vehicle (398 ± 9 g; $p < 0.05$). There was no significant difference in body weight among sedentary and trained animals treated with AAS.

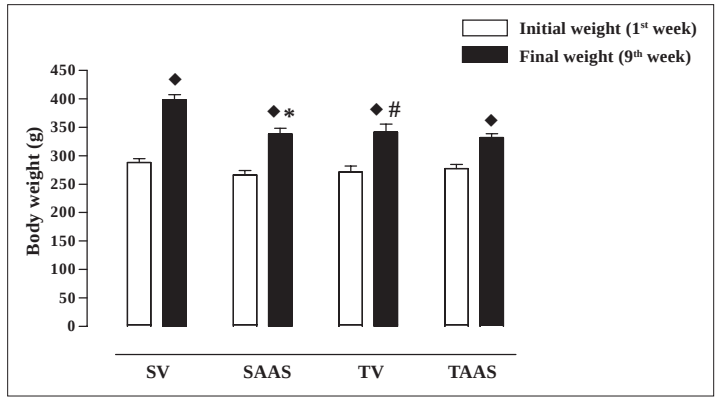

Fig. 1 *– Body weight evolution (g) of sedentary rats or rats submitted to swimming physical training, treated with vehicle or AAS for nine weeks. ♦ Significant difference in relation to the first week, in the same group. * Statistically different from the respective group treated with vehicle, in the first week. # Statistically different from the respective sedentary group, in the same week (p < 0.05) (n = 9-14) (SV – sedentary + vehicle; SAAS – Sedentary + AAS; TV – trained + vehicle; TAAS – trained + AAS).*

Physical training significantly diminished the plasmatic concentrations of triglycerides in animals treated with vehicle (46 ± 4 mg/dL vs. 104 ± 1 mg/dL) and in rats treated with AAS (44 ± 3 mg/dL vs. 101 ± 6 mg/dL; $p < 0.05$; figure 2A). Treatment with AAS did not alter the triglyceride concentrations in relation to treatment with vehicle ($p > 0.05$).

No statistical differences were observed in the blood glucose at rest, among the different experimental groups: sedentary vehicle (133 ± 5 mg/dL), sedentary AAS (128 ± 5 mg/dL), trained vehicle (131 ± 7 mg/dL) and trained AAS (139 ± 4 mg/dL) (figure 2B).

The trained group treated with vehicle presented significantly lower hepatic glycogen concentration (3.38 ± 0.57 mg/100 mg) than the respective sedentary group treated with vehicle (4.95 ± 0.11 mg/100 mg; $p < 0.05$; figure 3A). Trained rats treated with AAS also presented diminished hepatic glycogen concentration (2.62 ± 0.34 mg/100 mg) in relation to sedentary animals treated with AAS (4.43 ± 0.23 mg/100 mg; $p < 0.05$). There was no difference between treatment with AAS and vehicle in sedentary or trained animals ($p > 0.05$).

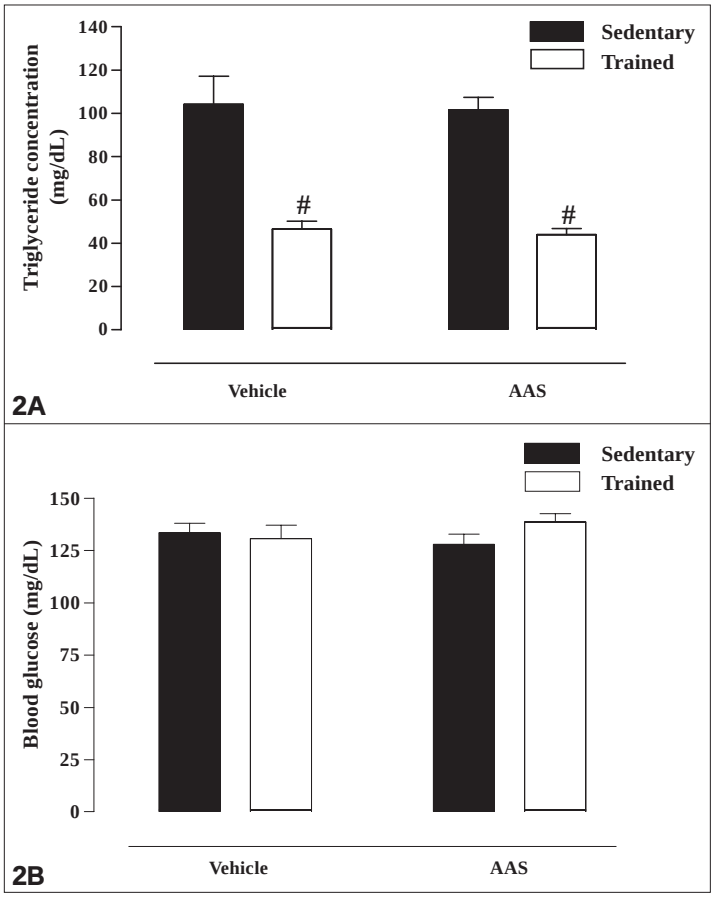

Fig. 2 – *Plasmatic concentration (mg/dL) of triglycerides* ***(2A)*** *and glucose* ***(2B)*** *in rats treated with AAS or vehicle, sedentary or submitted to swimming physical training for nine weeks. # Statistically different from the respective sedentary group (p < 0.05) (n = 7-14).*

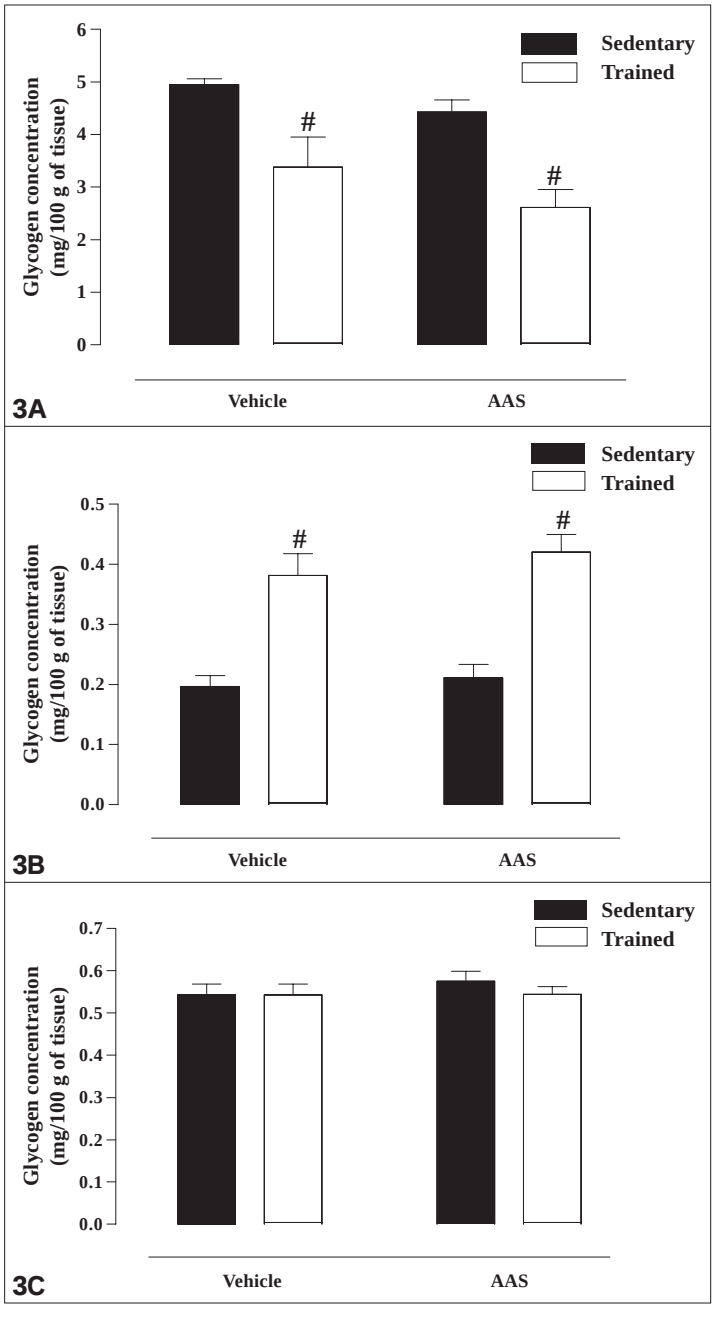

Fig. 3 – *Tissue glycogen concentration (mg/100 mg tissue) in liver* ***(3A)****, heart* ***(3B)*** *and soleus muscle* ***(3C)*** *of rats treated with AAS or vehicle, sedentary or submitted to swimming physical training for nine weeks. # Statistically different from the respective sedentary group (p < 0.05) (n = 7-13).*

The trained group treated with vehicle, presented significantly higher cardiac glycogen concentration (0.38 ± 0.04 mg/100 mg) than the respective sedentary group treated with vehicle (0.2 ± 0.02 mg/100 mg; p < 0.05; figure 3B). Trained rats treated with AAS also presented increased cardiac glycogen concentration (0.42 ± 0.03 mg/100 mg) in relation to the sedentary animals treated with AAS (0.21 ± 0.02 mg/100 mg; p < 0.05). When compared to treatment with vehicle, AAS did not have a significant effect on the cardiac glycogen concentration (p > 0.05).

Figure 3C presents data with reference to the soleus muscle glycogen concentration of the four experimental groups analyzed. No statistical differences were observed in the glycogen concentration in this muscle among the groups: sedentary vehicle (0.54 ± 0.03 mg/100 mg), trained vehicle (0.54 ± 0.03 mg/100 mg), sedentary AAS (0.57 ± 0.02 mg/100 mg) and trained AAS (0.54 ± 0.02 mg/100 mg; p > 0.05).

DISCUSSION

It is known that regular physical exercise can lead to changes in body composition, by increasing muscular mass and reducing body fat. When analyzing the results obtained with regard to body weight, it is observed that at the end of the experimental period, aerobically trained vehicle-treated animals presented lower weight gain than the respective sedentary group. During aerobic exercises, the glycogen reserves are used in the first minutes of activity and as the exercise proceeds, there is a reduction in glycogen use with concomitant increase in the use of fats[25]. Thus, it is believed that the physical training protocol led to increased aerobic metabolism in the trained vehicle-treated animals, reducing their body weight gain.

With regard to the influence of AAS on body weight, the data in the literature are still controversial. The result obtained in this study show that AAS treatment had a significant negative effect on body weight gain only in the sedentary group. It is believed that this difference was not observed among trained animals because the physical training itself promoted the adaptations necessary for their body weigh reduction, and AAS had no additional effect on it. Although AAS stimulated protein synthesis and increased water retention, which could lead to body weight gain, it is known that in excessive concentrations it may inhibit growth and body weight gain[26]. These effects result from appetite inhibition, hydro-electrolytic imbalance and increased lipid oxidation, due to greater carnitine palmitoyltransferase enzyme activity[27].

Several studies have demonstrated that physical exercise reduces the levels of cholesterol, triglycerides and LDL-cholesterol, and also increases HDL-cholesterol serum concentration[28]. In the present study, a significant reduction in plasmatic triglyceride con-

centration was observed in the animals submitted to aerobic physical training. In the lipid oxidation processes that occur during aerobic exercises lasting for over 30 minutes, the intramuscular free fatty acids and triglycerides are used as energy sources[25] and the lipids from the circulation are the main substrates used during the post-exercise recovery processes, which justify the reduced plasmatic triglyceride concentrations observed in the trained animals.

The use of excessive doses of AAS also promotes alterations in lipid metabolism. However, it was found that these alterations are related to the circulating lipoprotein concentrations, and have no direct influence on the plasmatic triglycerides concentrations. Thus, the results obtained in the present study are in accordance with the literature, since the use of AAS did not have any influence on the plasmatic triglyceride concentrations.

Considering that under physical exercise conditions, fast mobilization and redistribution of substrates for muscular activity performance occur, so that innumerable alterations and hormonal secretions and metabolism become necessary to maintain homeostasis[29]. Human[30] and animal[31] studies have shown that exercise is a potent stimulator of glucose uptake by the skeletal muscle.

Since no statistical differences in blood glucose at rest were observed among the different experimental groups at the end of the nine-week training period, it would suggest that the rate of tissue glucose uptake and insulin secretion by the pancreas of the animals, 14 hours after the last training session, could have been similar. Studies show that in the first 48 post-exercise hours, there is a progressive increase in insulinemia, the factor responsible for the increase in glucose uptake without any alteration in blood glucose[3].

Ramamani *et al.*[15] studying the effect of testosterone on glucose metabolism, observed that the absence of male sex hormones, induced by castration, increases the blood glucose without altering the circulating insulin concentration. With hormone replacement therapy (testosterone), blood glucose returns to its normal values, and the plasmatic concentration of insulin remains unchanged. Thus, it is believed that AAS may play an independent, but similar role to that of insulin in the mechanism of glucose uptake by the skeletal muscles.

It is known that hepatic tissue plays an important role in blood glucose control, particularly during physical exercise. This takes place by means of hepatic glycogenolysis and by neoglycogenesis processes at more advanced stages the physical exercise. According to results of this study, it was observed that physical exercise would appear to have induced effective hepatic glycogen mobilization, since trained animals presented lower concentration of this substrate after exercise, when compared to sedentary animals treated with vehicle or AAS. It is important to remember that the animals were sacrificed 14 hours after the last swimming session, and because this is the recovery period, the tissue hepatic glycogen concentrations probably were not fully reestablished. It is worth emphasizing that AAS administration did not have any significant effect with regard to this parameter.

It was demonstrated that the aerobic physical exercise promotes various adaptations to the heart tissue, related to its morphology, function and energy metabolism, increasing the glucose uptake as well as its glycogen reserves[32]. Such adaptations enable the development and maintenance of the cardiac muscle work during physical exercise, thus contributing to the delay in the onset of fatigue.

During physical exercise, the selection of the energy substrate to be used by the heart muscle is a result of the combination of several factors like, for instance the competition among energy substrates (fatty acids, lactate and glucose), the concentration and type of energy reserves present in the organism of each individual, the intensity and duration of the physical exercise performed and hence the hormonal adjustments set off as response. It is known that the high blood concentrations of fatty acids and lactate diminish cardiac glycogen oxidation, thus saving the use of this substrate[33]. As the trained animals treated with AAS or vehicle presented a lower triglyceride blood concentration, probably as a result of the degradation of this substrate used during exercise, it is believed that the blood concentration of fatty acids probably increased. If this hypothesis is true, the use of the heart glycogen may have been saved, leading to the development of the supercompensation mechanism of this substrate in the heart muscle. It is worth emphasizing that since the dosage of the plasmatic fatty acids was not performed, this is only a supposition and the data associated with cardiac metabolism must be cautiously interpreted.

Thus, as in the hepatic tissue and in the heart muscle, exercise also promotes alterations in the glycogen concentrations of the skeletal muscle. The glucose uptake of the skeletal muscular is mainly performed by two different types of transporters called as GLUT 1 and GLUT 4[34]. Physical training promotes a rise in the intrinsic activity and in the GLUT 4 translocation, and a rise in GLUT 4 RNAm cytosolic concentration, as well as an increase in the activity of enzymes connected with glucose metabolism[35]. Thus, individuals who do regular physical activity exhibit higher glycogen concentrations when compared to sedentary individuals[13]. According to Price *et al.*[36] glycogen re-synthesis after physical exercises occurs in two phases. The first phase is fast, insulin-independent and is developed during the first 45-60 minutes of the recovery phase. The second is slower, insulin-dependent and continues to develop until the glycogen reserves are fully re-established, which generally occurs 24 hours after exercises end. According to Nakatani *et al.*[3], the glycogen supercompensation mechanism peak in the skeletal muscles of rats is reached 24 hours after doing physical exercise, although the acute effect of exercise on muscle sensitivity to insulin expires within the first 18 hours[14].

It has been demonstrated that the development of the glycogen supercompensation mechanism is directly related to the increase in the exercise-induced glucorticoids and free fatty acids concentration, so that the higher the concentration of these substances in the blood stream is, the lower the stimulus for glycogenolysis will be. In this study, no significant differences in as regards glycogen concentration in the soleus muscle after the application of the experimental protocol were found, probably because the animals were sacrificed 14 hours after the last exercise session, in other words, while the glycogen reserves were still being recovered. Moreover, it should be emphasized that the soleus muscle fibers specificity may also have contributed to this result, as this muscle is predominantly oxidative (type I fibers), it presents low glycolytic enzyme content and hence lower capacity to synthesize this substrate. Although there is data in the literature reporting increase in glycogen synthetase I activity and glycogen reserves in the soleus muscle of rats treated with AAS[5], the nandrolone administration regimen used in the present study did not promote alterations on this parameter either.

Based on the results presented, the response of the skeletal muscle, heart muscle and hepatic tissue related to glycogen metabolism and storage is found to be different. These results are in agreement with those described by Poland *et al.*[37] who demonstrated that after intraperitoneal administration of dexamethasone, in an attempt to mimic part of the adaptations that occur during physical training, the glycogen supercompensation peak in the cardiac muscle occurs within 6 hours, while in the soleus muscle and hepatic tissue, it generally only occurs 17 hours after the glucocorticoid administration.

Thus, it may be concluded that regular aerobic physical exercises for nine weeks attenuated the animals' body weight gain. Furthermore, aerobic physical training promoted reduction in the plasmatic triglyceride concentrations and the glycogen supercompensation mechanism was observed only in the cardiac tissue. Except for the attenuating effect on the body weight gain,

the use of supraphysiological doses of AAS in the regimen established, did not promote any additional alterations of the parameters analyzed, beyond those obtained as response to the physical training. The use of such substances is not free of innumerable side effects, and in human beings, the risks increase as a function of the combined use of different anabolic agents and the daily stress everyone is submitted to. The negative effects of the interaction between these two factors may be evidenced by the higher mortality rate (approximately five times higher) among AAS users when compared to non-users[38]. Taking into consideration the absence of additional effects on the parameters evaluated, as result of the use of supraphysiological doses of AAS and the health risks originated from this practice, the need for publishing this information is reinforced, with the objective of inhibiting the indiscriminate use of these substances and to encourage further systematic studies to be developed on the subject.

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REFERENCES

1. Powers SK, Howley ET. Bioenergética. In: Powers SK, Howley ET, editores. Fisiologia do exercício – Teoria e aplicação ao condicionamento e ao desempenho. São Paulo: Manole, 2000;21-44.
2. Wahren J. Glucose turnover during exercise in healthy man and in patients with diabetes mellitus. Diabetes 1979;28:82-8.
3. Nakatani A, Han D, Hansen PA, Nolte LA, Host HH, Hickner RC, et al. Effect of endurance exercise training on muscle glycogen supercompensation in rats. J Appl Physiol 1997;82:711-5.
4. Foss ML, Keteyian SJ. Medicamentos e recursos ergogênicos. In: Foss ML, Keteyian SJ, editores. Bases fisiológicas do exercício e do esporte. Rio de Janeiro: Guanabara Koogan, 2000;445-62.
5. Van Breda E, Keizer HA, Geurten P, Van Kranenburg G, Menheere PP, Kuipers H, et al. Modulation of glycogen metabolism of rat skeletal muscles by endurance training and testosterone treatment. Pflugers Arch 1993;424:294-300.
6. Cartee GD, Young DA, Sleeper MD, Zierath J, Wallberg-Henriksson H, Holloszy JO. Prolonged increase in insulin-stimulated glucose transport in muscle after exercise. Am J Physiol 1989;256:494-9.
7. Parssinen M, Seppala T. Steroid use and long-term health risks in former athletes. Sports Med 2002;32:83-94.
8. Clarkson PM, Thompson HS. Drugs and sport. Sports Med 1997;24:366-81.
9. Rabkin JG, Wagner GJ, Rabkin R. A double-blind, placebo-controlled trial of testosterone therapy for HIV-positive men with hypogonadal symptoms. Arch Gen Pscychiatry 2000;57:141-7.
10. Kuipers H, Wijnen JA, Hartgens F, Willems SM. Influence of anabolic steroids on body composition, blood pressure, lipid profile and liver functions in body builders. Int J Sports Med 1991;12:413-8.
11. Franke WW, Berendonk B. Hormonal doping and androgenization of athletes: a secret program of the German Democratic Republic government. Clin Chem 1997;43:1262-79.
12. Cunha TS, Cunha NS, Moura MJCS, Marcondes FK. Esteróides anabólicos e a prática desportiva. Braz J Pharmac Sci 2004;40:165-79.
13. Greiwe JS, Hickner RC, Hansen PA, Racette SB, Chen MM, Holloszy JO. Effects of endurance exercise training on muscle glycogen accumulation in humans. J Appl Physiol 1999;87:222-6.
14. Kawanaka K, Nolte LA, Han DH, Hansen PA, Holloszy JO. Mechanisms underlying impaired GLUT-4 translocation in glycogen-supercompensated muscles of exercised rats. Am J Physiol Endocrinol Metab 2000;279:E1311-8.
15. Ramamani A, Aruldhas MM, Govindarajulu P. Differential response of rat skeletal muscle glycogen metabolism to testosterone and estradiol. Can J Physiol Pharmacol 1999;77:300-4.
16. Pope HG Jr, Katz DL. Affective and psychotic symptoms associated with anabolic steroid use. Am J Psychiatry 1988;145:487-90.
17. Norton GR, Trifunovic B, Woodiwiss AJ. Attenuated beta-adrenoceptor-mediated cardiac contractile responses following androgenic steroid administration to sedentary rats. Eur J Appl Physiol 2000;81:310-6.
18. Marcondes FK, Vanderlei LCM, Lanza LLB, Spadari-Bratfisch RC. Stress-induced subsensitivity to catecholamines depends on the estrous cycle. Can J Physiol Pharmacol 1996;74:663-9.
19. Ostman-Smith I. Adaptative changes in the sympathetic nervous system and some effector organs of the rat following long term exercise or cold acclimation and the role of cardiac sympathetic nerves in the genesis of compensatory cardiac hypertrophy. Acta Physiol Scand 1979;477:1-118.
20. Dubois M, Gilles KA, Hamilton JK, Rebers PA, Smith F. Colorimetric method for determination of sugars and related substances. Anal Chem 1956;28:350-6.
21. Lo S, Russel JC, Taylor AW. Determination of glycogen in small tissue samples. J Appl Physiol 1970;28: 234-6.
22. Tanno AP, Bianchi FJ, Moura MJCS, Marcondes FK. Atrial supersensitivity to noradrenaline in stressed female rats. Life Sci 2002;71:2973-81.
23. Spadari RC, De Moraes S. Repeated swimming stress and responsiveness of isolated rat pacemaker to chronotropic effect of noradrenaline and isoprenaline: role of adrenal corticosteroids. Gen Pharmacol 1988;19:553-7.
24. Silva CA, Polacow ML, Guirro R, Tanno AP, Silva HC, Paro D, et al. Tratamento com metformina induz elevação no conteúdo de glicogênio no fígado, nos músculos e nas ilhotas de Langerhans. PUC-SP Ciências Biológicas e do Ambiente. 1999;1:53-71.
25. Coyle EF. Metabolismo lipídico durante o exercício. Sports Science Exchange 1997;15:20-6.
26. Carson JA, Lee WJ, Mcclung J, Hand GA. Steroid receptor concentration in aged rat hindlimb muscle: effect of anabolic steroid administration. J Appl Physiol 2002;93:242-50.
27. Guzman M, Saborido A, Castro J, Molano F, Megias A. Treatment with anabolic steroids increases the activity of the mitochondrial outer carnitin palmitoyltransferase in rat liver and fast-twitch muscle. Biochem Pharm 1991;41:833-5.
28. Ferguson MA, Alderson NL, Trost SG, Essig DA, Burke JR, Durstine JL. Effects of four different single exercise sessions on lipids, lipoproteins, and lipoprotein lipase. J Appl Physiol 1998;85:1169-74.
29. Marliss EB, Kreisman SH, Manzon A, Halter JB, Vranic M, Nessim S. Gender differences in glucoregulatory responses to intense exercise. J Appl Physiol 2000; 88:457-66.
30. Wahren J, Felig P, Hendler R, Ahlborg G. Glucose and amino acid metabolism during recovery after exercise. J Appl Physiol 1973;34:838-45.
31. Baldwin KM, Winder WW, Terjung RL, Holloszy JO. Glycolytic enzymes in different types of skeletal muscle: adaptation to exercise. Am J Physiol 1973;225: 962-6.
32. Kinney LaPier TL, Rodnick KJ. Effects of aerobic exercise on energy metabolism in the hypertensive rat heart. Phys Ther 2001;81:1006-17.
33. Goodwin GW, Taegtmeyer H. Improved energy homeostasis of the heart in the metabolic state of exercise. Am J Physiol Heart Circ Physiol 2000;279:H1490-501.
34. Silva CA, Polacow MLO, Guirro R, Tanno AP, Silva HC, Rodrigues D. O efeito do fenobarbital sobre as reservas de glicogênio no músculo sóleo desnervado em ratos. Revista Brasileira de Fisioterapia 1998;3:35-40.
35. Ploug T, van Deurs B, Ai H, Cushman SW, Ralston E. Analysis of GLUT 4 distribution in whole skeletal muscle fibers: identification of distinct storage compartments that are recruited by insulin and muscle contractions. J Cell Biol 1998; 142:1429-46.
36. Price TB, Laurent D, Petersen KF, Rothman DL, Shulman GI. Glycogen loading alters muscle glycogen resynthesis after exercise. J Appl Physiol 2000;88:698-704.
37. Poland JL, Poland JW, Honey RN. Differential response of rat cardiac and skeletal muscle glycogen to glucocorticoids. Can J Physiol Pharmacol 1982;60:634-7.
38. Parssinen M, Kujala U, Vartiainen E, Sarna S, Seppala T. Increased premature mortality of competitive powerlifters suspected to have used anabolic agents. Int J Sports Med 2000;21:225-7.