REVIEWS

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Effect of Vitamin E on the Physical Work Capacity

Oddziaływanie witaminy E na obciążenie fizyczne

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Abstract

It has been widely noted that vitamin E shows numerous beneficial effects through its antioxidant properties and beyond; consequently, vitamin E is expected to prevent degenerative diseases. In the field of sports medicine, many studies dealing with vitamin E have been conducted, originally from the point of view of its effects on physical performance. Although some earlier studies indicated that vitamin E supplementation could improve physical performance, defects in the study design or statistical analysis were pointed out at a later time. The majority of subsequent, well-controlled studies have reported no significant effect on physical performance from vitamin E supplementation. In conclusion, the authors suggest that endurance exercise may promote free radical generation in the body, and vitamin E may play an important role in preventing the free radical and DNA damage associated with endurance exercise. There is also evidence of free radical involvement in exercise-induced muscle injury. Vitamin E supplementation might be expected to prevent muscle and DNA damage caused by exercise in humans (**Adv Clin Exp Med 2006, 15, 6, 1063–1071**).

Key words: vitamin E, free radical, physical exercise.

Streszczenie

Dotychczas zostały dokładnie opracowane informacje dotyczące działania witaminy E, które potwierdzają, że nie tylko jej właściwości antyutleniające, ale również inne mogą zapobiegać pojawianiu chorób związanych ze zmianami zwyrodnieniowymi. W badaniach dotyczących medycyny wysiłku fizycznego podkreślono wpływ witaminy E na działania, które wysiłkowi towarzyszą. Potwierdza się, że podawanie witaminy E w formie suplementów polepsza zdolność organizmu do wysiłku fizycznego, co dokładnie wyjaśniono na podstawie dalszych badań, w tym analizy statystycznej. Wiele z nich potwierdziło pozytywny wpływ działania witaminy E na zmiany spowodowane obciążeniem fizycznym. Sugerują, że pełni funkcję ochronną w organizmie, w tym również, że może ograniczać uwalnianie się wolnych rodników po wysiłku fizycznym. Wolne rodniki uwalniane pod wpływem obciążenia fizycznego mogą uszkodzić DNA, a nawet mięśnie. Witamina E podawana w formie suplementów powinna zapobiegać patogennym zmianom w mięśniach osób wykonujących wysiłek fizyczny, które mogą powstawać na skutek uszkodzenia DNA (**Adv Clin Exp Med 2006, 15, 6, 1063–1071**).

Słowa kluczowe: witamina E, wolne rodniki, wysiłek fizyczny.

Physical training is known to increase the antioxidant defense system and reduce exercise-induced oxidative stress. However, intense physical aerobic and anaerobic training and competition, such as that imposed on professional rugby players, can induce an increase in oxidative stress which may be implicated in the onset of overtraining. The authors suggest that oxidative stress and antioxidant measurement is significant in the biological follow-up of athletes [1, 2]. Exercise appears to increase reactive oxygen species, which can result in damage to cells. Exercise results in increased amounts of malondialdehyde in the blood and pentane in the breath; both serve as indirect indicators of lipid peroxidation. However, not all studies report increases; these equivocal results may be due to the large inter-subject variability in response or the lack of specificity of the assays [3,

4]. Are antioxidant supplements necessary for individuals who exercise regularly? Should antioxidant supplements be part of the "nutritional game plan" of athletes, to maintain lower free radical levels or normal synthesis DNA? These are common questions directed to fitness leaders, athletic trainers, and other health professionals who are consulted about the role of antioxidants in a healthy, active lifestyle. The reason for this interest in antioxidants is the finding that highly reactive chemical species, called free radicals, may increase during exercise [5]. A free radical is broadly defined as a molecule containing one or more unpaired electrons in its outer orbit. During oxidative metabolism, much of the oxygen consumed is bound to hydrogen during oxidative phosphorylation, thus forming water. However, it has been estimated that 4–5% of the oxygen consumed during respiration is not completely reduced to water, but forms free radicals. Thus, as oxygen consumption increases during exercise, a concomitant increase occurs in free radical production and lipid peroxidation. The body contains an elaborate antioxidant defense system that depends on the dietary intake of antioxidant vitamins and minerals and the endogenous production of antioxidant compounds such as glutathione. Vitamins C and E and beta-carotene are the primary vitamin antioxidants. In addition to glutathione, there are numerous enzymes involved in the quenching or removal of free radicals [4, 6–9].

Chemistry of Free Radicals

A free radical is a molecule that contains an unpaired electron in its outer orbit and that can exist independently. Molecular oxygen is a diradical, containing two unpaired electrons with parallel spin configurations. Because electrons must have opposite spin to occupy the same orbit, electrons added to molecular oxygen must be transferred one at a time during its reduction [10, 11], resulting in several highly reactive intermediates [10]. The complete reduction of oxygen to H_2O requires four steps and the generation of several free radicals and H_2O_2, which is not a free radical in itself because it contains no unpaired electrons. H_2O_2 is, however, considered a reactive oxygen species (ROS) because of its ability to generate highly reactive hydroxyl free radicals through interactions with reactive transition metals [12]. The complete reduction of oxygen is summarized in the following equations:

$$O_2 + e^- \rightarrow O_2^{\cdot-} \text{ superoxide radical}$$

$$O_2^{\cdot-} + H_2O \rightarrow HO_2^{\cdot} + OH^- \text{ hydroperoxyl radical}$$

$$HO_2^{\cdot} + e^- + H \rightarrow H_2O_2 \text{ hydrogen peroxide}$$

$$H_2O_2 + e^- \rightarrow {}^{\cdot}OH + OH^- \text{ hydroxyl radical}$$

Each of these oxygen-derived intermediates is considered highly reactive because their unstable electron configurations allow for the attraction of electrons from other molecules, resulting in another free radical that is capable of reacting with yet another molecule. This chain reaction is thought to contribute to lipid peroxidation [13, 14], DNA damage [15], and protein degradation [16] during oxidatively stressful events. Although all the intermediates are potentially reactive, the intermediates vary in their biological importance. The superoxide radical ($O_2^{\cdot-}$) is the most well-known oxygen-derived free radical [10] and, unlike the other oxygen-derived intermediates, can lead to the formation of additional reactive species [17]. In particular, the protonation of $O_2^{\cdot-}$ results in the formation of perhydroxyl radical $HO_2^{\cdot}$, a much stronger radical than $O_2^{\cdot-}$. Additionally, $O_2^{\cdot-}$ acts as a Bronsted base in aqueous solutions to shift the acid-base equilibrium to form a hydroperoxyl radical, thereby forming H_2O_2 in acidic environments [10, 11]. The most well-described consequence of the generation of free radicals and ROS is lipid peroxidation [13]. *In vitro*, the interaction between free radicals and lipids involves three processes: initiation, propagation, and termination. During initiation, conjugated dienes are formed through the abstraction of a hydrogen atom from a backbone methylene group of a lipid [18]. Although not as well described, free radicals can damage DNA [15]; however, no direct measures are available to quantify such damage *in vivo*. In summary, the univalent reduction of oxygen produces a series of free radicals that interact with lipids, DNA, and proteins. This interaction degrades proteins and promotes DNA-strand breakage and damage to other genomic structures. These reactive species affect lipids as well, compromising the integrity of polyunsaturated fatty acids which, in turn, can affect the homeostatic environment of the cell.

Vitamin E

It is still unclear whether exercise induces lipid peroxidation in the human body or not. Also, the beneficial effect of vitamin E supplementation on exercise-induced lipid peroxidation has not yet been established [14]. However, it is proposed that as a result of exercise, vitamin E may be mobilized from tissue stores and redistributed in the body to prevent oxidative damage. Therefore the authors are convinced that vitamin E contributes to preventing exercise-induced lipid peroxidation. It has

also been indicated that strenuous endurance exercise may enhance the production of oxidized low-density lipoprotein (LDL), which plays a key role in the initiation and progression of atherosclerosis. It is also suggested that this enhanced production of oxidized LDL could be reduced if a higher vitamin E status is maintained. Supplementation with 100 to 200 mg of vitamin E daily can be recommended for all endurance athletes to prevent exercise-induced oxidative damage and to reap the full health benefits of exercise [19, 20]. Another study was performed in order to determine the association between pre-race plasma vitamin E concentration and performance in sled dogs competing in the 1998 Iditarod Race, where a total of 323 dogs (48%) were withdrawn from the race at various distances from the start. The median finishing time for 39 teams was 11.5 d and the winning time was 9.2 d. Dogs with pre-race plasma vitamin E concentrations > 40.7 μg/ml were 1.9 times more likely to finish ($p = 0.0006$) and had 1.8 times less risk of being withdrawn for every mile run ($p = 0.03$) than were dogs with plasma vitamin E concentrations between 16.3 and 40.7 μg/ml. Neither a team's mean pre-race vitamin E concentration nor the proportion of dogs within a team with high (> 40.7 μg/ml) vitamin E concentration was associated with team speed. Dogs with higher plasma vitamin E concentrations had enhanced endurance compared with dogs with lower plasma vitamin E concentrations, but the plasma vitamin E status of a team was not associated with team speed [21]. In a third study the authors evaluated the effects of RRR-α-tocopherol (500 IU/day, 8 days) on *in vivo* cytokine response and cytoplasmic expression of inducible nitric oxide synthases (iNOS) and the antioxidant stress protein hem oxygenase-1 (HO-1) in human leukocytes after exhaustive exercise. Thirteen men were investigated in a double-blind, placebo-controlled, cross-over study with a washout period of 28 days. The exercise procedure consisted of an incremental treadmill test followed by a continuous run until exhaustion at 110% of the individual anaerobic threshold (total duration 28.5 ± ± 0.8 min). HO-1 and iNOS protein were assessed in monocytes, lymphocytes, and granulocytes using flow cytometry [3]. Plasma interleukin-6 (IL-6) and IL-8 were measured by ELISA. IL-6 rose significantly, whereas IL-8 did not exhibit significant changes after exercise. Changes in IL-6 were not affected by RRR-α-tocopherol. Exercise induced an increase in iNOS protein primarily in monocytes and granulocytes. A small but significant increase in HO-1 protein was noticed in monocytes and granulocytes. RRR-α-tocopherol did not show any significant effects on cytoplasmic expressions of iNOS and HO-1 at rest and after exercise. In conclusion, exhaustive exercise induces the expression of iNOS and HO-1 in human leukocytes by a mechanism that is not sensitive to RRR-α-tocopherol supplementation [22].

Child et al. [23] tested the hypothesis of the ability of natural body antioxidants to scavenge free radicals in the serum of trained runners. The experimental design included measuring peak VO_2, the ability to scavenge free radicals in serum, and the plasma concentration of malondialdehyde (MDA) were assessed in 18 male runners. The participants' characteristics (mean ± *SEM*) were height: 1.77 ± 0.01 m, mass: 71.4 ± 1.2 kg, age: 31 ± 1 years, and weekly training distance: 45 ± ± 5 km/week. Venous blood samples were collected at rest. Serum total antioxidant capacity (TAC) was determined using a chemiluminescence technique. This involved the oxidation of luminol in a reaction catalyzed by horseradish peroxidase. Serum antioxidant protection was quantified relative to a soluble vitamin E analogue (Trolox) and expressed as Trolox equivalents (Trolox Eq.). MDA was determined using a highly specific assay using HPLC with fluorimetric detection. Peak VO_2 was determined from expired gas measurements collected during an incremental running test on a motorized treadmill. Data were analyzed using Pearson correlations. Serum TAC was 500 ± 26 mmol Trolox Eq./l, with a plasma MDA concentration of 1.5 ± 0.1 mmol/l and serum urate concentration of 274 ± 12 mmol/l. Peak VO_2 was 63 ± 1 ml/kg/min. Significant correlations were observed between peak VO_2 and serum TAC ($r = 0.365$, $p < 0.05$), peak VO_2 and serum urate ($r = 0.463$, $p < 0.05$), and serum urate and serum TAC ($r = 0.807$, $p < 0.001$). Plasma MDA and serum TAC were not significantly correlated ($r = 0.026$, $p > 0.05$). These data demonstrate that the ability to quench free radicals in serum is increased in relation to the maximum ability to consume oxygen; however this response does not appear to provide any additional protection against peroxidative damage at rest. Another study was on antioxidant status and titers of autoantibodies (Abs) against oxidized low-density lipoproteins (ox-LDL-Abs) investigated in top soccer (S; n = 21, age: 24.6 ± 4.3 years) and basketball (B; n = 3000 mIU/ml) players. The ox-LDL-Abs were found in half the players (12 S and 4 B), with a maximum reaching 6000 mIU/ml (normal range: 200–600 mIU/ml), showing *in vivo* LDL oxidation. There was no correlation between ox-LDL-Ab titers and cholesterol, LDL cholesterol, or antioxidant levels. Nevertheless, plasma vitamin E concentration was lower in athletes having high levels of ox-LDL-Ab compared with those with normal levels (8.49 ± ± 3.14 μg/ml vs. 10.39 ± 2.55 μg/ml), but this dif-

ference was not statistically significant. In conclusion, these data suggest that potential atherogenic and cardiovascular risks, as reflected by high titers in ox-LDL-Ab, may exist in some top athletes despite an unaltered antioxidant status [20, 24].

To study the association between plasma antioxidants (β-carotene and α-tocopherol) and lung function in Dutch adults aged 20–59 y, a random sample (n = 367) was drawn from all participants (men and women) aged 20–59 y with reproducible lung function. The study involved completion of a general questionnaire and a physical examination comprising expiratory volume in 1 s (FEV_1), forced vital capacity (FVC), and plasma levels of β-carotene and α-tocopherol. Subjects with a high plasma β-carotene level (90%, i.e. 0.57 μmol/l) tended to have a higher FEV_1 (73 ml, *s.e.m.* = 60 ml; $p = 0.22$) and a higher FVC (147 ml, *s.e.m.* = 76 ml; $p = 0.05$) than subjects with a low plasma β-carotene level (10%, i.e. 0.11 μmol/l) after adjustment for age, height, gender, smoking status, pack-years of smoking, and alcohol consumption. There was no difference in lung function between subjects with high and low plasma α-tocopherol concentrations. The results suggest, with borderline statistical significance, that subjects with high plasma β-carotene tended to have a higher FVC than subjects with low plasma β-carotene concentration. The difference in FEV1 between high and low levels of plasma β-carotene tended to be in the same positive direction as that of FVC but did not reach the set statistical significance level. There was no relation between plasma α-tocopherol and lung function [25].

Physical activity is known to induce oxidative stress in individuals subjected to intense exercise. In the following study, the authors investigated the lipoprotein profile and plasma antioxidant status in a group of soccer players engaged in a regular training program. As was expected for aerobic exercise, high-density lipoprotein-cholesterol (HDL-C) and HDL3-C levels were significantly increased in the sportsmen ($p < 0.05$). Total plasma antioxidant capacity was 25% higher in sportsmen than in controls ($p < 0.005$). Accordingly, plasma hydrosoluble antioxidant levels (ascorbic acid and uric acid) were found to be significantly elevated in the soccer players ($p < 0.005$). In addition, these subjects showed high concentrations of α-tocopherol in plasma compared with controls ($p < 0.005$). Furthermore, an increase in plasma superoxide dismutase activity was also observed in relation to exercise ($p < 0.01$). The elevation in plasma activities of antioxidant enzymes and the higher levels of free radical scavengers of low molecular mass may compensate the oxidative stress caused by physical activity. High levels of high-density lipoprotein in plasma may offer additional protection by inhibiting low-density lipoprotein oxidation and thus liposoluble antioxidant consumption. Therefore, soccer players under regular training show an improved plasma antioxidant status in comparison to sedentary controls [26]. Strenuous physical activity is known to increase the production of reactive oxygen species (ROS), associated with depletion of antioxidant defense. Other authors evaluated the level of lipid peroxidation and antioxidant components in the blood of sportsmen under resting conditions and compared the data obtained with those in age- and sex-matched sedentary controls. A significant increase was noted in the levels of thiobarbituric acid reactive substances (TBARS) and conjugated dienes, while a decrease was observed in ascorbic acid and glutathione levels in sportsmen. α-tocopherol was unaltered in the plasma of sportsmen compared with controls. The activity of superoxide dismutase was increased (for 52%) and glutathione peroxidase was decreased (for 43%) in the erythrocytes of sportsmen compared with controls. Basal glutathione levels were negatively correlated with conjugated dienes and maximal oxygen uptake (VO_{2max}) of the subjects. Dietary supplementation with antioxidative vitamins has been shown to be beneficial in combating oxidative stress without enhancing performance, while exogenous glutathione was found to influence the endurance capacity of athletes. Such studies demonstrate the critical role played by glutathione and suggest that intervention trials should include a mixture of antioxidants rather than a single antioxidant [27]. A study of 44 athletes of various sport disciplines undergoing training for endurance showed the chemiluminescences method to be an important parameter indicating that a person is trained for physical exertion. The broad-spectrum adaptogenic agents Elton and Leveton reduced in *in vitro* experiments the super-weak luminescence of urine, which is evidence of their direct antioxidant effect. Twenty-day administration of Elton and Leveton reduced the chemiluminescence and the level of malonic dialdehyde in the urine of highly skilled athletes and increased their physical working capacity as tested by bicycle ergometry with gradually increasing physical loads [28]. Uteshev and Laskova [29] found that essential, tocopherol acetate, and lidocaine hydrochloride enhance the immune response to T-dependent antigen under active physical loading. An essential such as Elton induces the appearance of immunostimulating properties in heavy erythrocytes, whereas tocopherol acetate and lidocaine hydrochloride increase the resistance of light erythrocytes to the effect of blood serum compounds

(extracted from swimming animals) which induce the immunosuppressive properties in them.

The Relationship Between Nutrition and Antioxidant Supplementation in Sports

The relationship between nutrition and sport has been studied extensively in recent decades. Nevertheless, research interest was focused mainly on the role of dietary macro- and micronutrients as ergogenic aids. Today there is increasing support for the hypothesis that nutrient status also has relevance in the prevention and rehabilitation of systemic and muscular stress induced by intense physical exercise [1, 17]. Increased muscular stress is indicated by a rise in creatine kinase and myoglobin; systemic stress is associated with characteristic immunological and hormonal changes and an acute-phase response. During and following exercise, the course of cytokines (especially interleukin 6) and acute-phase proteins (C-reactive protein, fibrinogen) as well as cortisol levels are an indirect measure of the exercise intensity and the individual ability to cope with physical stress. It has been shown that dietary intake and, consequently, the systemic or intracellular concentrations of minerals such as magnesium and zinc, vitamins with antioxidant capacity (vitamins E, C, and β-carotene), and the composition of fatty acids can be related to the exercise-induced stress response [30, 31]. Therefore, the study dealt specifically with the impact of these nutritional components on the reduction of sport-specific muscular damage and systemic stress, especially under the aspect of increased losses during and following intense physical exercise [32]. Previous studies indicated that fish oil supplementation increases red blood cell (RBC) deformability, which may improve exercise performance. Exercise alone, or in combination with an increase in fatty acid unsaturation, however, may enhance lipid peroxidation. The effects of a bicycle time trial of approximately 1 h on RBC characteristics and lipid peroxidation were studied in 24 trained cyclists. After three weeks of fish oil supplementation (6 g/day) without or with vitamin E (300 IU/day), trial performance, RBC characteristics, and lipid peroxidation were measured again. RBC deformability appeared to decrease during endurance exercise. After correction for hemoconcentration, plasma total tocopherol concentrations decreased by 0.77 μmol/l (p = 0.012) or 2.9% and carotenoid concentrations by 0.08 μmol/l (p = 0.0008) or 4.5%. Endurance exercise did not affect the lag time and rate of *in vitro* oxidation of low-density lipoproteins (LDLs), but the maximum amount of conjugated dienes formed decreased by 2.1 ± 1.0 μmol/mmol LDL cholesterol (p = 0.042) or 1.2%. Fish oil supplementation with and without vitamin E did not affect RBC characteristics or exercise performance. Both supplements decreased the rate of LDL oxidation, and fish oil supplementation with vitamin E delayed oxidation [33]. The amount of dienes, however, was not affected. The supplements also did not change the effects of exercise. The authors concluded that the changes observed during endurance exercise may indicate increased oxidative stress, but further research is necessary to confirm this. Fish oil supplementation does not improve endurance performance, but it also does not cause or augment changes in antioxidant levels or LDL oxidation during exercise [19].

Despite considerable interest in the anticarcinogenic and anti-atherosclerotic effects of carotenoids and α-tocopherol, little is known about the determinants of these serum micronutrients. The association of lifestyle factors, including alcohol use, physical activity, and dietary habits, with serum levels of carotenoids (lycopene, lutein, cryptoxanthin, and β-carotene), retinol, and α-tocopherol were studied in 194 healthy men aged 24–60 years who smoked > 15 cigarettes/day. A self-administered questionnaire ascertained consumption frequency of 12 food items, alcohol consumption, levels of physical activity, and the number of cigarettes smoked per day. Of the dietary items studied, total vegetable intake was significantly and positively associated with β-carotene levels, as was fruit intake, with serum levels of each carotenoid. Tofu intake was unexpectedly, and strongly, related to decreased levels of cryptoxanthin and β-carotene. None of the food items were materially related to serum levels of retinol and α-tocopherol. Alcohol consumption was most strongly and inversely associated with levels of all the carotenoids except lutein, whereas it was positively associated with retinol level, but not with α-tocopherol level. Frequency of participation in sports was significantly and positively associated with both retinol and α-tocopherol levels. The number of cigarettes smoked per day was unrelated to each micronutrient level in this study of moderate or heavy smokers. The consumption of vegetables and fruits is an important determinant of serum carotenoids levels even in smokers. Alcohol consumption is inversely associated with carotenoids levels, although the mechanism for this is not clear. Tofu and physical activity influence serum levels of antioxidative micronutrients, and these relationships need further study [1, 34,

35]. The effect of antioxidant supplementation on acute exercise-induced lipid peroxidation and antioxidant potential was measured in serum and low-density-lipoprotein (LDL) samples. Eight endurance athletes repeated a 31-km running exercise twice with an interval of 4 wk. During the 4 wk before the runs, the subjects took in a single-blinded randomized order of either a combination of antioxidant supplements (the antioxidant trial: 294 mg vitamin E, 1000 mg vitamin C, and 60 mg ubiquinone daily) or placebo (the placebo trial). Venous blood samples were taken before and immediately after the 31-km run in both trials. Antioxidant supplementation raised the LDL antioxidant potential (TRAP) (40% and 30%, p = 0.0031), serum TRAP (9% and 10%, p = 0.0037), and serum α-tocopherol concentration (by 59% and 66%, p = 0.0004) in both pre- and post-exercise samples, respectively. The supplementation did not, however, affect the concentration of LDL diene conjugation (DC) or of serum DC. Physical exercise increased serum DC (by 18% and 10%, p = 0.0004) but not LDL-DC, and the quantity of the increment of serum DC was not affected by antioxidant intervention. The major cause of the increased LDL-TRAP and serum TRAP after antioxidant supplementation was apparently the elevation of the serum α-tocopherol concentration [36–38].

It has been widely indicated that several pathological conditions depend upon concomitant risk factors rather than a unique one, and also that the putative protective factors do not act alone. For these reasons it could be useful to consider subjects who present sufficiently homogeneous lifestyles (i.e. nutrition and physical activity). The experiments were carried out in a free-living community in order to clarify the possible correlations and differences among plasma metabolic and antioxidant markers in non-agonistic athletes. The subjects were divided in two main groups according to age (35–44 and 45–54 years) without considering the activity they performed, and Duncan's analysis of variance revealed that they showed similar characteristics and only the triglyceride levels were different. A clear negative correlation was found between vitamin E and VO_{2max} in both age groups, a negative correlation was also found between CoQ10 and VO_{2max} in the younger subjects and, finally, CoQ10 and vitamin E were also positively correlated in this first group. It appears, therefore, that people with a higher aerobic capacity have lower circulating levels of antioxidants [39, 40].

The Relationship Between Antioxidant Supplementation and Free Radical Level During Exercise

The effects of eight weeks of 35-min aerobic cycle training (3 times/wk) on indexes of male and female human vastus lateralis muscle antioxidant status were investigated. The training resulted in significant elevations in whole body maximal O_2 consumption and muscle citrate synthase activity [10]. Despite this, muscle superoxide dismutase, catalase, and glutathione peroxidase activities were not significantly altered by the training protocol. In addition, training did not affect muscle vitamin E (α- and γ-tocopherol) concentrations. Glutathione status, determined as the concentrations of reduced glutathione (GSH), oxidized glutathione (GSSG), total glutathione (GSH + 2 × × GSSG), and the GSH/GSSG ratio, was unaffected by the training protocol. There were no significant differences between males and females in any indexes of muscle antioxidant status. These results indicate that the moderate aerobic training typically performed by regularly exercising humans did not positively alter endogenous antioxidant status. This suggests that short-term aerobic training increases the capacity for flux through the citric acid cycle without necessarily increasing the ability to handle potential free radicals generated by the enhanced electron flux [1, 41]. There is growing evidence that oxygen free radical production and subsequent lipid peroxidation are normal sequelae to the rise in oxygen consumption concomitant with exercise. In addition, increased lipid peroxidation has also been shown in vitamin B6-deficient rat plasma, liver, and kidney. To investigate the potential for a role of vitamin B6 in exercise-induced oxidative stress, 36 male Sprague-Dawley rats received 0 (n = 12), 2 (n = 12), and 8 (n = 12) mg pyridoxine (PN)-HCl/kg in their diet and were trained by a 9-week swimming program. After 9-weeks of training, six rats (exhausted: E rats) of each vitamin group were exercised to exhaustion by swimming, while the other six rats rested (nonexhausted: NE rats). Ascorbate, ascorbate free radical, and antilipoperoxidant capability (AC) were evaluated in plasma. These parameters were higher in E rats than in NE rats. Free radical-mediated lipid peroxidation was measured in tissue and plasma by evaluating the content of thiobarbituric acid reactive substances (TBARS). This index of peroxidation was significantly increased in the livers of the E rats but not in the plasma,

heart, and gastrocnemius muscle. Concentration of TBARS in liver was the highest in the vitamin B6-deficient rats (consuming 0 mg PN-HCl/kg in diet) and the lowest in vitamin B6-sufficient rats (consuming 8 mg PN-HCl/kg in diet). Vitamin E (α-tocopherol) levels in the liver and heart were negatively related to vitamin B6 levels in the diet. Independently of vitamin B6, liver and muscle α-tocopherol levels were significantly higher in E animals than in NE animals [42]. There is good evidence, according to presented results, that exercise induced an oxidative stress, as indicated by a significant increase in ascorbyl radical levels in the plasma. The effects of vitamin B6 deficiency on free radical metabolism are low in trained rats. In contrast, exhaustive exercise induced modifications in the metabolic pathways of vitamin C and E, objectivized by variations in the levels of vitamin C in the plasma and vitamin E in liver [43].

The effect of vitamin E on protection against damage to DNA during exercise

The purpose of this study was to investigate the effect of repeated exercise on oxidative damage to DNA in 10 well-trained long distance runners who participated in an eight-day training camp. The average running distance during the camp session was 30 ± 3 km/day. The amount of urinary 8-hydroxy-deoxyguanosine (8-OHdG) excretion was used to estimate the oxidative DNA damage. Urine samples were collected for both a three-day control period as well as throughout the camp session. Blood samples were drawn after overnight fasting both before and after the session. Urinary 8-OHdG excretion was significantly increased during the session compared with the control period (265.7 ± 75.5 vs. 335.6 ± 107.4 pmol/kg/day, $p < 0.05$). The content of 8-OHdG in the lymphocyte DNA on the day after finishing the camp session did not differ from that before the session. Plasma TBARS, LDH, CK, CK-MB, and myoglobin significantly rose after the camp session ($p < 0.05$). The plasma β-carotene levels tended to rise after the session, while the plasma α-tocopherol levels increased significantly after the session ($p < 0.05$). These results indicate that repeated exercise augments oxidative stress and the DNA is also injured by exercise-induced reactive oxygen species. However, the oxidative damage to DNA is not accumulated by consecutive exercise, although it is sustained as long as the exercise is repeated [44].

In conclusion, the authors suggest that endurance exercise may promote free radical generation in the body, and vitamin E may play an important role in preventing the free radical and DNA damage associated with endurance exercise. Although there is evidence of free radical involvement in exercise-induced muscle injury, vitamin E supplementation might be expected to prevent muscle and DNA damage caused by exercise in humans.

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