REVIEW/DERLEME

ASSESSMENT OF NITRATE'S IMPACT ON EXERCISE PERFORMANCE

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ABSTRACT

This study aims to provide insights into nutritional and ergogenic strategies that support athletic performance by examining the physiological changes occurring during and after exercise. Research in the field of exercise physiology highlights the significance of proper nutrient intake and supplementation in enhancing performance. In this context, studies conducted between 2014 and 2024 were reviewed to evaluate the effects of nitrate on exercise performance. During exercise, glycogen stores are primarily used for energy; as these stores are depleted, the creatine phosphate and lactic acid pathways become active. Lactic acid accumulation contributes to muscle fatigue, whereas exercise-induced adaptations lead to an increase in mitochondrial density, making energy production more sustainable. Additionally, oxidative stress levels rise during physical activity, while the body's antioxidant defense mechanisms become more active. Along with supplements such as creatine, caffeine, and L-carnitine, nitrate—known as a precursor of nitric oxide—has been shown to promote vasodilation, enhancing oxygen and nutrient delivery to muscles and thereby improving performance. The findings indicate that nitrate supplementation may increase endurance performance by approximately 3% and can be beneficial when consumed prior to exercise.

Keywords: Ergogenic aids, Exercise, Nitrates, Nutrition, Physical performance

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INTRODUCTION

Exercise is defined as planned and repetitive movements (1). The response of the cardiovascular system to exercise is examined in two ways: acute and chronic. Acute responses are changes that occur in the body during exercise, while chronic changes are permanent adaptations resulting from the body's adjustment to these acute responses. During exercise, adrenaline and noradrenaline are secreted and the vagus nerve is stimulated. At the same time, oxygen consumption and carbon dioxide production increase. For energy requirements during exercise, glycogen stores in the muscles are primarily used (2). After glycogen stores are depleted, energy is obtained from creatine phosphate, and when this energy is insufficient, the lactic acid pathway is used and lactate accumulates in the muscles (3). Lactic acid levels increase initially and then decrease towards the end of the exercise, showing a changing pattern. After physiological adaptation to exercise is achieved, the number of mitochondria in the muscles increases and ATP production continues despite lactic acid accumulation (2). These changes and damage occurring during exercise are considered physiological stress. The cortisol hormone released during exercise is also an indicator of this stress (4). This stress is associated with the production of free radicals and reactive oxygen species during exercise. Protein and glutathione oxidation increase during acute exercise (5). Oxidative stress and inflammation are nowadays considered as fundamental factors underlying many diseases. These are not only limited to the direct oxidation of biomolecules and enzymes but are also related to physiological adaptation mechanisms by affecting biological processes such as redox signaling, cellular metabolism, the TCA cycle, and the methionine cycle. Similarly, inflammation is a natural defense mechanism developed by the body against harmful stimuli. However, when it becomes chronic, it can damage cells and tissues (6,7,8,9). Free radical species, especially reactive oxygen species (ROS) and reactive nitrogen species (RNS), perform important physiological functions by activating and regulating many signaling pathways. Therefore, maintaining redox balance is of critical importance for the normal functioning of cells. In this context, maintaining the balance between oxidants and antioxidants (both enzymatic and non-enzymatic) properly is necessary for the healthy functioning of cells and organisms (10). However, especially when free radical species are present at high levels, they can exert damaging effects by oxidizing biological molecules such as proteins, lipids, and nucleic acids (6). Oxidative stress is also of great importance as it can lead to trauma, stroke, and the emergence of chronic diseases (11). In response to increased oxidative stress after exercise, increases in antioxidant responses such as superoxide dismutase and glutathione peroxidase enzymes are observed. Additionally, plasma α-tocopherol levels decrease after exercise (12). In addition to increasing the production of free radicals and related molecules, exercise also strengthens the body's antioxidant responses. Different types of exercise such as aerobic, anaerobic, or mixed training lead to changes in redox balance and oxidative stress levels. These changes are balanced by changes in the expression of the body's antioxidant systems in response to increased ROS and RNS production (13). In this regard, biological systems, cellular processes, and organisms have developed specific adaptation mechanisms to cope with exercise-induced oxidative stress. Reaching a certain level of oxidative stress is necessary during exercise for physiological and metabolic adaptations to maintain redox homeostasis (14). However, external interventions aimed at balancing oxidative stress may alter the physiological adaptations provided by exercise. It is shown that antioxidant supplements may negatively affect the benefits of exercise training (16). Additionally, increased oxygen consumption and insufficient oxygen levels lead to the production of more reactive oxygen species. Increased reactive oxygen production causes muscle fatigue and muscle damage (14).

Exercise Performance and Some Ergogenic Aids

Exercise performance is evaluated by the speed at which an individual restores energy stores and systems to pre-exercise conditions (16). The recovery process after exercise occurs by replenishing the energy expended during exercise and removing accumulated lactic acid from the body. Sleep, smoking, alcohol, massage, and nutrition are among the factors that affect the recovery process (2). Creatine, which plays an important role in exercise physiology, is taken into the body not only through endogenous synthesis but also through dietary sources such as fresh meat and fish. It is known that creatine, a widely used nutritional supplement by athletes and individuals who exercise, improves exercise performance by increasing intramuscular creatine concentration by approximately 40% (17). Caffeine, known as 1,3,7-trimethylxanthine, is a compound that dissolves in both water and lipids and is absorbed from the stomach and small intestine (18). Caffeine significantly increases exercise performance and has an effect that reduces fatigue after exercise (19). While short-term ketogenic-low carbohydrate diet application reduces exercise performance, there are also studies showing that it increases exercise performance by reducing fat mass (20,21). L-carnitine, a derivative of amino acids in various forms, is responsible for the transport of long-chain fatty acids from the cytosol to the mitochondrial matrix. In addition, its role in storing energy as acetyl-carnitine and its antioxidant effects draw attention regarding its impact on exercise performance. It positively affects exercise performance by protecting glycogen stores during exercise and reducing lactate accumulation (17). n-3 supplementation is reported to improve exercise performance by supporting protein synthesis in muscle (22). Another ergogenic aid thought to positively affect exercise performance is nitric oxide (17).

Nitric Oxide

The first study on the chemical structure of nitric oxide (NO) was published by Joseph Priestley in 1772. In 1914, Sir Henry Dale reported that acetylcholine increased blood flow and relaxed blood vessels in rabbits in a study he conducted on rabbits (23). Subsequently, Furchgott reported that a substance secreted from the vascular endothelium caused relaxation in the vessels, and this relaxation only occurred if the endothelium was intact. He named this substance Endothelial Derived Relaxing Factor (EDRF). It was discovered in 1987 that NO and its derivatives were required for the release of EDRF (24,25). Nitric oxide (NO) is an important free radical in the body in terms of signal transmission and regulatory functions. It plays a role in processes such as vasodilation, mitochondrial respiration, glucose and calcium balance, muscle contraction, and fatigue. Due to its short half-life, NO must be continuously produced. There are two main pathways for NO production in the body. These pathways occur via nitric oxide synthase (NOS) and the nitrate-nitrite conversion (26). The precursors of nitric oxide are L-arginine and nitrate (NO3-). Nitric oxide synthesis is carried out by nitric oxide synthase. Changes in blood flow, insufficient oxygen, vasoactive substances, etc., stimulate nitric oxide synthesis. The final products of the reactions occurring in the body are nitrite and nitrate (27). Dietary nitrate consists of one nitrogen atom and three oxygen atoms and is commonly found in foods such as beetroot, spinach, and arugula (28). It is thought that nitrate in foods increases NO levels and provides better performance in sports (29). In the presence of NO, the same performance can be achieved with less oxygen. This effect is thought to stem from NO's impact on processes such as energy efficiency, Ca+2 transport, mitochondrial respiration, muscle fatigue, and vasodilation in the human body (30). The vasodilation effect of nitric oxide (NO) leads to the expansion of blood vessels and thus provides more blood flow to the muscles. This ensures more oxygen and nutrients are transported to the muscles, thus delaying fatigue during exercise and increasing performance (31). The use of compounds known as NO precursors such as L-arginine and L-citrulline may promote muscle hypertrophy (growth) and support strength adaptations. NO increases the efficiency of oxygen and ATP utilization in muscles, enabling muscles to work more efficiently during exercise. It is also reported to increase exercise performance by facilitating the removal of markers that cause post-exercise fatigue, such as lactic acid (32).

The Effect of Nitrate on Exercise Performance

Although the metabolism of nitrate and nitrite in the human body is not yet clear, it is known that the concentration of nitrate and nitrite is higher in skeletal muscle compared to plasma. Following nitrate consumption, the amount of sialin in skeletal muscle increases. This suggests that sialin serves as a nitrate carrier molecule. It is also known that muscle nitrate concentration decreases depending on exercise (37). When studies evaluating the effect of nitrate on exercise performance are examined, it is shown that consumption of beetroot juice containing nitrate particularly increases maximum and average power output during the first half of a 30-second sprint test. It has also been shown that maximum power is reached in a shorter time (33). In the sarcoplasm, NO increases calcium release and reduces the rate of phosphocreatine breakdown. It is reported that nitrate supplementation in the range of 5–19 mmol, taken in single or multiple doses over 15 days, can be used to increase anaerobic performance, tolerance during high-intensity exercise periods, and efficiency. Furthermore, it is thought that its use in elite athletes is controversial and therefore may be more beneficial for athletes using anaerobic energy pathways before competitions (30). It is stated that training status may be a factor in the effect of nitrate supplementation on exercise tolerance and performance. In trained athletes who maintain muscle oxygenation through regular training, dependence on the NO pathway decreases and the effect of nitrate is observed to be lower. In a reviewed meta-analysis study, no significant difference was reported between nitrate supplementation and exercise performance with an application duration ranging from 3 to 15 days. While it is reported that 5–9 mmol of nitrate for a maximum of 15 days can contribute to exercise performance, it is suggested that this amount can be taken as single or multiple doses. The most effective dose reported for exercise performance is 5–9 mmol, and its dietary sources are considered to be reliable (34). In another study, nitrate supplementation of 6–12 mmol/day taken 2–3 hours before exercise for 6–15 days was reported to be safe (35). When the exercise performance of participants who consumed 140 mL of beetroot juice 2.5 hours before exercise was evaluated, it was reported that consumption for 4 days increased exercise performance more compared to acute intake (36). In addition to dietary intake, it is known that nitrate is stored in the muscles in the human body, and this storage is affected by dietary nitrate intake. This nitrate stored in skeletal muscle may contribute to NO formation during exercise and may affect exercise performance (37). The effect of nitrate on exercise performance is reported as 3%, and its intake 90 minutes before exercise is shown as an ergogenic aid (38).

Dietary Sources of Nitrate

The highest nitrate sources are listed as beetroot, spinach, and arugula. In addition to nitrate, beetroot also contains many bioactive compounds (34). When the effects of beetroot, spinach, chard, and wild asparagus (uşkun) on exercise performance are examined, positive effects are observed only in beetroot. It is also reported that nitrate-depleted beetroot increases exercise performance due to its polyphenol content. Dietary nitrate slightly affects exercise performance, especially in individuals performing endurance exercise, and this effect varies depending on the composition of the food (39). Current studies showing the effects of beetroot juice on exercise performance, oxidative stress, and muscle are presented in Table 1.

Table1. Studies on beetroot juice supplementation

Study Type	Participants	Intervention	Outcome	References
Randomized Controlled Double-Blind Placebo-Controlled	14 semi-professional female volleyball players	Effect of 50 mL beetroot juice on exercise-induced muscle damage	Improvements observed in parameters such as muscle endurance, perceived muscle soreness, and edema	39
Randomized Controlled Double-Blind Placebo-Controlled	16 elderly individuals	Supplementation with beetroot juice containing 18.2 ± 6.2 mmol NO_3^- for two weeks	No changes in oxidative stress markers; however, increases observed in Vmax and Pmax	40
Randomized Controlled Double-Blind Placebo-Controlled	9 professional tennis players	Supplementation with 70 mL beetroot juice containing 6.2 mmol NO_3^- to assess its effects on performance	Acute intake reported to provide no performance benefits during matches; considered to have minimal ergogenic value	41
Randomized Controlled Double-Blind Placebo-Controlled	11 amateur male athletes	70 mL beetroot juice containing either 400 mg or 6.4 mmol·L^{-1} NO_3^- administered 120 minutes pre-training	Beetroot supplementation may positively affect heart rate and endurance, though no significant difference found between the two dosage levels	42

CONCLUSION

It has been observed that the cardiovascular system, energy metabolism, and skeletal muscles undergo various adaptations during exercise. The depletion of glycogen stores in the course of acute exercise, along with the activation of the creatine phosphate and lactic acid pathways, indicates that energy production processes are efficiently regulated. Furthermore, the increase in oxidative stress and the consequent activation of antioxidant defense mechanisms can be regarded as an integral component of the body's physiological response to exercise. Ergogenic aids, particularly creatine, caffeine, L-carnitine, and nitric oxide precursors, have been found to exert favorable effects on exercise performance. It has been demonstrated that creatine and caffeine enhance energy production and endurance capacity, whereas L-carnitine supports energy efficiency by playing a pivotal role in the metabolism of fatty acids. Additionally, nitric oxide precursors have been shown to facilitate vasodilation, thereby promoting the delivery of greater amounts of oxygen and nutrients to the musculature, ultimately improving exercise performance. The acute and chronic adaptations induced by exercise exert substantial influence on individuals' overall health status and physical performance. The acute cardiovascular response to exercise is critically important for the regulation of blood flow and the adequate delivery of oxygen to the working muscles. The recruitment of alternative energy pathways following glycogen depletion reflects the body's ability to adapt to varying exercise intensities. In particular, the accumulation of lactic acid and the resultant muscle fatigue emerge as principal limiting factors during exercise performance. The relationship between oxidative stress and exercise is directly associated with exercise intensity and duration. The elevated production of reactive oxygen species may contribute to muscle damage and fatigue; however, endogenous antioxidant defense mechanisms attempt to mitigate these deleterious effects. In this context, the significance of the post-exercise recovery process is paramount. The beneficial effects of ergogenic aids such as creatine, caffeine, and L-carnitine on exercise performance explain their widespread use among athletes and individuals who engage in regular physical activity. Notably, nitric oxide precursors have been shown to enhance exercise performance by delaying the onset of muscular fatigue and increasing oxygen delivery to skeletal muscles.

IMPLICATIONS

In conclusion, the physiological adaptations that occur during exercise constitute critical determinants that directly affect both individual health status and athletic performance. The appropriate use of ergogenic aids may support these adaptations and contribute to performance enhancement. These findings may serve as a reference in the formulation of exercise programs and nutritional strategies for both athletes and individuals who participate in regular physical activity. Nonetheless, considering the variability of individual needs, the utilization of such aids should be tailored according to personal requirements and health status.

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