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Creatine supplementation in sport and medicine - a review of recent reports

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Abstract:

Introduction and objective

The role of creatine as a dietary supplement to enhance ergogenic performance in strength sports is well established and researched, both among professionals and amateurs. In this article, we will focus not only on analysing creatine supplementation as an agent used in sport, but also as a supplement that may find a medical application.

Review methods

A literature search of Google Scholar and PubMed medical databases from the last eight years (2016-2024) was performed.

Articles were searched in English using the following keywords: Creatine, Supplementation, Sport, Athletes

Abbreviated description of the state of knowledge

The role of creatine in strength sports is firmly established. Recent reports present creatine as an agent with many other uses. Endurance sports, rehabilitation or injury prevention are just a few of the areas mentioned where creatine finds its use. In the medical sciences, it is of interest to fields such as neurology, psychiatry, cardiology, geriatrics or rheumatology. Although many misconceptions have grown up around creatine, one of the best confirming its safety may be the fact that there are reports of benefits for pregnant women and the foetus.

Summary

Research shows the extensive use of creatine in various sports and medical fields. The high safety profile and efficacy in resistance training has been confirmed and is now known to an increasing number of people, not only in competitive sport. New promising reports in many areas of medicine and sport are described in an increasing number of reports, with the need for further research, often using more widely available modern technologies.

Keywords: Creatine, sport, activity and health

Introduction

Creatine (methylguanidinoacetic acid) is an endogenously formed compound that is synthesised mainly in the kidneys and liver from the amino acids glycine, methionine and arginine. Exogenously, it is supplied to the body especially with meat: especially red meat, and also in

seafood. The vast majority of creatine is found in skeletal muscle (approximately 95 %), with the remainder of the compound found in the testes and brain (approximately 5 %). [1] [2] Creatine's primary role in the body is to resynthesise adenosine triphosphate (ATP) by transferring the N-phosphoryl group from phosphoryl-creatine (PCr) to adenosine diphosphate (ADP), as well as buffering energy by its transfer from the mitochondria to the cytosol of the cell. It also reduces the leakage of calcium ions (Ca^{2+}) from the sarcoplasmic reticulum, which translates into increased muscle cell strength. Creatine also has antioxidant properties, reducing reactive oxygen species by coupling them to ATP. [3] The structure of the creatine molecule is shown in Figure 1.

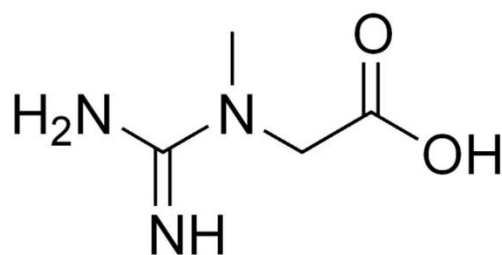


Fig. 1. Chemical structure of the creatine molecule.

Due to the beneficial effects of the mechanisms described above, creatine is one of the agents that athletes at both the professional and amateur level reach for. It is one of the best researched compounds used in sport with documented benefits, such as increased physical performance and decreased protein breakdown - leading to increased muscle mass. [4] Creatine supplementation is most strongly associated as a measure used to benefit during resistance training, where its position as a muscle gainer is firmly established. It also improves the performance of the athletes using it during intensive, short-duration exercises such as sprinting (100 m, as well as multiple sprints) and has been used for a long time. Despite the widespread opinion of its indifferent or even harmful role in other forms of exercise (e.g. endurance sports), its usefulness as a dietary supplement that may also have a beneficial effect in endurance sports is also being increasingly analysed. [5] It may be quite surprising how much research in recent years has been devoted to the effect of creatine as a supplement with beneficial effects on central nervous system (CNS) function, especially in the elderly population. [2][3][6] This is not the only age group benefiting from supplementation with this compound. Despite the fact that most studies have been conducted on adult men, ergogenic benefits have also been shown in women, as well as in children and adolescents. [4] Creatine benefits have also been reported among

vegetarians [7] and may have good effects in people being treated for depression, among others. [8] Furthermore, it has shown promising results in studies in patients with type two diabetes and also in people with insulin resistance. [9]

In a 2021 article published by Jose Antonio and colleagues, an attempt was made to answer the most common questions and concerns regarding creatine supplementation. As stated, despite the large number of peer-reviewed publications on the subject, questions still frequently arise regarding elementary issues, namely the safety and efficacy of taking creatine. It was pointed out that, apart from the population most commonly identified with creatine use, i.e. athletes and amateurs training to increase muscle mass, it also has a positive effect on recovery processes and training performance. Issues of beneficial effects related to musculoskeletal function in subjects, especially in the older age group, were raised, but the potential benefits of creatine use in younger age groups: children and adolescents, as well as women, were pointed out. The most relevant issues of taking this supplement were explained, such as: At recommended doses (3-5 g/day or 0.1 g/kg body weight/day), creatine is relatively well tolerated and effective, and taking higher doses, the so-called loading phase, is not necessary. When used in recommended doses, it does not cause renal dysfunction in healthy individuals and rarely causes water retention. It has been shown that there is no increase in body fat with supplementation. No correlation has been found between creatine use and alopecia. No advantage of other forms of creatine over monohydrate has been found. [1] Creatine supplementation strategies are presented in Table 1.

Tab. 1. Creatine supplementation strategies.

STRATEGIES FOR CREATINE SUPPLEMENTATION	
SATURATION PHASE	PERMANENT SUPPLEMENTATION
Saturation (charging) phase 20-25 g/day for 5-7 days	3-5 g/day each day until discontinued
Sustaining phase 3-5 g/day each day until discontinued	

The following article reviews multi-ingredient pre-workout supplements containing substances such as caffeine, beta-alanine or creatine in different proportions, among others. The authors devote a great deal of attention to the synergistic effects of the individual substances, while analysing each of them separately. They draw attention to the need to analyse the composition of individual preparations and the percentage of substances. In the context of creatine, they conclude that its use is safe even in a regimen that includes a 'loading' phase, consisting of

consuming large amounts of the supplement (20 grams/day or 0.3 grams/kilogram of body weight/day) followed by supplementation at doses of approximately 3-5 grams per day. They show that intake of creatine in appropriate doses, along with other supplements for at least 28 days is likely to be sufficient to improve exercise performance. [10]

In the article below, the authors focus on assessing the safety profile of creatine in the renal context. They conclude that the deterioration of renal function shown in several animal studies was not reflected in clinical studies with a control group. Creatine intake may lead to an increase in serum creatinine levels in some individuals, but this is not the same as renal dysfunction, as creatine is converted spontaneously to creatinine. They indicate that in studies assessing renal function using methods considered reliable, creatine supplementation is safe in healthy individuals, but further studies are needed in patients with pre-existing renal disease. [11]

The authors of the following article analysed studies of direct measures of skeletal muscle growth in individuals using resistance training and creatine supplementation. In a study including methods such as ultrasonography, computed tomography and magnetic resonance imaging, they found a slight increase in direct measures of skeletal muscle hypertrophy (especially in the younger population) in both the lower and upper body. [12]

Another study demonstrating the direct effects of creatine and its impact on training performance was conducted by Massimo Negro and colleagues. After administration of a creatine-based multi-ingredient pre-workout supplement, maximal force production and fatigue performance during resistance exercise were analysed. By monitoring blood lactate levels, task completion time and superficial electromyographic signals, volunteers who consumed a creatine-based multi-ingredient pre-workout supplement or placebo before exercise were compared. The creatine-enriched formulation was shown to result in greater improvements in superficial electromyographic descriptors, exercise fatigue and task completion time compared to placebo. [13]

In the following article, the authors, while mentioning the effectiveness of creatine in resistance sports, analyse its use as a supplement that can be applied in endurance sports. As a definition, they take endurance performance understood as the activity of many muscle groups, which is cyclic and lasts more than (approximately) 3 minutes. They mention its beneficial effects as a means of reducing oxidative stress causing inflammation. At the same time, they recall the increase in muscle mass, which in endurance sports can have negative effects. For those supplementing with creatine, they find that the results of time trials are mixed depending on the discipline, and they see benefits in disciplines where 'endurance spurts' are important, i.e. those

in which athletes have to show the highest intensity of effort, e.g. during the final phase of a race. They cite sports such as rowing, mountain biking and cross-country skiing, among others, as potentially applicable. [5]

Further researchers are attempting to answer a question that comes up very often in the context of creatine use, namely: when is it best to take it and is it really that important to take it before, after or even during exercise.

In their study, Darren G. Candow and colleagues conclude that there is a lack of conclusive data regarding the greater effectiveness of creatine intake in a specific pattern. Mentioning different supplementation regimens, such as daily intake vs. intake only on training days, staggered vs. occasional intake immediately before/after training, they are unable to identify the most effective and preferred method. They show a small number of studies, with methodological limitations (e.g. no use of placebo) and indicate the need for further studies. [14]

Other researchers also show a lack of consensus in relation to the best time to take creatine in relation to training. They mention the fact that, although there are reports indicating the benefits of taking it post-exercise, methodological limitations make it impossible to draw practical conclusions. Based on the current research, it is not possible to conclude which moment of supplementation is recommended and further scientific studies, which have been reliably conducted, are needed. [15]

An interesting analysis was undertaken by researchers led by Annamaria Del Franco, who undertook a holistic presentation of the role of creatine in cardiac energy metabolism and an assessment of myocardial creatine deficiency and clinical evaluation of its use in patients with heart failure. Reduced creatine content is a characteristic feature of patients with advanced heart failure. However, the benefits of creatine and phosphocreatine supplementation have not been clearly demonstrated. The authors point to the need for randomised trials and point to the important role of magnetic resonance spectroscopy as a non-invasive means to estimate the energy response of applied metabolic therapies. In addition, they state that future studies should focus on creatine supplementation in patients with heart failure in whom creatine deficiency has been assessed, by analysing the measurement of absorbed creatine versus therapeutic dose. [16]

In the following article, the authors address the benefits of creatine supplementation in vegetarians in relation to the non-diet group. Due to the natural occurrence of creatine in meat, vegetarians often suffer from creatine deficiency, which means that supplementation can have

a measurable effect. In the studies analysed, creatine intake was shown to contribute to an increase in lean body mass (especially in type II muscle fibres) and also muscle strength and endurance. In addition, it had a beneficial effect on brain functions such as memory and intelligence and also caused an increase in insulin-like growth factor-1. The authors conclude that creatine supplementation in vegetarians may have numerous benefits.[7]

Creatine has also been assessed as a factor that may affect the body's sugar metabolism. The researchers first highlight the documented role of creatine in resistance training and also mention the increasing number of reports of its potential in neurodegenerative diseases or muscular dystrophy. They present evidence that creatine supplementation can improve glucose metabolism in both healthy individuals and those with known insulin resistance (including patients with type two diabetes). Creatine itself has been shown to increase insulin secretion (in in vitro studies), increase muscle glycogen stores and also reduce hyperglycaemia in animals. The benefits of supplementation are particularly noticeable when it is combined with physical training. They point to the increased transport of glucose into muscle cells via the glucose transporter type 4 (GLUT-4) to the sarcolemma as a direct mechanism for the beneficial effect when combined with exercise. As a conclusion, despite promising research on the role of creatine as a factor influencing glycaemic control, they state that further research is needed. [9]

In the study, led by Scott C. Forbes, the researchers focus on the role of creatine as a factor affecting brain function. They show that creatine supplementation, together with guanidinoacetic acid, has the effect of increasing the amount of creatine contained in the human brain. It may contribute to alleviating symptoms of depression, have a beneficial effect on cognitive function, and may also be beneficial in alleviating symptoms associated with conditions following central nervous system injury, such as concussion, among others. They highlight the rationale for further research on creatine supplementation in the context of anxiety disorders, post-traumatic stress disorder and neurodegenerative diseases. [8]

In the literature reviewed, much more information can be found on the potential role of creatine as a beneficial factor influencing central nervous system function.

In a subsequent article, the authors demonstrate that in healthy individuals, creatine monohydrate supplementation has a beneficial effect on memory. Among all age groups, the analysis showed that the most beneficial effects were found in the elderly, especially in those aged 66-76 years. [6]

Creatine supplementation may have a positive effect on cognitive function was assessed in a study by Hamilton Roschel and colleagues. They assessed that creatine intake may have a

positive effect on cognitive functions, especially if their impairment is triggered by acute stressors such as sleep deprivation or exercise, among others. In addition, a beneficial role has been found in Alzheimer's disease, senior citizens, depression or mild traumatic brain injury. [3]

The multifactorial role of creatine as a dietary supplement is described in the following article. The authors indicate that it can have an impact on injury prevention, acceleration of post-exercise recovery, beneficial effects on thermoregulation and even rehabilitation. They mention the use of creatine in the treatment of neurological conditions such as Parkinson's disease, Huntington's disease, muscular dystrophy, as well as fibromyalgia or osteoarthritis. They touch on the benefits of supplementation in depression, as well as pregnancy, showing that creatine supplementation can benefit both the mother and the foetus. [2]

The broad population benefits of creatine use are also described in other articles, where the role of creatine supplementation is demonstrated and described as safe for both short- and long-term intervals, for both sexes and virtually all age groups. [17]

In the elderly population, the role of creatine supplementation has been confirmed not only as a means of directly increasing muscle strength and muscle volume. Creatine may have an effect on inhibiting sarcopenia and also indirectly increasing the ability to perform activities of daily living and thus functionality in older people. [18] Among the elderly, creatine supplementation together with resistance training may have a better effect in preventing sarcopenia than resistance training alone, and thus have an impact on healthy ageing. [19]

The benefits of creatine supplementation can be noted not only as a factor affecting muscle strength or reducing the risk of muscle damage during training. [20] Creatine supplementation has applications and benefits throughout life, for example as a dietary supplement that promotes faster recovery from injury and in the management of chronic diseases. [4]

Conclusions

In summary, creatine, as a dietary supplement in recent reports, is firmly established in strength training, as evidenced by numerous scientific studies. However, the potential benefits of its use are proving to be, or may prove to be in the future, much broader. Studies in virtually every age group, from pregnant women to children, healthy adults, people with multiple medical conditions or seniors, prove the safety and numerous benefits of its use. Intensive research as an adjunct to therapies for disorders of the central nervous system (e.g. Alzheimer's disease) or for mental health (e.g. depressive disorders) is showing promising results. Creatine may also

prove important as an adjunct therapy in patients with sugar management disorders such as insulin resistance or type two diabetes. Creatine supplementation is also used in some endurance sports, may accelerate rehabilitation and contribute to injury prevention especially in older age groups. Of interest is its important role in special populations such as vegetarians, where its numerous benefits have been proven. Studies on supplementation in patients with heart failure also appear promising and, thanks to modern technologies such as magnetic resonance spectroscopy, among others, may find clinical application in the future. One may be tempted to conclude that it is wrong to simplify the role of creatine as a supplement used, by professionals and amateurs alike, exclusively in resistance training. Its applications are or have promising prospects of proving to be an agent used far more widely, not only in sport, but also in many areas of medicine.

Disclosures:

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