Current aspects about oxidative stress, physical exercise and supplementation*

Vinicius Fernandes Cruzat, Marcelo Macedo Rogero, Maria Carolina Borges and Julio Tirapegui

ABSTRACT

Oxygen reactive species (ORE) are usually produced by the body metabolism. However, ORE present the ability to remove electrons from other cellular composites, being able to cause oxidative injuries in several molecules. Such fact leads to a total loss of cellular function. Physical exercise practice increases ORE synthesis, besides promoting muscular injury and inflammation. After a physical exercise set, the recovery phase begins, where several effects positive to health are observed, including increase in resistance to new injuries induced or not by exercise, a fact which is considered an 'adaptation' process. Many studies though, have reported that this recovery is not reached by individuals who are submitted to intense and extended exercises, or even, who have high training frequency. Nutritional alternatives have been widely studied, in order to reduce the effects promoted by extenuating exercise, among which vitamin E, vitamin C, creatine and glutamine supplementation is included. This review has the aim to approach the current aspects concerning the ORE formation, the cellular injury and inflammation processes, the adaptation to the kinds of aerobic and anaerobic exercise, besides possible nutritional interventions.

Keywords: Oxygen reactive species. Adaptation. Vitamins. Creatine. Glutamine.

INTRODUCTION

Regular practice of physical activities associated with a balanced diet may be an important factor in health promotion. However, frequent performance of high intensity or exhaustive physical exercises may increase susceptibility to injuries, promote chronic fatigue and overtraining, partially due to the high synthesis of oxygen reactive species (ORS). Experimental evidence mentions that these composites may be involved with the development of many physiopathological processes such as aging, cancer, inflammatory diseases and atherosclerosis.

On the other hand, the ORS may also have effects considered positive over the immune system and play essential metabolic functions for the cellular homeostasis. The formation mechanisms of the ORS in the muscular injury and inflammation are some of the aspects approached in this review. Moreover, several nutritional alternatives have appeared in the trial to decrease oxidative stress and improve athletic performance. Within this context, this paper also presents some aspects of vitamin E and vitamin C, creatine and glutamine supplementation, with the purpose to contribute with updated information on comprehension of this process.

MUSCULAR INJURY INDUCED BY EXERCISE

Skeletal muscle injury caused by physical exercise may vary from a muscular fiber ultrastructural injury to trauma involving complete muscle rupture. Post-injury pain induced by exercise frequently has its peak between 24 to 48 post-exercise hours. Muscular injury induced by performance of an eccentric exercises bout may be derived from connective tissues rupture ligated to adjacent myofibrils from the muscular cell itself, from the basal laminate adjacent to the plasmatic membrane, the plasmatic membrane of the muscular cell, the sarcomere, the plasmatic reticule, or even of a combination of these components[1-4].

Muscular fibers injuries are usually evaluated by the determination of the reflux of cytosolic enzymes specific for blood circulation, combined with histological techniques or ultrastructural evaluation through electronic microscopy in order to evaluate the local effects. The morphological and ultrastructural characteristics of the injury induced by exercise are well reported in animal and human models. Injuries of small areas of muscular fibers may be observed immediately after exercise. The injury usually becomes more extensive during the next 48-72 post-exercise hours. The histological observation of the injured muscle may be characterized by the myofibrillar rupture, irregular structures of the Z lines, sarcolemma rupture, irregular location of organelles, increase of the mitochondrial density and the myofibrillar proteins and cytoskeleton content[3-4].

The increase of cytosolic proteins in the circulation after exercise reflects the muscular injury. The evaluated proteins are usually the creatine kinase (CK), lactate dehydrogenase (LDH), aspartate aminotransferase and the myoglobin, which are not normally able to trespass the plasmatic membrane. The plasma concentration of the 3-methylhistidine amino acid also increases with the muscular injury. The presence of these proteins and amino acids in the blood circulation reflects a significant alteration in the structure and permeability of the myofibrillar membrane. The determination of the CK seric activity has been widely used in studies evaluating muscular injury induced by exercise. The CK post-exercise muscular reflux peak is dependent on the type of exercise performed. Although a detectable increase in the activity immediately after exercise may occur, the peak of this enzyme is usually reached between 24 and 72 post-exercise hours[4-5]. Tiidus and Ianuzzo[6] showed that both exercise intensity and duration independently affect the enzymatic seric activity and the muscular pain; however, intensity is the variable with the highest effect.

MUSCULAR INFLAMMATION INDUCED BY EXERCISE

Eccentric exercises performed by individuals with no exercise habit may cause muscular injuries which are characterized by late muscular pain, muscular fibers rupture, release of muscular proteins within the plasma, acute phase immune response and decrease of physical performance. The consumption of adenosine triphosphate (ATP), the alteration in the calcium homeostasis and the ORS production have been shown in the injury and muscular necrosis etiology[1-5] (figure 1).

After eccentric exercise, there are alterations in the population of circulating inflammatory cells. Initially, neutrophils and later

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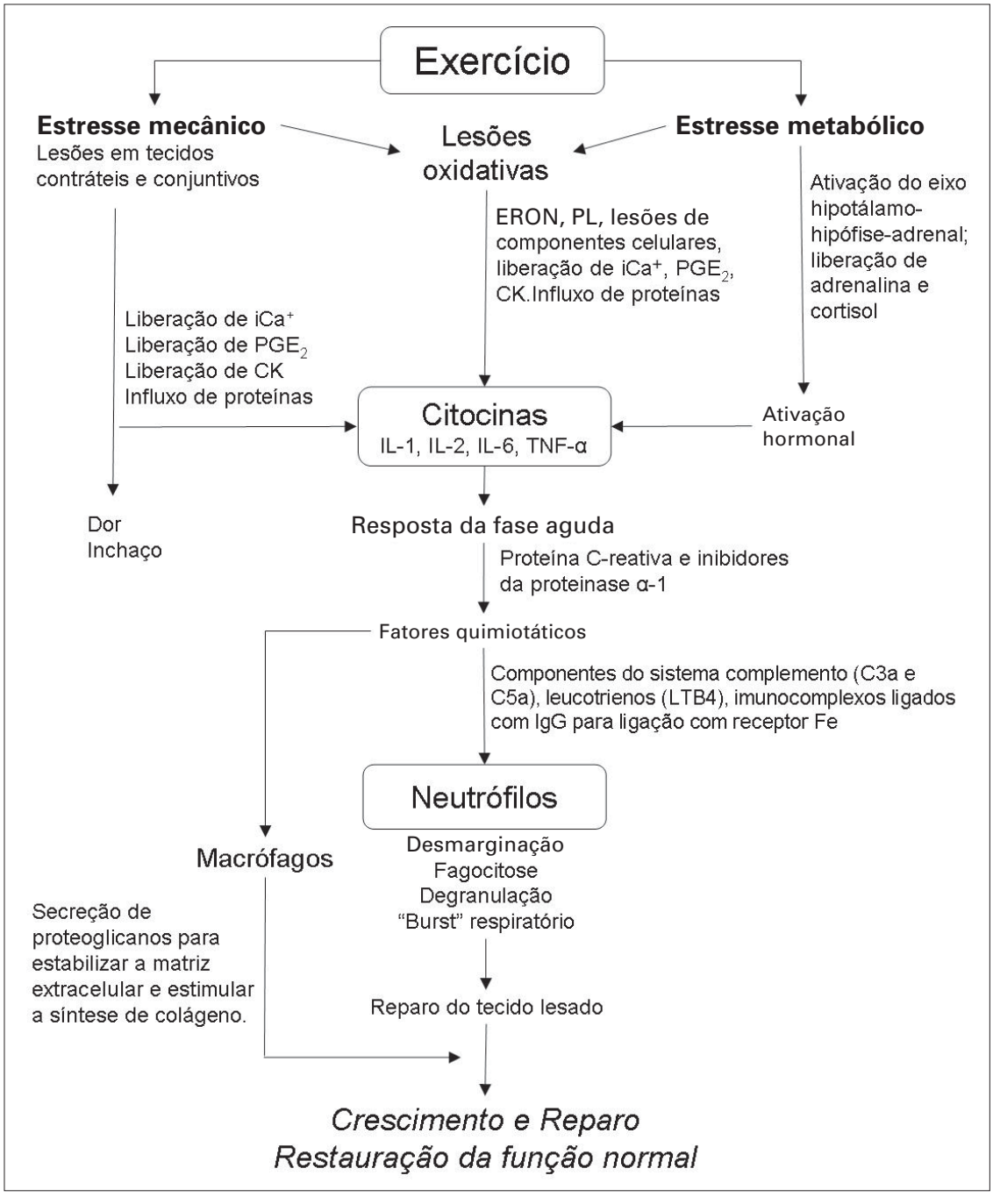

Figure 1 *– Theory of the Physiological processes promoted by physical exercise.*
Abbreviators: ONRS = Oxygen and Nitrogen Reactive Species; LP = Lipid Peroxidation; iCa^+ = intracellular calcium, PGE_2 = Prostaglandine E_2, CK = Creatine kinase, TNF-α = Necrosis tumoral factor-α, IL-1 = Interleukin-1, IL-2 = Interleukin-2, IL-6 = Interleukin-6, C3a = Protein C3a of the complement system; C5a = Protein C5a of the complement system; Fe = Iron; LTB4 = Leukotriene B4. Adapted from Pyne[9].

monocytes and lymphocytes are recruited for the inflammation site, where they produce ORS and proteolytic enzymes in order to clean and repair the injured tissue. The neutrophils infiltration is promoted by chemoetactic factors, including prostaglandins, tumoral necrosis factor (TNF)-α, interleukin (IL)-1β and IL-6. These two last cytokines are known to increase in response to exercise. The neutrophils fagocyte the injured muscular fiber through the activation of the nicotinamide adenine dinucleotide phosphate oxidase enzymatic system (NADPH) and the release of proteolytic enzymes from their intracellular granules. This response is not specific and therefore, may lead to injury of normal cells adjacent to the injured site[4,7].

Initially, there is synthesis of pro-inflammatory cytokines, TNF-α and IL-1β, which in return stimulate the IL-6 synthesis. This cytokine acts as primary mediator of the acute phase reaction, stimulating the hepatic production of acute phase proteins, such as the reactive protein C (RPC) and inhibitors of proteases (for instance, protease α-1 inhibitor). The IL-6 limits the inflammatory response extension since it increases the anti-inflammatory cytokines synthesis. The acute phase response reestablishes depleted or injured proteins and reverts the deletereal effects of the initial inflammatory response. From this view point, the IL-6 plays a more restoration than pro-inflammatory role. The IL-6 also stimulates the hypophysis gland to release the adrenocorticotrophic hormone (ACTH), which subsequently promotes the increase of the cortisol hormone release from the adrenal cortex[8-10].

The relationship between exercise, cytokines and the immune system is relevant for many different reasons. Firstly, the cytokines synthesis by immune system cells is one of the mechanisms through which the intrinsic and acquired immunities are activated or enlarged, a fact which increases the immune competence and

boosts the beneficial effects of exercise. Moreover, the exercise model may aid in the elucidation of the role the cytokines play as local regulators and circulating of the endocrine function in individuals submitted to exhaustive trainings.

ADAPTATION OF THE ANTIOXIDANT SYSTEM INDUCED BY PHYSICAL EXERCISE

Aerobic exercise

Different strategies have been used in studies with volunteers and normal or genetically modified animals over the last years in a trial to increase the antioxidant capacity of the individual, such as the supplementation with antioxidants, dietetic restrictions and medicine. None of these isolated alternatives have shown increase of the defense capacity of the body or reduction of the effects of the aerobic metabolism[11]. However, according to Finkel and Holbrook[12], the most efficient strategy in increasing the endogenous amount of antioxidants may be a greater induction of the oxidative stress itself, which would gradually stimulate the cellular antioxidant mechanisms and would increase the resistance to injuries induced by exercise[13-16]. It is worth mentioning that the greatest part of the effects induced by physical exercise (increase of muscular mass, improvement of the cardiovascular system, reduction of the incidence of diseases and infections and others) is mainly due to the adaptations induced over the several body systems, including the endogenous antioxidant system[14,16].

The frequency and intensity in which the physical exercise is performed alter the balance in which the physical exercise is performed as well as the balance between pro-oxidants and antioxidants[17]. Ji *et al.*[18] have demonstrated that acutely, the skeletal muscle submitted to an isolated load of exhaustive work produced an increase of the lipid peroxidation (LP) and stimulated the activity of several antioxidant enzymes such as glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase (CAT). According to the authors, the synthesis of these enzymes not only shows increase of oxidative stress, but also stimulates adaptations in the antioxidant defense mechanisms. Normally, these adaptations may start fast (~ 5 min) after each exercise performance, occurring the repairing of tissue injuries produced by the oxidative stress. Concomitantly, these adaptations influence in the body preparation for a new stress, increasing the activity of the cellular antioxidant system[19-20].

In the majority of the cases, it is verified that the greater the exercise intensity (≥ 70% of the maximal oxygen uptake [$\dot{V}O_{2máx}$]), the higher the ORS synthesis is[11,21]. Individuals who are submitted to intense and prolonged exercises or exhaustive training, or even, who have a very high training frequency may surpass the capacity of the endogenous antioxidant system and, consequently, promote severe muscular injuries, causing a local inflammatory process and oxidative stress. All these facts are involved in the reduction in performance, training volume and possibly overtraining[20,22-23].

The effects of the aerobic exercise are not limited to the activity of enzymatic antioxidants, since effects over the non-enzymatic antioxidants can also be observed. Some studies show that the glutathione (GSH), the main non-enzymatic cellular antioxidant, or the relationship between the GSH and its oxidized form (GSSG) may be reduced during physical exercise[18,24]. After intense and prolonged exercises, the plasma concentration of other non-enzymatic antioxidants such as vitamin E, vitamin C and uric acid tends to increase[28]. The vitamin E and vitamin C supplies seem to be mobilized in the trial to reduce the oxidative stress promoted by the ORS. The isolated increase in the uric acid concentration cannot be considered a specific response of the adaptation to the oxidative stress, since it is a final product of the purines cycle. The uric acid however, significantly contributes to the reduction of the oxidative stress. Generally speaking, the set of alterations in the non-enzymatic antioxidants may promote an increase in the total capacity of antioxidants, showing an adaptation to the physical training[25-26].

Anaerobic exercise

Among the exercises classified as anaerobic, we verify the explosion ones (sprint), the endurance ones (concentric and eccentric) and the Wingate tests. Although the protocols are fairly diversified and vary according to each sport, many studies demonstrate a significant increase of oxidative stress in exercises with supramaximal intensities[27-30].

The increase of the ORS synthesis in anaerobic exercises may occur in different ways, such as the activation of the electrons transportation chain, the increased synthesis of the xantine oxidase and NADPH oxidase enzymes, the prolonged ischemia process and tissue reperfusion and the phagocyte activity (figure 2)[11,27,31]. Additionally, the increase of the lactic acid synthesis, catecholamine and the increased inflammatory process after anaerobic exercises with supra-maximal intensities also significantly contribute to the ORS production[31].

In the ischemia and muscular reperfusion process an increase of the oxidative stress may occur during and after exercise, especially due to the purines catabolism[31]. More specifically, during the tissue ischemia, the ATP is degraded to adenosine diphosphate (ADP) and monophosphate (AMP), due to high demand of energy by the muscular tissue. Once the oxygen availability (O_2) during the schemic process is reduced, the AMP is continually degraded to hypoxanthine, which is converted in xantine and, later to uric acid by the xantine oxidase enzyme, together with the reduction of the O_2, producing superoxide radical ($\bullet O_2^-$) and hydrogen peroxide (H_2O_2)[32]. The moment the tissue is reperfunded, that is, during muscular relaxation, the

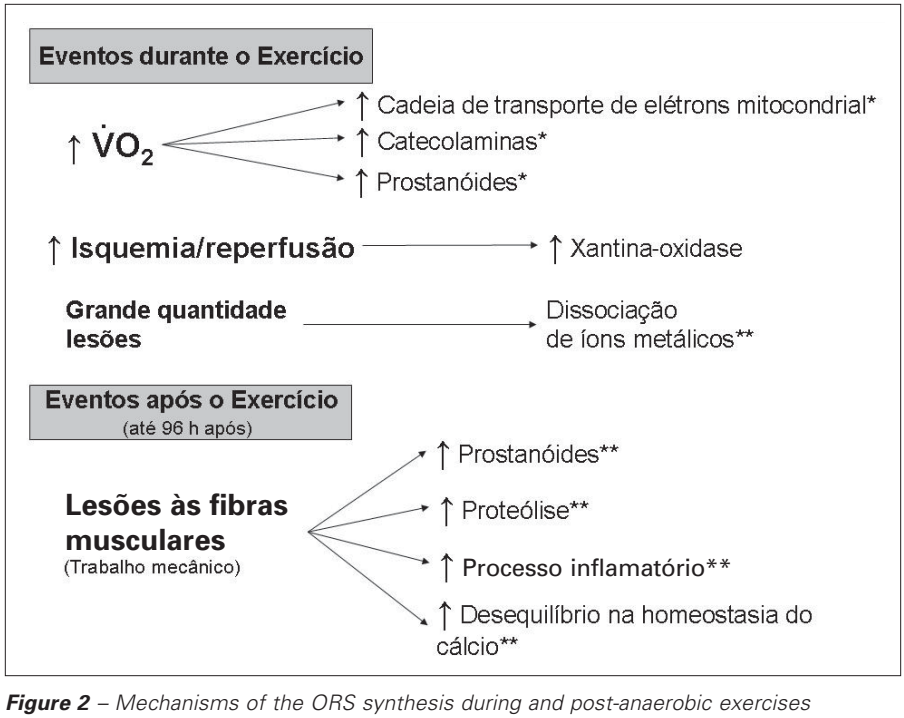

Figure 2 *– Mechanisms of the ORS synthesis during and post-anaerobic exercises*
$\dot{V}O_{2máx}$ = O_2 maximum volume. * ORS synthesis especially post explosion exercises. ** ORS synthesis especially post endurance exercises. Adapted from Bloomer, Goldfarb[31].

process of O_2 reduction becomes increased, also making hydroxyl radical ($\bullet OH^-$). The conversion of the xantine desidrogenase enzyme to its oxidized form, xantine oxidase has been proposed, through intracellular proteases activated by Ca^{2+}, it used the O_2, which accepts electrons and becomes steady. The role of the xantine oxidase enzyme in the ORS synthesis during exercises is not clear yet and further studies should be conducted[27].

Although acute sessions of anaerobic exercises increase the ORS synthesis, with consequent appearance of injuries, in a situation of chronic training favorable adaptations to the antioxidant system may occur[14,19]. Individuals trained in activities predominantly anaerobic present a reduced anaerobic stress and a lower number of injuries, when compared with non-trained individuals[27,29,31].

Hellsten *et al.*[28] have examined the effects of explosion training over the activity of some antioxidant enzymes, including the glutathione peroxidase (GPx), glutathione redutase (GR) and the superoxide dismutase (SOD). During six weeks, the individuals trained three times a week; in the seventh week however, the training was performed two times per day during the seven days (overload). An increase in the activity of the GPx and GR enzymes has been observed only at the end of overload week, showing that both the anaerobic exercise volume and intensity are determinant in the promotion of the adaptation of the antioxidant system. Probably, the increase of the oxidative stress imposed to the body during periods of high work volume promotes transitory increase of the activity of antioxidant enzymes [17]. Within this context, Atalay *et al.*[33] have observed in rats submitted to a six-week exercise protocol with supra-maximal intensity an increase in the muscular concentration of total GSH, GPx, glutathione-S transferase (GST) and GR. These results however, were obtained through a treadmill protocol with intensity equivalent to 200% of the $\dot{V}O_{2máx}$ of the animals, which makes the extrapolation difficult for humans.

Few investigations have studied the effects of anaerobic exercises over the activity of non-enzymatic antioxidants. In a study which used the Wingate test of 30 s at supra-maximal intensity, the individuals presented an increase in the non-enzymatic antioxidants concentration, including uric acid and vitamin C and a reduction in the concentration of vitamins A and E[30]. A reduction in the GSH concentration was observed, a fact which may be concerned with the regeneration of vitamins C and E. The repeated synthesis of ORS during the ischemia process and muscular reperfusion and inflammation, promoted by the anaerobic exercises practice, may result in the increase of the non-enzymatic antioxidants concentration, a mechanism characteristic of the training adaptation process. Nevertheless, further studies are needed in order to evaluate the effects of the anaerobic exercises over the non-enzymatic antioxidants[27,31].

SUPPLEMENTATION

Vitamin E

Supplementation with α-tocoferol is used by many athletes with the aim to improve physical performance. However, no study has demonstrated improvement in performance after supplementation in non-deficient individuals[34-35].

Due to α-tocoferol efficiency in reacting with peroxyl radicals, many studies have been conducted with the purpose to evaluate the effect of α-tocoferol supplementation in the LP, caused by oxidative stress induced by physical exercise. Goldfarb *et al.*[35] have observed smaller concentrations of lipidic hydroperoxides and thiobarbituric acid reactive substances (TBARS) in the plasma and in muscular fibers of rats submitted to intense exercise and supplemented for five weeks with α-tocoferol (250 UI α-tocoferol/kg of diet). Metin *et al.*[36] also verified reduction in the TBARS concentration in rats supplemented with α-tocoferol (30 mg/kg/day) and training in swimming. Rokitzki *et al.*[34] have reported that cyclists taking 300 mg of α-tocoferol/day during 20 weeks presented lower concentration of malonaldehyde (MDA), a product from the LP, after exhausting exercise, when compared with the control group.

α-tocoferol supplementation may be efficient in reducing the oxidative stress and the number of cells injuries after exhaustive exercise. Rokitzki *et al.*[34] have observed that the supplementation promoted lower plasma concentration of CK in response to endurance exhaustive exercise practiced by athletes. Sachek *et al.*[37] verified this effect up to 24 hours after running exercise at 75% $\dot{V}O_{2máx}$ in young males, supplemented with 1000 UI/day of vitamin E during 12 weeks.

Other investigations[38-39], however, did not observe positive effects of α-tocoferol supplementation, neither in the oxidative stress nor in the control of muscular injuries. The discrepancy between the studies' results may be due to the lack of standardization of several variables, such as type, exercise duration and intensity, the amount of supplemented vitamin, the supplementation duration, the used methods for evaluation of the LP, the time in which the samples are collected, age, the diet and physical conditioning of the individuals involved in these studies[37,39].

Vitamin C

Since vitamin C is an hydrosoluble antioxidant capable of regenerating the tocoferoxil radical and reacting with the ORs and peroxil radicals in aquouse phase, different researchers evaluated the influence of vitamin C supplementation in the oxidative stress induced by physical exercise. Goldfarb *et al.*[40] administered doses of 500 or 1.000 mg of vitamin C/day to volunteers during two weeks, and at the end of this period, a 30-minute run at 75% of $\dot{V}O_{2max}$ was performed. After the exercise, the supplemented group presented lower amount of carbonylated proteins comparing to the control group. Therefore, there was not influence of the supplementation over the TBARS concentrations. Palmer *et al.*[41] have observed that supplementation with 1.500 mg of vitamin C/day for seven days before and during an ultramarathon did not attenuate the oxidative stress after the event. The inefficiency of the vitamin C supplementation over the LP was attributed to the fact that this vitamin is located in aqueous compartments, being less efficient in neutralizing lipophilic radicals, not directly reacting with radicals generated in the lipidic membrane.

Vitamin C supplementation for a longer period may cause benefits concerning pain and muscular injuries. From a non-habitual exercise bout, Thompson *et al.*[42] evaluated the effect of two weeks of vitamin c supplementation over recovery. The supplemented group received two doses of 200 mg of vitamin C/day and, two weeks after the beginning of supplementation, the individuals were submitted to an intense and prolonged exercise protocol. The CK and myoglobine concentration was not altered by the supplementation. However, the supplementation attenuated the increase of the MDA concentration and muscular pain, benefiting the recovery of the muscle function. The authors have also verified that the plasma concentration of IL-6 was lower two hours after exercise in the group supplemented with vitamin C comparing with the placebo group.

In another investigation, Thompson *et al.*[43] studied the post-exercise effect of vitamin C supplementation over recovery, from the performance of an intense, prolonged and non-habitual exercise bout. Immediately after the activity, the supplemented group took 200 mg of vitamin C. Such nutritional intervention was repeated once again at the same day and in the morning and night of the two following days. The plasma vitamin C concentration of the supplemented group increased 1 hour after the end of the exercise and remained high during three post-exercise days. The CK and myoglobin concentrations however, were not affected by supplementation, and both the pain and the recovery of muscular function were not different between groups. Maxwell *et al.*[38] reported that vitamin C supplementation in the dose of 400 mg/day for three

weeks before and for one week after eccentric exercise resulted in increase of blood concentration of vitamin C. According to the authors, the supplementation promoted an increase in the tissue storages of vitamin C, which would have resulted in greater release of this vitamin in the circulation during the exercise. Nevertheless, influence of vitamin C supplementation or physical exercise in LP indicators after the activity has not been observed.

Creatine

Creatine synthesis occurs in the liver, kidneys and pancreas, having as precursors three distinct amino acids: arginine, glycine and methionine. Besides the endogenous synthesis, creatine can be provided through diet in the amount of approximately 1 g of creatine/day, especially through the ingestion of animal origin products, such as beef and fish[44-45]. About 95% of body creatine is stored in the muscular tissue where more than 70% is in phosphorilized form[44].

The great majority of studies show that creatine acute supplementation may rapidly increase strength and muscular strength gain, especially through the increase of intracellular water volume. These effects are usually associated with improvement in physical performance[44,46]. However, recently, some research has been conducted with the purpose to find other relevant benefits of the creatine supplementation, including some effects over the cellular oxidative stress and recovery of muscular tissue injuries, especially those promoted by exhaustive exercises of longer duration[45,47].

From research such as the one by Vergnani *et al.*[48], where the crucial antioxidant role of the amino acid anginine in the removal of $\bullet O_2^-$ endothelial cells radicals was demonstrated, it was raised the hypothesis that creatine had also an effect on the cellular redox metabolism. One of the first evidence of the contribution of creatine in the reduction of the oxidative stress was described by Lawler *et al.*[49], where the supplement administration resulted in a lower amount of $\bullet O_2^-$ radicals and peroxynitrite ($\bullet OONO^-$). However, lower amounts of H_2O_2 and LP were nor observed, which suggested that the antioxidant properties of creatine may be selective and very limited.

Studies concerning creatine and cellular volume demonstrate that greater pick up of sodium ions, induced by increased intracellular creatine concentration increases the cell volume, a factor considered anabolic, once the cellular volume considerably affects the protein turnover, promoting greater protein synthesis and increasing the availability of substrates for the many systems involved in the tissue repairing process[45,49-50]. The hypothesis that creatine attenuates the oxidative stress was tested by Santos *et al.*[51], where the effect of creatine acute administration was evaluated (4 doses of 5 g/day for 5 days) over some injury and inflammation markers, after a 30 km run. The results demonstrated a lower CK, LDH, prostaglandin-E_2 (PGE_2) and TNF-α concentration in the group supplemented with creatine, when compared with the control group. These facts show that creatine was able to decrease cellular injuries and inflammation induced by exhaustive exercises. Corroborating these results, Kreider *et al.*[52] have also verified that creatine acute supplementation reduced the concentration of some parameters indicative of muscular injury (CK and LDH) in athletes submitted to a long season of intense training.

Glutamine

Glutamine is the most abundant free amino acid in plasma and muscular tissue and it is used in high concentrations by cells of fast division, including enterocytes and leucocytes, in order to provide energy and favor the nucleotides synthesis. Approximately 80% of the body glutamine is found in the skeletal muscle, and it this concentration is 30 times higher than in the one in the plasma[53-55].

Among the organs involved in the glutamine synthesis are the skeletal muscle, lungs, liver, brain and possibly the adipose tissue which present activity of the glutamine sintetase enzyme. On the other hand, tissues which are primarily glutamine consumers – cells of the intestinal mucosa, leucocytes and cells of the renal tubule – have high activity of the glutaminase enzyme. Under certain conditions, such as reduced carbohydrates availability, the liver becomes a glutamine site consumer[54,56].

The effects of exercise over the glutamine metabolism are not completely clear. Factors such as exercise intensity and duration, nutritional status of the individuals and differences in blood sample collection, way of storing the plasma samples and the biochemical techniques of glutamine concentration measurement are responsible for the contradictory data presented by different authors[57].

Countless investigations have demonstrated a significant decrease of the plasma and tissue glutamine concentrations during and after intense and prolonged exercise. Among the mechanisms which lead to the decrease of plasma and muscular glutamine concentrations during and after prolonged exercise, we highlight the increase of cortisol hormone concentration, which stimulates both the muscular glutamine reflux and the glutamine pick up by the liver. Thus, greater availability of glutamine in the liver, joined with decrease of the storages of hepatic glycogen and the cortisol concentration promote higher hepatic noeoglycogenesis stimulus from the glutamine amino acid[58-60].

Another mechanism implied in the decrease of glutaminemia during prolonged physical exercise refers to the increase of blood lactate concentration which alters the blood pH (metabolic acidosis) and favors higher pick up of glutamine by the kidneys. The elimination of hydrogen ions (H^+) by the kidneys involves the providing of ammonia derived from glutamine. The ammonia made from the glutamine escapes from the renal tubule cells through a passive diffusion process and links to H^+ protons making ammonium ions (NH_4^+). The loss of hydrogen ions aids in the maintenance of the acid-basic balance[57,61]. Besides these facts, the increase of the pick up of glutamine by the immune system cells, especially when activated, may collaborate for the decrease of the glutaminemia induced by exercise[55].

Glutamine is also essential for the GSH synthesis; which represents the main cellular antioxidant of the body. The glutamine depletion, especially in the intracellular medium, may contribute for an imbalance between the oxidant agents, such as the ORS and the antioxidants, favoring the oxidation of substances essential to the cellular integrity and the LP, which increases the tissue injury[62]. In a study by Fläring *et al.*[63], individuals after having been submitted to metabolic stress events – abdominal region surgeries – were supplemented for three days with glutamine. The results showed that the intervention with glutamine attenuated the GSH depletion, a fact which improved the recovery of patients. Therefore, the glutamine supplementation may represent a nutritional intervention efficient in the recovery of individuals with traumas and submitted to situations extremely catabolic, such as the ones derived from the physical exercise, once it attenuates the degradation of the storages of body antioxidants[64-65].

Studies relating glutamine and cellular volume demonstrate that the transportation of this amino acid for the intracellular medium concomitantly promotes an increase in the pick up of sodium ions, which increases the cell's volume and may be considered as an anabolic signal, once the cellular volume favorably alters the protein turnover, promoting the protein synthesis and increasing the availability of substrates for the several systems involved in the tissue repairing process[50]. However, the effectiveness o glutamine supplementation has been argued due to the fact that approximately 50% of this amino acid is metabolized by cells of the intestinal mucosa[53,66]. An alternative to be able to transport the barrier of the intestinal cells has been the utilization of dipeptides of glutamine such as the alanyl glutamine[66]. It is absorbed and passes to the

blood stream and being able to serve later as substrate for other tissues, including mainly the muscular one[58-60,66].

CONCLUSION

The formation of ORS is inherent to the aerobic metabolism and tends to promote LP and cellular oxidative injuries. Nevertheless, some studies demonstrate that the increase in the ORS synthesis is also important to the body homeostasis and to the suitable functioning of the antioxidant system. Therefore, the gradual increase in ORS production promoted by the performance of aerobic or anaerobic physical exercises may increase the resistance to new stresses, an effect known as training adaptation. Regardless the kind of exercise performed, individuals who are submitted to intense and prolonged exercises or exhaustive trainings, or even, who have a very high training frequency are exposed to severe muscular injuries, a consequent inflammatory process and chronic oxidative stress, facts which imply in performance harm, training volume decrease and possibly overtraining. Different research has shown that the vitamin E supplementation, creatine and glutamine may attenuate the oxidative stress or reduce the amount of cellular injuries derived from exhaustive physical exercises. Other components such as vitamin C may have little or no effect over the supplementation; however, the reduction of its body supplies may contribute to the increase of the oxidative stress.

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