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Introduction

Health practitioners are frequently questioned by patients about the effectiveness and safety of various dietary supplements promoted as performance-enhancing ergogenic aids. Creatine monohydrate has received much attention in this regard, enjoying widespread use across the North American athletic population, with U.S. retail sales of the product reaching $200 million per year as of 1998. Creatine is one of the few supplements in sports nutrition with extensive research to support its performance-enhancing claims. As such, practitioners should be aware of the research pertaining to its safe and effective application for athletes, and emerging studies implicating its potential role as an adjunctive treatment in the management of certain cardiac conditions, neurodegenerative diseases, musculoskeletal rehabilitation, and as an anti-aging intervention for older subjects.

Physiological Considerations

It is widely accepted that creatine supplementation can increase muscle strength and mass. Creatine is an amino acid that is stored in muscle in the form of creatine phosphate. During explosive or intense exercise, creatine phosphate is broken down by a specific enzyme to yield creatine, phosphate and free energy. Free energy released from the breakdown of creatine phosphate is used to regenerate ATP, the fuel that powers muscle contraction.

The normal daily requirement for creatine is about two grams for a person weighing 70 kg. Animal protein (especially meat) normally provides at least half that amount, with approximately one gram per day synthesized by the liver. A half-pound of raw meat contains about one gram of creatine, but fish is also a good source.

A number of recent studies have demonstrated that short-term creatine supplementation increases creatine phosphate stores in skeletal muscle by 10 to 40 percent. In combination with proper training, creatine supplementation leads to an increase in muscle mass, thought to occur from increased protein synthesis, as
the muscle lays down more contractile myofilaments (protein bands that contract and generate force). Increased muscular fluid retention may also participate in muscle volume gains with creatine use.\textsuperscript{5-7} Creatine has also been shown to provide antioxidant properties, which may be of some significance, as free radicals generated from exercise can affect muscle fatigue and protein turnover.\textsuperscript{24}

Creatine supplementation may also allow athletes to train harder (due to increased available energy for muscle concentration), promoting strength gains and increased muscle size due to hypertrophy (larger muscle fiber size).\textsuperscript{2,3}

The established protocol for creatine used by athletes involves a loading dosage of 20 to 25 grams per day for the first five to seven days. Typically, an athlete will mix a heaping teaspoon of creatine monohydrate crystals into a glass of juice to obtain about five grams of creatine. During the loading phase, the athlete does this on four or five occasions throughout the day to achieve an intake of 20-25 grams. After the loading phase is completed, the maintenance daily dosage is usually five to 10 grams per day. Recent reports suggest that taking creatine with glucose (a simple carbohydrate) may increase the amount of creatine absorbed by the muscles. As such, some manufacturers combine creatine with carbohydrates in a premixed product to help improve creatine delivery to muscles.\textsuperscript{25}

**Clinical Applications and Mechanism of Action**

1. **Increased Strength and Performance Athletes**

Several studies have shown that creatine supplementation improves performance in repeated bouts of high-intensity strength work and repeated sprints, which are primary determinants and requirements for many sports.\textsuperscript{8-14,16-18} In short, substantial evidence suggests that creatine supplementation can increase lean body mass, muscular strength and sprint power.\textsuperscript{24}

Significant gains in strength and lean mass often occur in the first six weeks of creatine supplementation, when combined with proper training and diet. In one study, college football players who took creatine supplements for 28 days during resistance and agility training had significant gains in lean mass when compared to players who took a placebo.\textsuperscript{15}

Individual response to creatine supplementation varies, but it is not uncommon to see a 5-10-pound increase in body weight within the first six weeks.
Approximately 80 percent of creatine studies have reported a performance-enhancing effect. This is quite impressive when you consider the fact that creatine is not structurally or functionally related to anabolic steroids, and that creatine supplements are not banned by the International Olympic Committee or the National Collegiate Athletic Association. Creatine use is based on the same principle as carbohydrate loading, in that an athlete is manipulating dietary intake to optimize muscle creatine phosphate stores for more explosive power and enhanced performance.

Athletes requiring repeated bouts of explosive power may also benefit from creatine supplementation, as demonstrated by M. Izquierdo, et al. Among other positive benefits revealed in their study of 19 trained athletes were that short-term creatine supplementation (20 grams per day for five days) enhanced repeated sprint performance and attenuated decline in jumping ability after repetitive high-power-output exercise bouts (MRPB). Similar results have been documented by G. Cottrell, et al., in subjects performing repeated sprint cycling. These studies have important implications for many sports, such as hockey; basketball; soccer; volleyball; lacrosse; football; tennis; and any sport requiring repeated bouts of all-out, lower-extremity, explosive power or jumps.

2. Neuromuscular Diseases

Creatine supplementation in humans has reportedly enhanced power and strength in normal subjects and in patients with various neuromuscular diseases. Clinical studies in patients with amyotrophic lateral sclerosis (ALS); Huntington’s disease; Parkinson’s disease; Duchenne muscular dystrophy; McArdle’s disease; and myasthenia gravis have shown that creatine supplementation can increase strength and thus provide symptomatic treatment and improved quality of life for many of these patients.

3. Heart Failure

Creatine supplementation has been shown to improve exercise capacity in patients with heart failure in some studies. Along with coenzyme Q10, hawthorn extract and L-carnitine, creatine is one of few natural health products that has been shown to reverse certain parameters of heart failure. As reported by K. Witte, et al., there is evidence for a possible role for micronutrient deficiency in heart failure, of which creatine may be one of the principal factors.

4. Musculoskeletal Rehabilitation
Creatine was shown to speed recovery of muscular power in a double-blind, placebo-controlled study involving 20 male and female students whose right legs were immobilized in casts for a period of two weeks. Those given creatine during and after leg immobilization displayed more muscular power and greater muscle size after three to 10 weeks of physical rehabilitation than did subjects who took the placebo.  

5. Anti-aging in Older Subjects

Creatine provided to active subjects over 70 years of age, and subjects 59-72 years of age, has resulted in significant gains in several indices of muscle performance, including maximal dynamic and isometric strength; lower body mean power; lower extremity functional capacity; fat-free mass; increased lean mass; and endurance power. These studies suggest that creatine may help to forestall or reverse muscular atrophy and progressive weakness that occurs during aging, and may be useful as an intervention to improve the ability of certain elderly individuals to perform functional living tasks, decreasing dependency and enhancing the quality of life.

Other studies have noted that younger individuals responded to creatine more efficiently than older subjects; muscular phosphocreatine stores were shown to increase, on average, by 35 percent in young subjects (<24 years of age) and seven percent in older subjects (<70 years of age) after five days of creatine supplementation (20 grams per day). As such, it may take longer to maximize stores in older subjects using creatine.

Absorption and Utilization

Creatine absorption from the intestinal tract is very efficient. Studies show that a 6-8-gm oral load results in approximately 50 percent of the ingested creatine being excreted in the urine. Thus, researchers are still working to identify the ideal single, daily and cumulative doses of creatine for various applications. Other studies demonstrate that a five-gram oral load of creatine, followed by 93-gram oral load of simple carbohydrate in solution (water) at 30 minutes post-creatine intake (four times per day), resulted in a 60-percent increase in total muscle creatine, compared to subjects ingesting the same amount in the absence of a simple carbohydrate drink. Subjects ingesting creatine and the simple carbohydrate drink had higher insulin levels, and significantly less creatine lost in their urine, indicating that higher insulin levels are likely a key to greater muscle uptake and utilization of creatine, and a reduction in urinary loss. Thus, it is accepted that creatine utilization is enhanced by concurrent ingestion of a simple carbohydrate drink (e.g.,
fruit juice).\textsuperscript{25}

Additionally, concurrent administration of creatine and glycogen has revealed that creatine enhances muscle levels of glycogen (glycogen supercompensation) beyond that attainable from glycogen loading alone. As supercompensation of muscle glycogen is also an ergogenic factor in exercise performance, the combination of creatine and carbohydrate loading appears to improve performance by increasing muscle creatine and muscle glycogen.\textsuperscript{27}

\textbf{Adverse Side-Effects and Toxicity}

As for the safety of creatine supplementation, a 1997 study showed that short-term creatine use (20 grams per day for five days) did not increase markers of kidney stress in five healthy men.\textsuperscript{13} A study comparing creatine users (for up to five years) to control subjects has shown that creatine users have no remarkable differences in their creatine, urea and plasma albumin clearances compared to controls. The researchers concluded that oral creatine supplements, regardless of length of use, did not induce detrimental effects in the kidneys of healthy individuals.\textsuperscript{29-31} To date, no liver abnormalities have been noted in short-term creatine challenge studies.\textsuperscript{30} However, individuals with pre-existing kidney disease should be cautious, as evidenced by the development of kidney dysfunction in a 25-year-old soccer player taking creatine who previously had been treated for focal segmental glomerulosclerosis of the kidney. His kidney function returned to normal after discontinuing creatine supplementation.\textsuperscript{28}

Some experts suggest that compulsory regular kidney and liver monitoring should accompany the use of creatine, due to the increased burden placed upon the liver and kidneys.\textsuperscript{30} As pointed out by other experts, creatine is normally found in cardiac muscle; brain; testes; and skeletal muscle - tissues that have been largely unstudied with respect to the effects of creatine.\textsuperscript{32} The U.S. Food and Drug Administration (FDA) has advised athletes to consult physicians or health care professionals before embarking on any scheme of creatine loading or supplementation.\textsuperscript{28} Nevertheless, few adverse side effects have been reported, despite its widespread use among young athletes. Other infrequently reported side-effects include gastrointestinal disturbances and muscle cramps.\textsuperscript{30}

In children and younger athletes, the safety of creatine supplementation has not yet been investigated. Until all safety issues have been evaluated, experts strongly recommend against the use of creatine among adolescent athletes.\textsuperscript{33}
Overall, creatine appears to be safe for healthy adults. It’s a low-molecular-weight compound that is excreted in the kidneys by simple diffusion. In the maintenance phase, athletes consume only slightly more creatine (3-5 grams per day) than is generally found in the diet, which is usually about two grams per day.\textsuperscript{10,11}

There are no well-known drug-nutrient interactions with creatine at this time.\textsuperscript{38}

Summary

Supplementation with creatine has been shown to improve various parameters of athletic performance and body composition in athletic subjects. It may also be of therapeutic value for a number of health conditions and used as an anti-aging intervention in older individuals. Debate continues over issues of long-term safety, whether or not there should be prescreening kidney filtration evaluation prior to introducing creatine supplementation, and minimum of age at which creatine can be safely administered. It is important to ensure that patients with a history of kidney disease or impairment avoid the use of creatine, and practitioners should be sure to address this question when it is being discussed. In my own practice, I discourage the use of creatine supplementation in athletic patients under the age of 16 or 17, who are seeking to improve their strength, muscle size or performance. This is a position I intend to maintain until further safety and toxicity studies are in place to show that a young, developing body can safely handle this intervention without undue side-effects, including of renal and liver damage.

Please take time to listen to Dr. Meschino’s interviews on ChiroWeb.com. The subjects of the first three are: Combining Traditional, Complementary and Natural Interventions, The Benefits of Melatonin, and Using Natural Remedies to Manage Women’s Health Issues. Each interview is packed with important information available to you and your patients. You can listen to the interviews at www.chiroweb.com/audio/meschino. There is a link on the directory page for your feedback.

References


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