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Review Article

Use of Creatine as a Nutritional Supplement during Endurance Training

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Abstract

Creatine supplementation shows greatest benefits when applied with the aim of improving strength and endurance in anaerobic exercise. Nevertheless, there is also evidence of benefits from supplementation for endurance exercise such as cycling, middle distance, team sports or HIIT. The aim of this review is to evaluate the potential benefits of creatine as a nutritional supplement during endurance exercise, as well as identify the potential mechanisms may influence.

There are many types of creatine, but the most evidence-based and most widely consumed is creatine monohydrate. Most effective way to achieve gains is by performing a loading phase with the intake of 5 g of creatine monohydrate (or 0.3g/kg body weight) four times a day for a period of 5-7 days. Once muscle creatine stores are fully saturated, an intake of 3-5g/day is usually sufficient to maintain them. In the case of endurance activities, improved performance is attributed to an increase in phosphocreatine resynthesis and muscle creatine content. The response to supplementation can differ greatly among individuals, usually depending on the individual's initial phosphocreatine stores. Potential mechanisms that could affect training adaptations include an increase in exercise intensity, the role of creatine in aerobic metabolism and finally its antioxidant properties. Nevertheless, further research is needed to fully understand its impact on training adaptations in endurance sports. According to the results of some studies, the best time to consume creatine is after exercise; consumption of 5 g of creatine after exercise shows improvements in body composition (gains in fat-free mass and loss of fat mass). In addition to its efficacy, it is also considered a safe supplement, and is approved and recommended by several official organizations. It is true that in some specific cases, such as in polymedicated, elderly or postmenopausal women, adverse effects may occur after supplementation. However, in most cases this will be unusual. Finally, additional applications of creatine have recently been identified that enhance recovery, warm-up exercise tolerance, injury prevention and rehabilitation, and neuroprotection of the brain and spinal cord, as well as other potential medical uses in different clinical contexts. In summary, creatine supplementation seems to have benefits in endurance exercise, although more studies are still needed to specify which parameters are improved in each type of exercise, also considering the influence of other factors such as age or gender.

Keywords: Creatine; Creatine Monohydrate; Supplement; Sport; Exercise; Resistance Training; Endurance; Ergogenic Aid

Abbreviations

AIS: Australian Institute of Sport; EFSA: European Food Safety Authority; ASADA: Australian Sports Anti-Doping Authority; AEPSAD: Spanish Agency for Health Protection in Sport; PCr: Phosphocreatine; CK: Creatine kinase; ATP: Adenosine triphosphate; HIIT: High Intensity Interval Training; ROS: Reactive Oxygen Species; SCI: Spinal Cord Injuries; TBI: Traumatic Brain Injuries

Introduction

Supplements are increasingly used worldwide due to their easy accessibility, relatively low cost and associated health benefits. Creatine is one of the most popular especially in athletes and exercising individuals for improving muscle mass, performance and recovery, also its use is considered safe in the short and long term in different populations [1,2].

The Australian Institute of Sport (AIS) uses an ABCD classification system to classify sports foods and supplement ingredients into four groups based on scientific evidence and other practical considerations that determine their suitability, safety and effectiveness in enhancing sports performance. The AIS includes creatine in Group A, which means that it has a strong scientific evidence base for use in specific situations, provided that a specific intake protocol is followed [3].

Other bodies such as EFSA (European Food Safety Authority), the Australian Sports Anti-Doping Authority (ASADA), AEPSAD (Spanish Agency for Health Protection in Sport) and the American College of Sports Medicine also categorize creatine as an effective and safe supplement, despite the many myths and controversies that have existed [4].

The prevalence of creatine use among athletes and military personnel in survey-based studies is typically estimated to be approximately 15-40%. Its usage is more frequently observed among male strength/power athletes. In contrast, female athletes have reported a considerably lower rate of creatine use, ranging from 0.2 to 3.8% across various sports [5].

There are numerous studies that support the use of creatine as an ergogenic aid during anaerobic exercise. Previously, it was in this type of exercise that was mainly consumed [6]. Currently, creatine supplementation has increased in both anaerobic and aerobic exercise. It is used in all training modalities, as benefits have also been demonstrated in endurance sports by increasing glycogen storage and protein endurance [7]. However, this evidence is less or not well known in endurance performance, defined as large muscle mass activities that are cyclical in nature and have a duration longer than 3 min [6].

Thus, the aim of this review is to evaluate the potential benefits of creatine as a nutritional supplement during endurance exercise, as well as identify the potential mechanisms may influence according to the evidence shown in the studies published to date.

Creatine metabolism

Creatine is a non-protein amino acid compound present mostly in muscle cells (~95%), but also in the brain and testes. It can be obtained through dietary sources too, such as seafood, red meat, and poultry. About two-thirds of intramuscular creatine is phosphocreatine (PCr) and the remainder is free creatine. Total creatine storage in muscle varies between individuals, with the average being around 120 mmol/kg dry muscle mass. However, it appears that in most individuals the maximum storage is approximately 160 mmol/kg dry muscle mass [3,5].

It is notable for its energetic function, providing immediate energy for the muscle to respond to short duration, high intensity exercises. Creatine exhibits a high rate of energy production, but the muscle's storage capacity is limited, allowing for approximately 8-10 seconds of maximal exercise [3].

It combines with a phosphate group to form PCr via the enzyme creatine kinase (CK). During intense exercise, the energy released from the hydrolysis of PCr to creatine and phosphate can be used to resynthesize adenosine triphosphate (ATP), which is the main source of energy for muscle cells. In addition, the CK/PCr system helps transport energy from the mitochondria to the cytosol [5].

Some of the intramuscular creatine is degraded to creatinine and excreted in the urine (1-2%). The body needs to replenish about 1-3 g of creatine daily to maintain normal levels. Half of the daily requirement is usually obtained from the diet, while the remainder is synthesized in the liver and kidneys from arginine, glycine and methionine [5].

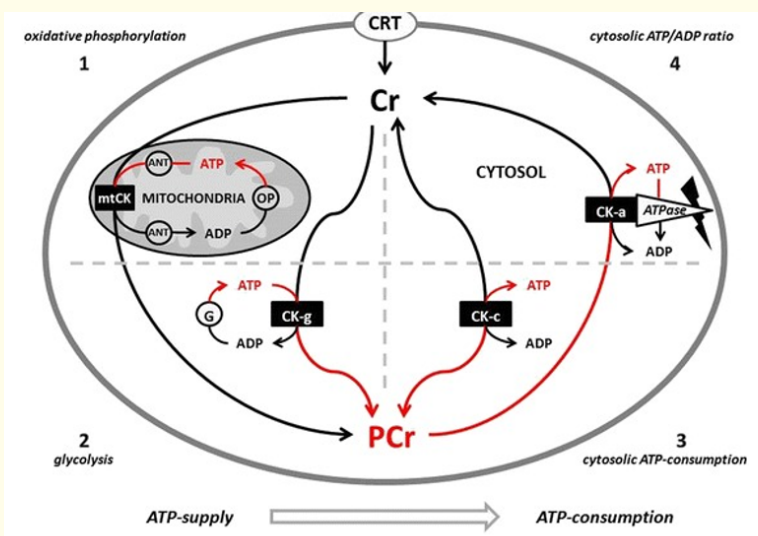

Figure 1: Proposed Creatine Kinase/Phosphocreatine (Ck/Pcr) Energy Shuttle. Crt: Creatine Transporter; Ant: Adenine Nucleotide Translocator; Atp: Adenine Triphosphate; Adp: Adenine Diphosphate; Op: Oxidative Phosphorylation; Mtck: Mitochondrial Creatine Kinase; G: Glycolysis; Ck-G: Creatine Kinase Associated With Glycolytic Enzymes; Ck-C: Cytosolic Creatine Kinase; Ck-A: Creatine Kinase Associated With Subcellular Sites Of Atp Utilization; 1 – 4 Sites Of Ck/Atp Interaction. From Kreider And Jung.

Some people are deficient in creatine synthesis due to inborn errors in the enzymes responsible and are therefore dependent on dietary intake to maintain normal levels. Vegetarians, in general, have lower intramuscular creatine stores (90-110 mmol/kg dry muscle) and in consequence may derive greater benefit from creatine supplementation. On the other hand, larger athletes performing intense training may require 5-10g/day of creatine to maintain optimal body creatine stores. Also, individuals with certain clinical conditions may need higher doses of creatine (10-30 g/day) to compensate for deficiencies in creatine synthesis and/or provide therapeutic benefit in various disease states [5].

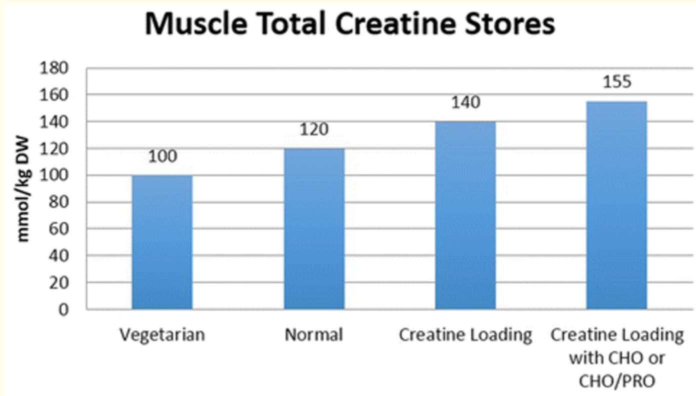

Figure 2: Approximate Muscle Total Creatine Levels In Mmol/Kg Dry Weight Muscle Reported In The Literature For Vegetarians, Individuals Following A Normal Diet, And In Response To Creatine Loading With Or Without Carbohydrate (Cho) Or Cho And Protein (Pro). From Kreider And Jung.

Types of creatine. creatine monohydrate

The EFSA warns of the importance of the composition of the supplement, avoiding impurities such as creatinine, dicyandiamide, dihydro1,3,4-triazine, heavy metals, mercury, cadmium, lead, or arsenic among others, to prevent the occurrence of adverse effects. Creatine is not commercialized in its pure state due to its instability. The water molecule provides stability, so creatine monohydrate is the most used form. It is usually consumed in powder form [4].

Creatine monohydrate contains 88% creatine and 12% water. As well as being the most studied, it is the most economical, although it can cause fluid retention and gastrointestinal discomfort, and some people are even non-responders. The purest type of creatine is alkaline or "buffered", it is resistant to the acid pH of the stomach, so it reaches the blood in a pure state and the muscle takes full advantage of it. As it is more easily absorbed, a smaller dose is needed, so it does not produce as much fluid retention or gastrointestinal discomfort, but its disadvantage is that the price is higher compared to creatine monohydrate [4].

In addition to these two main forms, there are creatine derivatives, such as hydrochloride, creatine citrate, creatine nitrate, creatine serum, creatine ethyl ester, creatine malate, creatine phosphate or creatine gluconate. But these forms have been less studied and do not have as much scientific evidence as creatine monohydrate [1,4].

Materials and Methods

A literature review was carried out through various search engines such as "Google Scholar", "PubMed", "Scopus" or "Scielo", in which scientific articles were found with information of interest using keywords such as "creatine", "supplement", "sport", "exercise", "resistance training", "endurance" or "ergogenic aid", both in English and Spanish, either separately or in different combinations.

Of all the results obtained in the search, only articles in English and Spanish published from 2018 to 2023 were selected, apart from some previous studies that were considered relevant to the work. The most recent studies were prioritized, mainly reviews, medical journals, guidelines of sports and some meta-analyses.

Results and Discussion

Supplementation protocol

A normal diet providing 1-2 g of creatine per day will have a 60-80% saturation of muscle creatine reserves, so that an increase in muscle creatine and PCr of 20-40% can be achieved by dietary supplementation. According to the results of the different studies found, the most effective way to achieve this is by performing a loading phase with the intake of 5 g of creatine monohydrate (or 0.3 g/kg body weight) four times a day for a period of 5-7 days [5].

Once muscle creatine stores are fully saturated, an intake of 3-5 g/day is usually sufficient to maintain them. Accompanying creatine intake with carbohydrate and protein has been shown to promote greater creatine retention. An alternative supplementation protocol is to ingest 3 g/day of creatine monohydrate for 28 days, although this would result in a gradual increase in muscle creatine content compared to the faster loading method and therefore may have less effect on exercise performance and/or training adaptations until creatine stores are fully saturated. Studies show that once muscle creatine stores are increased, it will typically take 4-6 weeks for them to return to their initial concentration. In addition, it has been recommended that, due to the health benefits of creatine, people should consume around 3g/day of creatine in their diet, especially as they age. There is no evidence to suggest that muscle creatine levels fall below baseline after stopping creatine supplementation; therefore, it does not appear that in the long-term endogenous creatine synthesis is reduced [5,8].

In the initial days of creatine supplementation, individuals may experience a noticeable increase in body weight, often by several kilograms. This effect is primarily linked to the osmotic stimulation of water retention within cells and surrounding tissues. Additionally, there may be secondary contributions from protein and/or glycogen accretion, which together account for the observed increase in body weight during this early phase of creatine supplementation [8].

In terms of the response to creatine supplementation, there has been a large individual and great individual variability, with high and low responders [9]. Approximately 30% of individuals who use creatine supplements do not experience sufficient increases in creatine levels to enhance their athletic performance. This variation is influenced by the individual's initial phosphocreatine stores, as those with higher phosphocreatine levels may exhibit lower increases in creatine with supplementation. As a result, individuals who are less trained or at the beginning of their training season tend to benefit the most from creatine supplementation [4,10].

Furthermore, there is evidence of variability in intramuscular creatine accumulation based on gender and age. Women tend to have higher concentrations of creatine in their muscles compared to men, while creatine levels decrease with age [4]. However, the exact reasons for these gender and age-related differences in creatine accumulation are not fully understood.

In summary, the response to creatine supplementation can differ greatly among individuals, and those with lower initial phosphocreatine stores or who are less trained may experience the most significant performance benefits. Additionally, gender and age can also influence intramuscular creatine levels, with women generally having higher concentrations and creatine levels declining with age [9].

Creatine during endurance training

Creatine supplementation is also associated with improved performance in various sporting events, including sprinting, middle distance, team sports and high-intensity interval training (HIIT) within endurance sports. Performance enhancement is attributed to increased phosphocreatine resynthesis and muscle creatine content [4,9].

Despite the well-accepted role of creatine in enhancing performance, there has been limited research on its impact on training adaptations [9]. However, there are several potential mechanisms by which creatine supplementation may affect training adaptations: 1) Increased exercise intensity: creatine supplementation may increase exercise intensity, which is a crucial factor for training-induced improvements in mitochondrial respiration. By enhancing exercise intensity, it can offer additional benefits for endurance training, adaptation, and performance. 2) Participation in aerobic metabolism: besides its primary role in forming PCr, creatine may also participate in aerobic metabolism by connecting ATP production sites (glycolysis and oxidative phosphorylation) with subcellular ATP utilization sites (ATPases). This could lead to improved mitochondrial respiration, particularly in slow-twitch muscle fibers, potentially allowing greater work to be completed during training sessions and reducing oxygen cost during submaximal exercise. 3) Antioxidant actions: creatine has shown antioxidant properties, which can reduce the formation of reactive oxygen species (ROS), oxidative DNA damage, and lipid peroxidation after exercise. These actions may affect exercise-induced cell signaling and contribute to better training adaptations. Overall, while creatine supplementation has been extensively studied for its performance-enhancing effects, further research is needed to fully understand its impact on training adaptations in endurance sports [9].

Two studies conducted on active men who engaged in 4 weeks of HIIT while taking either creatine (10g/day) or a placebo reported significant improvements in critical power and ventilatory threshold in the creatine group, but not in the placebo group. However, there were no significant differences between the groups for variables such as VO_{2peak}, time to exhaustion at VO_{2peak}, anaerobic working capacity, or total work done during a ride to exhaustion at 110% of peak aerobic power. Likewise, similar research in active women did not find any differences in exercise-induced improvements in VO_{2peak}, ventilatory threshold, or 2-km time-trial performance (~2 min). It is worth noting that this study did not control for the menstrual phase, which has been shown to impact the blood lactate response to high-intensity exercise [9].

As with many other supplements, isolating the specific effects of creatine on performance from its impact on adaptations to training can be challenging. In situations where no training is involved, 5–7 days of creatine loading has shown increases in power at the lactate threshold and supra-maximal time to exhaustion, as well as reduced VO_2 during submaximal cycling [9].

In summary, creatine supplementation seems to have benefits in endurance exercise, although more studies are still needed to specify which parameters are improved in each type of exercise, also considering the influence of other factors such as age or gender.

Creatine timing

It appears that creatine supplementation before and after endurance training sessions has a positive effect on lean tissue mass and strength. Several meta-analyses have indicated that post-exercise creatine intake may produce greater muscle benefits compared to pre-exercise creatine intake [11]. Some research demonstrated that 5 g of creatine monohydrate ingestion after exercise resulted in greater improvements in body composition, specifically gains in fat-free mass and loss of fat mass, compared to pre-exercise creatine ingestion. However, this finding was not supported by a study in older adults. On the other hand, Candow et al. observed that 32 weeks of creatine supplementation (0.1 g/kg) in healthy older adults immediately after resistance training led to greater lean muscle mass compared to supplementation immediately before resistance training or resistance training alone [8].

The mechanism behind the greater lean muscle mass from post-exercise creatine supplementation was speculated to be related to increased skeletal muscle blood flow during resistance training, leading to higher creatine transport and accumulation in exercising muscles. However, it is essential to note that in this study, both pre and post-exercise creatine supplementation during resistance training increased upper and lower body strength compared to resistance training alone, with no significant difference between the two timing groups [8].

It is known that the highest plasma peak occurs approximately one hour after creatine intake, so the type of sport practiced will be another factor that will determine the best time for supplementation. Thus, for short, intense strength exercises, it is consumed during the first moments of training; for longer workouts, during the same workout and, for endurance exercises with a large anaerobic component (moderate intensity and greater volume), immediately afterwards [4].

More research is needed to thoroughly investigate the issue of timing of creatine supplementation, particularly with higher dosages, and its effects on muscle creatine content, body composition, and high-intensity exercise performance. Additionally, it is crucial to highlight that exercise can enhance the effectiveness of creatine storage in skeletal muscle due to increased muscle blood flow during exercise. Furthermore, co-ingestion of creatine with either carbohydrate (94g per 5g of creatine) or a combination of carbohydrate plus protein (47g + 50g per 5g of creatine, respectively) has been shown to enhance muscle creatine storage via an insulin-stimulating effect [8].

Adverse effects or contraindications

In general, creatine intake following established protocols is safe. There are some studies that suggest that creatine may increase the risk of musculoskeletal injury, dehydration, muscle cramps, gastrointestinal discomfort or impair renal function. However, these studies are few and insignificant [4,8,12].

The most common adverse effect is muscle cramps, which may be due to dehydration or disruption of the water balance that can be caused by the substance but is easily remedied by drinking more water. The potential damage to kidney function that creatine supplementation can potentially cause by increasing urinary creatinine excretion, which is an indicator of kidney function, is often questioned, but this only occurs if the person receiving the supplementation has previous kidney damage. On the other hand, it seems that, by increasing muscle hypertrophy, stiffness increases, so that some studies have shown that it decreases the range of extension and abduction of some parts of the body, which is counterproductive in sports where flexibility may be an important factor. In terms of body composition, creatine appears to increase total body mass and lean body mass. That is, being hydrophilic, the changes are due to changes in fat-free mass, but with respect to fat mass there seems to be controversy, as in some studies of creatine supplementation, fat mass remains stable while in others it decreases [12].

It is important to note that creatine loading may result in an increase in body mass due to water retention. However, despite this ~2.5% increase in body mass, well-trained cyclists subjected to creatine and carbohydrate loading reported increased power output during sprint efforts within a simulated 120 km time trial, with no difference in simulated uphill cycling compared to placebo [9].

Due to inter-individual variability in the action of creatine, these adverse effects may vary depending on the target population. Polymedicated individuals, who tend to be older, are more vulnerable and at greater risk of adverse effects of creatine; however, there are few scientific studies that consistently establish these potential effects. In people with genetic deficiencies or mutations, the scientific evidence is stronger. In other cases, such as postmenopausal women, isolated adverse effects may occur, usually gastrointestinal distress and muscle cramps [12].

Other benefits in sports

Recent studies have shown several additional applications of creatine supplementation that can be advantageous for athletes and individuals seeking to enhance their training adaptations. Some of these applications include [5]

- Enhanced recovery. It has been shown to enhance glycogen loading in muscles, which enhances energy availability during high-intensity exercise and may lead to improved performance, especially when creatine is combined with carbohydrates and protein. Other studies show that creatine supplementation can reduce inflammation and the release of muscle enzymes after intense exercise. This can contribute to a faster recovery process and reduce muscle soreness. Finally, Athletes who supplement with creatine tend to have better tolerance for high training volumes and overreaching. This increased capacity for training can lead to more effective adaptations and improved overall recovery.
- Injury prevention. Research has indicated that athletes who incorporate creatine supplementation into their training and competition routines tend to have a lower incidence of injuries compared to athletes who do not use creatine as part of their dietary supplementation. In a number of studies, individuals who use creatine experience lower incidence rates of various conditions such as muscle cramping, heat illness/dehydration, muscle tightness, muscle strains/pulls, non-contact injuries, and total injuries/missed practices compared to those who do not take creatine.
- Enhanced tolerance to exercise in the heat. Creatine monohydrate, like carbohydrates, possesses osmotic properties that aid in retaining a small amount of water in the body. As a result, creatine supplementation, whether taken alone or in combination with glycerol, can serve as an effective nutritional hyper-hydration strategy for athletes involved in intense exercise in hot and humid environments. This approach can help reduce the risk of heat-related illnesses in such conditions.

- Enhanced rehabilitation from injury. Due to its reported ability to enhance muscle mass and strength gains, creatine supplementation has garnered interest in its potential effects on muscle atrophy rates during limb immobilization and rehabilitation. Although not all studies demonstrate consistent benefits, evidence suggests that creatine supplementation may be beneficial in reducing muscle atrophy during immobilization and aiding in recovery during exercise-related rehabilitation in certain populations. As a result, creatine supplementation holds promise in assisting athletes and individuals with clinical conditions in their recovery from injuries.
- Brain and spinal cord neuroprotection. The risk of concussions and/or spinal cord injuries (SCI) in athletes engaged in contact sports has raised significant concern worldwide, both among sports organizations and the general public. Recent studies have presented compelling evidence suggesting that creatine supplementation may play a role in mitigating damage caused by concussions, traumatic brain injuries (TBI), and/or spinal cord injuries (SCI). This emerging research highlights the potential therapeutic effects of creatine supplementation in protecting athletes from the adverse effects of these traumatic injuries.

Other potential medical uses of creatine

In addition to the benefits in sport area, numerous researchers have been exploring the potential therapeutic advantages of creatine supplementation across various clinical populations. Conditions where benefits from creatine intake may be observed include creatine deficiency syndromes, neurodegenerative disease, ischemic heart disease, ageing and pregnancy [5].

Conclusion

Creatine, consumed in the form of creatine monohydrate, is a safe and effective ergogenic aid not only in strength/power activities, but also in endurance activities, if a specific supplementation protocol is followed, as it has been seen which increases the resynthesis of phosphocreatine and its muscular content. It also seems that it could improve adaptation to training through different mechanisms including an increase in exercise intensity, the role of creatine in aerobic metabolism and its antioxidant properties. These benefits appear to be greater when taking the supplement after training.

On the other hand, other applications of creatine have recently been identified that improve recovery, warm-up exercise tolerance, injury prevention, rehabilitation, and neuroprotection of the brain and spinal cord, as well as other potential medical uses in different clinical contexts. Despite the myths and controversies that have existed around the consumption of creatine, the appearance of adverse effects derived from this supplementation is rare.

The results obtained in this paper support the use of creatine in endurance sports, but more studies are needed to clarify which parameters improve depending on each type of exercise, considering the influence of other factors such as age or gender, as well as how to better understand the impact it has on training adaptations.

Conflict of Interest

The author declares no conflict of interest.

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