CREATINE SUPPLEMENTATION: ITS APPLICATION IN SPORTS PERFORMANCE, THE TREATMENT OF HEALTH CONDITIONS AND SAFETY PROFILE

JAMES MESCHINO DC, MS, ND

Introduction

Health practitioners are frequently questioned by their athletic patients about the effectiveness and safety of various dietary supplements promoted as performance-enhancing ergogenic aids. Creatine monohydrate is one of the sports supplements that has received much attention in this regard and has been shown to enjoy widespread use across the North American athletic population, with U.S. retail sales of the product reaching $200 million per year as of 1998. (1) Creatine is one of the few supplements in the sports nutrition area, where extensive research exists to support its performance-enhancing claims. As such, practitioners should be aware of the research pertaining to its safe and effective application for athletes, as well as the newly 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 now widely accepted that creatine supplementation can increase muscle strength and mass. (1,2,3,4) Creatine is an amino acid that is stored in muscle in the form of creatine phosphate. During explosive or intensive exercise, creatine phosphate is broken down by a specific enzyme to yield creatine, plus phosphate, plus free energy. The free energy released from the breakdown of creatine phosphate is used to regenerate ATP, which is the fuel that powers muscle contraction. (2)

The normal daily requirement for creatine is about 2 grams for a person weighing 70 kg. Animal protein (especially meats) 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 1 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% (3). In combination with proper training, creatine supplementation leads to an increase in muscle mass, which is thought to occur from increased protein synthesis, as the muscle lays down an increased number of contractile myofilaments (protein bands that contract and generate force). Increased muscular fluid retention may also participate in muscle volume gains with creatine use. (5,6,7) Creatine has also been shown to provide antioxidant properties. This may be of some significance as free radicals generated from exercise can affect muscle fatigue and protein turnover. (24)

It also appears that creatine supplementation may allow athletes to train harder (due to increased available energy for muscle concentration), which promotes strength gains, and increases muscle size due to hypertrophy (larger muscle fiber size). (2,3)

The established protocol for creatine supplementation used by athletes involves a loading dosage of 20 to 25 grams per day for the first 5 to 7 days. Typically an athlete will mix a heaping teaspoon of creatine monohydrate crystals into a glass of juice to obtain about 5 grams of creatine. During the loading phase, the athlete does this on 4 or 5 occasions throughout the day to achieve an intake of 20-25 grams. After the loading phase is completed, the maintenance daily dosage is usually 5 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 premix product to help improve creatine delivery to muscles (25).

Clinical Applications and Mechanism of Action

1. Increased Strength and Performance In 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. (8,9,10,11,12,13,14,16,17,18) In short, substantial evidence suggests that creatine supplementation can increase lean body mass, muscular strength, and sprint power. (24)

   Significant gains in strength and lean mass often occur in the first 6 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 the placebo. (15)

   Individuals may vary in their response to creatine supplementation, but it is not uncommon to see a 5 to 10 lb. increase in body weight within the first six weeks.

   Approximately 80% 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 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 their 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 nineteen trained athletes, they showed that short-term creatine supplementation (20 gms per day for 5 days) enhanced repeated sprint performance and attenuated decline in jumping ability after repetitive high-power-output exercise bouts (MRPB). (22) Similar results have been documented by G. Cottrell, et al, in subjects performing repeated sprint cycling. (23) 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 and/or jumps.

2. Neuromuscular Diseases

   Creatine supplementation in humans has been reported to enhance power and strength both in normal subjects and in patients with various neuromuscular diseases. (14,34,35) Clinical studies in patients with ALS (amyotrophic lateral sclerosis) (14), Huntington's disease, Parkinson's disease, Duchenne muscular dystrophy, McArdles disease (15), and myasthenia gravis (16) have shown that creatine supplementation can produce an increase in strength and thus, provide symptomatic treatment and improved quality of life for many of these patients. (14,15,16,39,40)

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. (36,37) 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 principle factors. (10,11,17)

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 supplementation during and after leg immobilization displayed more muscular power and greater muscle size after three to ten weeks of physical rehabilitation than did subjects who took the placebo. (18)

5. Anti-aging in Older Subjects

   Creatine supplementation provided to active subjects over 70 years of age, and subjects 59-72 years of age, have resulted in significant gains in several indices of muscle performance including, increased maximal dynamic and isometric strength, lower body mean power, lower extremity functional capacity, increased fat-free mass, increased lean mass and endurance power. These studies suggest that creatine supplementation may help to forestall or reverse muscular atrophy and progressive weakness that occurs during aging, and that creatine may be useful as an intervention to improve the ability of certain elderly individuals to perform functional living tasks, decreasing dependency and, enhancing their quality of life. (19,20)

   Other studies have noted that younger individuals respond to creatine supplementation more efficiently than do older subjects in that muscular phosphocreatine stores were shown to increase on average by 35% in young subjects (~24 years of age) and 7% in older subjects (~ 70 years of age) after five days of creatine supplementation (20 gms per day). As such, it may take a longer period to maximize creatine stores in older subjects on creatine supplementation. (21)

Absorption and Utilization

Creatine absorption from the intestinal tract is very efficient. Studies show that a 6-8 gm oral load of creatine results in approximately 50% 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. (26) Other studies demonstrate that a 5 gm oral load of creatine, followed by 93 gm oral load of simple carbohydrate in solution (water) at 30 minutes post-creatine intake (4-times per day), resulted in a 60% increase in total muscle creatine compared to subjects ingesting the same amount of creatine 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 is likely a key to greater muscle uptake and utilization of creatine, and a reduction on urinary loss. Thus, it is accepted that creatine utilization is enhanced by concurrent ingestion of a simple carbohydrate drink (e.g., fruit juice). (25)

Additionally, concurrent administration of creatine and glycogen reveal that creatine supplementation 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 appear to improve performance by increasing muscle creatine and muscle glycogen. (27)

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 5 days) did not increase markers of kidney stress in five healthy men. (13) A study comparing creatine users, for up to five years duration, 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 conclude that neither short-term, medium-term, nor long-term oral creatine supplements induce detrimental effects in the kidney of healthy individuals. (29,30,31) To date, no liver abnormalities have been evident in short-term creatine challenge studies. (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. (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. (30) As pointed out by other experts, creatine is normally found in cardiac muscle, brain, and testes, as well as skeletal muscle, and these former tissues have been largely unstudied with respect to the effects of creatine supplementation. (32) The Food and Drug Administration (FDA) has advised athletes to consult a physician or a health care professional before embarking on any scheme of creatine loading or supplementation. (28) Nevertheless, few reported adverse side effects from creatine use have been reported despite its widespread use among young athletes. (1)

Other infrequently reported side effects include gastrointestinal disturbances and muscle cramps. (30)

In regards to children and younger athletes, the safety of creatine supplementation has not yet been investigated in these individuals. Until all safety issues have been evaluated, experts strongly recommend against use of creatine among adolescent athletes. (33)

Overall, creatine supplementation 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 gm per day) than is generally found in the diet, which is usually about 2 gm per day. (10, 11)

There are no well-known drug-nutrient interactions for creatine at this time. (38)

Summary

Supplementation within 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 pre-screening kidney filtration evaluation prior to introducing creatine supplementation, and minimum of age at which creatine supplementation 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 creatine supplementation is being discussed. Note that many practitioners discourage the use of creatine supplementation in athletic patients under the age of 16 or 17 years of age, who are seeking to improve their strength, muscle size and/or performance.

References:

1. Kreider RB: Creatine, the next ergogenic supplement? Sportscience Training and Technology. Internet Society for Sports Science. Available at: http://www.sportsci.org/traintech/creatine/rbk.html. Accessed May 5, 1998.
2. Kreider RB: Creatine supplement: analysis of ergogenic value, medical safety, and concerns. Journal of Exercise Physiology Online 1998; 1(1). Available at: http://www.css.edu/users/tboone2/asep/jan3.html. Accessed May 5, 1998.
3. Bramberger M: The magic potion. Sports Illus 1998;88(16):58-65.
4. Bessman SP, Savabi F: The role of the phosphocreatine energy shuttle in exercise and muscle hypertrophy, in: Taylor AW, Gollnick PD, Green HJ (eds.), International Series on Sport Sciences: Biochemistry of Exercise VII. Champaign, IL, Human Kinetics, 1988, vol. 19, pp 167-178.
5. Ingwall JS: Creatine and the control of muscle-specific protein synthesis in cardiac and skeletal muscle. Circ. Res 1976;38(5 suppl 1):I115-I123.
6. Sipila I, Rapola J, Simell O, et al: Supplementary creatine as a treatment for gyrate atrophy of the choroid and retina. N Engl J Med 1981;304(5):867-870.
7. Almada A, Kreider R, Ferreira M, et al: Effects of calcium-HMB supplementation with or without creatine during training on strength and sprint capacity, abstract. FASEB J 1997; 11:A374.
8. Earnest CP, Snell PG, Rodriguez R et al.: The effect of creatine monohydrate ingestion on anaerobic power indices, muscular strength and body composition. Acta Physiol Scand 1995;153(2):207-209.
9. Burke LM, Pyne DB, Telford RD: Effect or oral creatine supplementation on single-effort sprint performance in elite swimmers. Int. J Sports Nutr 1996;6(3):222-223.
10. Dawson B, Cutler M, Moody A, et al.: Effects of oral creatine loading on single and repeated maximal short sprints. Aust J Sci Med Sports 1995;27(3):56-61.
11. Redondo DR, Dowling EA, Graham BL, et al: The effect of oral creatine monohydrate supplementation on running velocity. Int J Sports Nutr 1996;6(3):213-221.
12. Kreider RB, Ferreira M, Wilson M, et al.: Effects of creatine supplementation on body composition, strength, and sprint performance. Med Sci Sports Exerc 1998;30(1):73-82.
13. Poortmans JR, Auquier H, Renaut V, et al.: A Effect of short-term creatine supplementation on renal responses in men. Eur J Appl Physiol 1997;76(6):566-567.
14. Mazzini, L., Balzarini, C., Colombo, R., Mora, G, Pastore, I., De Ambrogio, R., Caligari, M. Effects of creatine supplementation on exercise performance and muscular strength in amyotrophic lateral sclerosis: preliminary results. J Neurol Sci, 2001 Oct 15; Vol. 191 (1-2), pp. 139-44
15. Persky, A.M., Brazeau, G.A. Clinical pharmacology of the dietary supplement creatine monohydrate. Pharmacol Rev, 2001 Jun; Vol. 53 (2), pp. 161-76
16. Stout, J.R., Eckerson, J.M., May, E., Coulter, C., Bradley-Popovich, G.E. Effects of resistance exercise and creatine supplementation on myasthenia gravis: a case study. Med Sci Sports Exerc, 2001 Jun; Vol. 33 (6), pp. 869-72
17. Witte, K.K., Clark, A.L., Cleland, J.G. Chronic heart failure and micronutrients. J Am Coll Cardiol, 2001 Jun 1; Vol. 37 (7), pp. 1765-74
18. A leg to stand on. Better Nutrition, May 2002, Vol. 64 Issue 5, p.20

19. Chrusch, M.J., Chilibeck, P.D., Chad, K.E., Davison, K.S., Burke, D.G. Creatine supplementation combined with resistance training in older men. Med, Sci Sports Exerc., 2001 Dec; Vol. 33 (12), pp. 2111-7
20. Gotshalk, L.A., Volek, J.S., Staron, R.S., Denegar, C.R., Hagerman, F.C., Kraemer, W.J. Creatine supplementation improves muscular performance in older men. Med Sci Sports Exerc, 2002 Mar; Vol. 34 (3), pp. 537-43
21. Rawson, E.S., Clarkson, P.M., Price, T.B., Miles, M.P. Differential response of muscle phosphocreatine to creatine supplementation in young and old subjects. Acta Physiol Scand, 2002 Jan; vol. 174 (1), pp. 57-65
22. Ezquierdo, M., Ibañez, J., González-Badillo, J.J., Gorostiaga, E.M. Effects of creatine supplementation on muscle power, endurance, and sprint performance. Med Sci Sports Exerc, 2002 Feb; vol. 34 (2), pp. 332-43
23. Cottrell, G.T., Coast, J.R., Herb, R.A. Effect of recovery interval on multiple-bout sprint cycling performance after acute creatine supplementation. J Strength Cond Res, 2002 Feb; Vol. 16 (1), pp. 109-16
24. Lawler, J.M., Barnes, W.S., Wu, G., Song, W., Demaree, S. Direct antioxidant properties of creatine. Biochem Biophys Res Commun, 2002 Jan 11; Vol. 290 (1), pp. 47-52
25. Green, A.L., Hultman, E., Macdonald, I.A., Sewell, D.A., Greenhaff, P.L. Carbohydrate ingestion augments skeletal muscle creatine accumulation during creatine supplementation in humans. Am J Physiol, 1996 Nov; Vol. 271 (5 Pt 1), pp. 821-6
26. Burke, D.G., Smith-Palmer, T, Holt, L.E., Head, B., Chilibeck, P.D. The effect of 7 days of creatine suppelmentation on 24-hour urinary creatine excretion. J Strength Cond Res, 2001 Feb; Vol. 15 (1), pp. 59-62
27. Nelson, A.G., Arnall, D.A., Kokkonen, J, Day, R., Evans, J. Muscle glycogen supercompensation in enhanced by prior creatine supplementation. Med Sci Sports Exerc, 2001 Jul; Vol. 33 (7), pp. 1096-100
28. Culpepper, R. Michael. Creatine supplementation: Safe as steak? Southern Medical Journal, Sep98, Vol. 91, issue 9, p. 890-3
29. Poortmans, J.R., Francaux, M. Long-term oral creatine supplementation does not impair renal function in healthy athletes. Med Sci Sports Exerc, 1999 Aug; Vol. 31 (8), pp. 1108-10
30. Poortmans, J.R., Franczux, M. Adverse effects of creatine supplementation: fact or fiction? Sports Med, 2000 Sep; Vol. 30 (3), pp. 155-70
31. Schilling, B.K., Stone M.H., Utter, A., Kearney, J.T., Johnson, M., Coglianese, R., Smith, L., O'Bryant, H.S., Fry, A.C., Starks, M., Keith, R., Stone, M.E. Creatine supplementation and health variables: a retrospective study. Med Sci Sports Exerc, 2001 Feb; Vol. 33 (2), pp. 183-8
32. Juhn, M.S., Tarnopolsky, M. Potential side effects of oral creatine supplementation: a critical review. Clin J Sport med, 1998 Oct; Vol. 8 (4), pp. 298-304
33. Dietary Supplement Information Bureau.www.intramedicine.com
34. Tarnopolsky, M., Martin, J. Creatine monohydrate increases strength in patients with neuromuscular disease. Neurology. Mar 1999; 52 (4): 854-7
35. Vorgerd, M., Grehl, T., Jager, M., et al. Creatine therapy in myophosphorylase deficiency (McArdle disease): a placebo-controlled crossover trial. Arch Neurol. Jul 2000; 57 (7): 956-63

36. Gordon, A., Hultman, E., Kaijser, L., et al. Creatine supplementation in chronic heart failure incrases skeletal muscle creatine phosphate and muscle performance. Cardiovasc Res. Sep 1995; 30 (3): 413-8
37. Andrews, R., Greenhaff, P., Curtis, S., et al. The effect of dietary creatine supplementation on skeletal muscle metabolism in congestive heart failure. Eur Heart J. Apr 1998; 19 (4): 617-22
38. Healthnotes, Inc., 2001. www.healthnotes.com
39. Walter, M.C., Lochmüller, H., Reilich, P., et al. Creatine monohydrate in muscular dystrophies: A double-blind, placebo-controlled clinical study. Neurology 2000; 54: 1848-50
40. Felber, S., Skladal, D., Wyss, M. et al. Oral creatine supplementation in Duchenne muscular dystrophy: a clinical and 31P magnetic resonance spectroscopy study. Neurol Res 2000; 22: 145-50