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ENDURANCE EXERCISE AND ANTIOXIDANT SUPPLEMENTATION: SENSE OR NONSENSE?-PART 2

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KEY POINTS

- Prolonged exercise at 65-80% VO_2max increases the production of radicals in the contracting skeletal muscles. This exercise-induced radical production often results in oxidative damage to skeletal muscle fibers and contributes to muscle fatigue.
- Antioxidant supplements are widely available and are commonly consumed by endurance athletes. Arguments exist both for and against the use of antioxidant supplementation.
- The strongest argument supporting antioxidant supplementation exists in endurance athletes who do not consume a well-balanced diet. Specifically, if a nutritional evaluation reveals that the athlete is deficient in antioxidant intake (e.g., consumption below the recommended daily allowance [RDA] for antioxidant vitamins), dietary supplementation designed to achieve the RDA standard for antioxidant vitamins appears warranted.
- The major argument against antioxidant supplementation is the possibility that megadoses of antioxidants (e.g., vitamin E and C) can diminish the training response to endurance exercise.
- Although exercise-induced radical production can contribute to muscle fatigue during endurance exercise, studies demonstrate that supplementation with common antioxidants (e.g., vitamin E and C) do not improve exercise performance. Nonetheless, there are some suggestions that treatment with N-acetylcysteine can delay fatigue at work rates between 65-80% VO_2max.

INTRODUCTION

It is established that contracting skeletal muscles produce radicals and that the rate of radical production in muscles intensifies as a function of the exercise intensity and duration (Powers & Jackson, 2008; Powers et al., 2011a). This exercise-induced increase in radical production often results in oxidative damage to both muscle proteins and lipids (i.e., oxidative stress). Moreover, exercise-induced increased production of radicals is a contributory factor to muscle fatigue during prolonged endurance exercise (Reid, 2008). The recognition that exercise-induced radical production can damage skeletal muscle fibers and contribute to muscle fatigue has inspired many people who engage in regular endurance exercise to consume antioxidant supplements.

This Sports Science Exchange article is the second of a two-part series that discusses endurance exercise, oxidative stress and antioxidant supplementation. Part 1 of this series introduced exercise-induced oxidative stress and discussed both endogenous (cellular antioxidants) and exogenous antioxidants (i.e., dietary antioxidants). The objective of the current report is to address two important questions related to endurance exercise and antioxidant supplementation: 1) Should endurance athletes supplement with antioxidants to protect against exercise-induced oxidative stress?; and 2) Does antioxidant supplementation improve endurance exercise performance? The article begins with a debate about whether antioxidant supplementation is justified in individuals engaging in endurance exercise training.

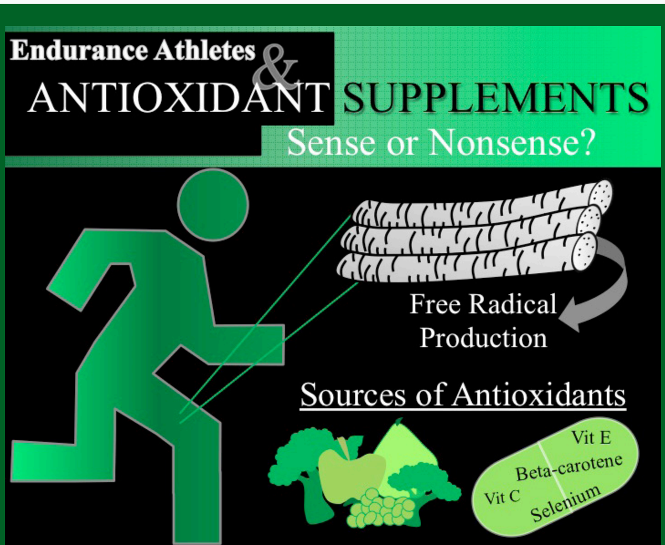
DOES ENDURANCE EXERCISE TRAINING INCREASE THE NEED FOR DIETARY ANTIOXIDANTS?

Performing an Internet search using the term "antioxidants" yields a large number of websites providing information about antioxidants. The scientific basis of the information contained in these sites is extremely variable. Nonetheless, many websites conclude that antioxidant consumption promotes good health and reduces the risk for many diseases (e.g., cancer, heart disease, etc.). Therefore, it is not surprising that nutritional supplements containing antioxidants are widely available for purchase both in retail stores and from Internet vendors. For example, common antioxidants offered by supplement companies include vitamin E, vitamin C and beta-carotene. Many other antioxidant products exist including grape extracts, resveratrol, lutein, lycopene, alpha lipoic acid, green tea complexes and numerous others. The large number of companies producing and selling antioxidant products suggests that antioxidant supplementation is widespread. Studies reveal that the incidence of antioxidant supplementation varies from country-to-country and across different segments of the population. Nonetheless, the use of antioxidant supplements is high around the world, as one study reported that ~62% of junior track and field athletes use nutritional supplements (Nieper, 2005). In the next segments we highlight arguments both for and against antioxidant supplementation in endurance athletes.

ARGUMENTS FOR ANTIOXIDANT SUPPLEMENTATION

Supporters of antioxidant supplementation for endurance athletes reason that because rigorous exercise training results in increased damaging radical production in skeletal muscles, antioxidant supplementation is essential to protect skeletal muscle fibers against oxidative damage. This notion is supported by experimental evidence demonstrating that vitamin C supplementation sufficiently blunts exercise-induced free radical production (Ashton et al., 1999).

Another argument used to support antioxidant supplementation is that many endurance athletes have diets that are deficient in antioxidants (Van Erp-Baart et al., 2004). Athletes who regularly restrict energy intake, have severe weight-loss practices, eliminate certain food groups or consume unbalanced diets are at the greatest risk for vitamin deficiency. Only a handful of dietary antioxidants have a designated Recommended Dietary Allowance (RDA). The RDAs for these include: vitamin C – 90mg for men and 75 mg for women, vitamin E – 15 mg and selenium – 55 μg. Therefore, supplementation with an antioxidant could be beneficial for individuals who consume a diet low in one or more of these antioxidants; however, consultation with a dietitian before beginning a supplementation regimen is advised.



Pros	Cons
May scavenge radicals during activity	Not proven to improve performance
Diet deficiency	Blunt training response

Figure 1. Antioxidant supplementation effects on endurance exercise training. Rigorous endurance exercise increases free radical production in skeletal muscle. Antioxidants obtained from the diet or supplements can protect against free radical damage. However, the benefits of supplementation are debated because high amounts of antioxidants have been shown to be ineffective and potentially detrimental.

ARGUMENTS AGAINST ANTIOXIDANT SUPPLEMENTATION

In contrast to the argument that antioxidant supplementation is warranted for endurance athletes, there are several arguments against antioxidant supplementation for endurance athletes. First, there is no evidence that exercise-induced radical production in skeletal muscle is harmful to human health. Indeed, it is well established that regular exercise reduces all-cause mortality and therefore, it seems unlikely that exercise-induced radical production is unhealthy (Lee et al., 2010). Further, regular endurance exercise training promotes increased enzymatic antioxidants in muscle fibers resulting in improved endogenous protection against exercise-mediated oxidative damage (Powers & Jackson, 2008). Hence, this training-induced increase in endogenous antioxidants may be adequate to protect against oxidative damage from other sources. Finally, if an endurance athlete maintains an isocaloric diet that is nutritionally well-balanced, it is likely that the individual does not need supplementary antioxidants above those consumed in the diet. Similar conclusions have been reached by other investigators in this field (Margaritis & Rousseau, 2008; Rodriguez et al., 2009).

Perhaps the strongest arguments against antioxidant supplementation for endurance athletes are the following. First, new studies reveal that antioxidant supplementation can prevent exercise-induced adaptations in skeletal muscle (Gomez-Cabrera et al., 2008; Ristow et al., 2009). Indeed, compelling evidence indicates that exercise-induced reactive oxygen species (ROS) production serves as a required signal to promote the expression of numerous skeletal muscle proteins including antioxidant enzymes, mitochondrial proteins and heat shock proteins (Powers & Jackson, 2008; Powers et al., 2011a). Another argument against antioxidant supplementation in athletes is that much of the current research does not support the notion that antioxidant supplementation is beneficial to human health. For example, a meta-analysis of 68 randomized antioxidant supplement trials (total of 232,606 human participants) concluded that dietary supplementation with beta-carotene, vitamin A and vitamin E does not improve health outcomes and may increase mortality (Bjelakovic et al., 2007). This detailed report concluded that the roles of vitamin C and selenium on human mortality are unclear and require further study before a recommendation can be rendered.

CAN ANTIOXIDANT SUPPLEMENTATION IMPROVE ENDURANCE PERFORMANCE?

Muscle fatigue is commonly defined as a reduction in the ability of a skeletal muscle to generate force (Gandevia, 2001). Exercise-induced muscle fatigue is a multi-factorial process and the specific causes of fatigue vary as a function of the type of exercise that produced the muscle fatigue (Ament & Verkerke, 2009). For example, the major contributory factors to fatigue during high-intensity contractions completed during resistance training type activities will be different from the factors that contribute to primary fatigue during lower-intensity, repeated contractions that take place during endurance type activities. Nonetheless, growing evidence indicates that radical production in skeletal muscles contributes to fatigue during prolonged exercise at submaximal intensities (i.e., 65-80% VO_2max) (Reid, 2008; Lamb & Westerblad, 2011). As mentioned previously, radical production increases in contracting skeletal muscles and low levels of radicals play an essential role in the regulation of muscle force production (Powers & Jackson, 2008). Indeed, low levels of radicals in contracting skeletal muscles are required to achieve optimum force production (Powers & Jackson, 2008). However, high levels of radicals can induce oxidative damage to muscle proteins and lipids and diminish muscle force production

(Reid, 2001). Therefore, a physiological basis exists to suggest that supplementing with antioxidants would improve muscular performance.

In this regard, when using in vitro experimental set-ups (i.e., isolated animal muscle preparations), antioxidants have been shown to delay fatigue during prolonged low-intensity contractions (Andrade et al., 1998). Additionally, well-controlled animal studies indicate that scavenging radicals via antioxidants can protect skeletal muscle against oxidative damage and also delay fatigue during prolonged submaximal exercise (Reid, 2008). In contrast, antioxidant scavengers are not effective in delaying muscle fatigue in animals performing high-intensity exercise (Reid, 2008).

Do radicals contribute to exercise-induced muscular fatigue in humans? The answer to this question remains under debate, but a growing number of studies suggest that acute administration of the antioxidant N-acetylcysteine (NAC) delays human muscle fatigue during prolonged submaximal exercise (Powers et al., 2011b). Specifically, NAC administration has been shown to delay muscular fatigue in humans during submaximal exercise tasks (e.g., electrically stimulated limb muscle, voluntary cycling exercise and repetitive handgrip exercise) (Reid, 2008). Similar to the aforementioned animal studies, NAC does not retard human muscle fatigue during high-intensity exercise (i.e., close to VO_2max) (Reid, 2008). A potential side effect is that the consumption of NAC can produce nausea in some individuals. Therefore, NAC supplementation may not improve endurance performance in those athletes who experience nausea when using this drug. Importantly, the long-term health effects of supplementation with NAC remain unknown.

In contrast to the findings that acute NAC administration can delay muscle fatigue during prolonged submaximal exercise, little evidence exists to support the concept that other more commonly used antioxidant supplements (e.g., beta-carotene, vitamin E and/or vitamin C) can improve human exercise performance (Peternelj & Coombes, 2011; Hernandez et al., 2012). Further, no evidence exists that antioxidant supplementation improves recovery from endurance exercise (Peternelj & Coombes, 2011; Hernandez et al., 2012).

PRACTICAL IMPLICATIONS

- Antioxidants exist in small quantities in foods and therefore, there is limited risk of an antioxidant "overdose" by consuming a diet rich in both fruits and vegetables. However, the ingestion of megadoses of antioxidants via dietary supplements (e.g., vitamin E) could blunt the training effects associated with endurance exercise. Therefore, consumption of megadoses of antioxidant supplements is not advised.
- Supplementation with common dietary antioxidants (e.g., vitamin E and C) does not improve exercise performance or accelerate recovery from exercise.
- Treatment with the antioxidant N-acetylcysteine has been shown to improve human exercise performance during submaximal exercise. However, N-acetylcysteine is associated with nausea in some individuals and the long-term health impact of the consumption of N-acetylcysteine remains unknown.

SUMMARY

The question of whether or not athletes should use antioxidant supplements remains an important and highly debated topic. Arguments for and against antioxidant supplementation exist and additional research will be required to firmly establish whether antioxidant supplementation is beneficial or harmful to athletes (Figure 1). However, at present, there is limited scientific evidence to recommend antioxidant supplements to athletes or other physically active individuals. In fact, the current evidence suggests that athletes should use caution when considering supplementation with high (mega) doses of antioxidants.

Although exercise-induced radical production can contribute to muscle fatigue during endurance exercise, research does not support the notion that commonly used antioxidant supplements (e.g., vitamin E or vitamin C) can improve human exercise performance. One exception may be supplementation with NAC, which has been shown to improve endurance capacity during prolonged exercise at 65-80% VO_2max. Nonetheless, the long-term effects of supplementation with NAC remain unknown.

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