Reviews

Proteins and Amino Acid Supplementation in Sports: Are They Truly Necessary?

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People all around the world spend billions of dollars on nutritional supplements, or – as they are often called – "ergogenic aids" (from the Greek *ergon*, meaning work). These substances are alleged to enhance athletic performance, decrease fatigue, change body composition and improve looks. Although true athletic success stems primarily from a combination of genetic endowment, training technique, equipment and proper nutrition, in a world that one-hundredth of a second could be the difference between fame and shame in the life of an athlete, nutritional supplements are becoming inseparable from sports.

Protein and amino acids are among the most popular "performance-enhancing" supplements. Since amino acids and proteins are essential for the synthesis of structural proteins and are involved in numerous metabolic pathways associated with exercise, it has been suggested that athletes require additional proteins either in their diet or as supplements. Although the use of supplements in sports is very common, limited clinical data are available in the medical literature on the effects of protein supplements on exercise performance.

This article will review some of the current available data on protein and amino acid supplements, their efficacy and safety.

Protein and amino acids

The current recommended daily protein intake for healthy adults is 0.8–1.2 g/kg/day. These recommendations are based mainly on nitrogen balance data from individuals who are usually sedentary.

The question of how much dietary protein is required for optimal athletic performance has been debated for more than 150 years. Most studies indicate that in order to maintain protein balance during intense endurance training, athletes should ingest from 1.0 to 1.8 g protein per kg body mass per day, while in intense resistance training protein intake should be increased up to 2.4 g protein per kg body mass per day [1]. In most instances, despite the fact that the suggested protein intake for athletes exceeds the recommended daily protein intake for sedentary individuals, an iso-energetic diet can provide the required amount of protein, and most studies agree that with a proper diet, protein supplementation is not needed. Thus far, there is no scientific evidence that

increased protein intake will enhance exercise capacity and increase muscle mass. It is likely that excess protein will simply be used as energy or stored as fat.

Several studies indicate that the timing of post-exercise protein supplementation is important for net muscle growth and recovery from exercise (especially if combined with carbohydrates). Oral protein supplement (10 g in liquid form) immediately after resistance training was shown to lead to skeletal muscle hypertrophy in elderly men with sarcopenia [2]. However, similar effects of immediate post-exercise protein supplementation were not reported in individuals with normal muscle mass or in trained athletes. Recently, Saunders et al. [3] reported that a carbohydrate beverage with additional protein calories produced significant improvements in time to fatigue, and reductions in muscle damage in endurance athletes. However, the authors concluded that further

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research is necessary to determine whether these effects were the result of higher total caloric content of the beverage or due to specific protein-mediated mechanisms. Overloading of protein may lead to high nitrogen load on the kidneys, as well as to dehydration, gout, calcium loss and gastrointestinal complaints [4].

Amino acids are the building blocks of proteins. Protein ingested in food is broken down by digestive enzymes and absorbed as amino acids. There are 20 common amino acids, of which 9 are considered essential. The term "essential" relates to the fact that these amino acids cannot be produced in sufficient amounts by the body so they must be provided by diet. However, all 20 amino acids are important for maintaining protein tissues. One of the commonly

purported benefits of amino acid supplementation is that certain amino acids (arginine, histidine, lysine, methionine, ornithine, phenylalanine) may stimulate the release of growth hormone, insulin, insulin-like growth factor-I and/or glucocorticoids, thereby promoting anabolic processes, leading to increases in fat-free mass. For example, intravenous arginine infusion is used clinically for stimulating growth hormone release in the evaluation of short stature in children [5]. Some preliminary clinical studies indicated that oral protein supplementation (20–60 g), arginine and lysine (1.2 g), and ornithine (70 mg/kg) may also increase growth hormone and IGF-I concentrations in the blood [6]. However, these findings have not been replicated by others [7] and it now appears that oral supplementation of amino acids fails to achieve the same hormonal stimulation that is observed when amino acids are administered intravenously. Moreover, most data suggest that growth hormone release during exercise is maximized under fasting conditions [8].

There is little evidence that supplementation of oral amino acids during training significantly affects body composition, strength, and/or muscle hypertrophy and exercise performance in healthy individuals [9]. The recommended daily intake of all amino acids (2–3 g/day) can be easily achieved by eating common foods such as eggs, yoghurt and milk. Therefore, the beneficial effects of amino acids supplementation in sports are questionable. Very high intake of amino acids may be associated with amino acid imbalance, direct toxic effects, diarrhea and muscle cramping [10].

Branched-chain amino acid

Branched-chain amino acids (leucine, isoleucine, valine) are essential amino acids that can be oxidized in skeletal muscle. Researchers have expended a considerable amount of effort on evaluating the effects of supplementation of BCAA acids on physiologic and psychological responses to exercise based on their role in protein metabolism as well as on the hypothetical role of BCAA in central fatigue [11].

BCAA in the muscle are able to transaminate pyruvate to form alanine, which is recycled to glucose in the Cori cycle. There is significant oxidation of these amino acids during exercise, and tracer studies that follow leucine are often used for estimating protein turnover. Some studies suggest that BCAA supplementation minimizes protein degradation and enhances recovery after exercise [11], while other studies have failed to confirm an enhancement of exercise performance following BCAA supplementation [12].

A number of studies have recently been conducted to evaluate whether carbohydrate and/or BCAA supplementation affects central fatigue during exercise, and/or signs and symptoms of overtraining. Central fatigue arises from increased levels of unbound tryptophan, which crosses the blood-brain barrier and leads to elevated levels of brain serotonin. A key factor in brain serotonin increase is the rise in the plasma ratio of free tryptophan to BCAA (tryptophan:BCAA), which compete for the same transporters in the brain. With exercise, the ratio changes due to enhanced oxidation of BCAA in the muscle and a rise in free fatty acids leading to displacement of

tryptophan from its binding sites, and elevation in its unbound brain levels leading to increased serotonin and central fatigue.

It has been hypothesized that supplementing BCAA will prevent the drop in plasma BCAA, attenuate the rise in free tryptophan:B-CAA ratio, and reduce the likelihood of fatigue. Analysis of the literature indicates that carbohydrate and/or BCAA supplementation during exercise can affect the ratio of free tryptophan to BCAA. For example, carbohydrate administration during exercise has been reported to attenuate free fatty acids release and minimize increases in the free tryptophan:BCAA ratio [13]. In addition, BCAA supplementation has been reported to increase plasma BCAA concentration and minimize and/or prevent increases in the ratio of free tryptophan to BCAA [14]. Studies also indicate that BCAA administration with or without carbohydrate prior to and during exercise can affect physiologic (muscle damage) and psychological (fatigue) responses to exercise [15].

Nevertheless, the effect of these nutritionally induced alterations in the free tryptophan to BCAA ratio on physical performance is still not clear. Most studies indicate that BCAA supplementation does not improve single-bout endurance performance, but these studies lacked power to delimit small but useful enhancements of performance [16].

Despite the intriguing theories on the potential role of BCAA on performance, to date there are no convincing data to support the use of BCAA as an enhancing supplement. Moreover, the use of supplemented BCAA leads to increases in ammonia level [17]. Ammonia, being toxic to the brain and the muscle tissue, may affect exercise capacity and performance.

> *There is some evidence to support the use of creatine and possibly HMB as ergogenic aids in specific situations*

Creatine

Creatine is a naturally occurring protein derived from the amino acids glycine and arginine. It is synthesized primarily in the liver in a two-step reaction. Most creatine is stored in skeletal muscle, primarily as phosphocreatine; the rest is found in the heart, brain, and testes. The daily requirement of creatine is approximately 2–3 g; about 50% is obtained from the diet, while the remainder is endogenously synthesized. Once in the muscle cell, creatine becomes phosphorylated by creatine kinase. Phosphorylated creatine serves as an available source of adenosine triphosphate within the muscle. During most exercises ATP is provided through oxidative phosphorylation in the mitochondria.

In some competitive sports, characterized by brief intense repetitive exercise bouts, this aerobic production is insufficient to

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IGF-I = insulin-like growth factor-I
BCAA = branched-chain amino acids

ATP = adenosine triphosphate

provide ATP demands. In these cases, anaerobic production of ATP becomes important, and production of ATP from phosphorylated creatine hydrolysis and anaerobic glycogenolysis is required.

Creatine is found in abundance in meat and fish, containing approximately 4–5 g creatine for 1 kg of food weight. Creatine ingestion reduces the endogenous creatine synthesis. Creatine supplementation has been proposed as a means to "load" muscle with creatine and phosphocreatine. In theory, an increased store of creatine or phosphocreatine would improve the ability to produce energy during high intensity exercise as well as improve the speed of recovery from such exercise.

Creatine supplement evolved as an ergogenic aid from its use by British sprinters and hurdlers in the 1992 Olympic Games in Barcelona. Since then, creatine has become the fastest selling and most researched ergogenic aid.

It is reported that creatine loading (20–30 g per day or 0.3 g per kg body mass per day for 5–7 days) may lead to a 10–30% increase in phosphorylated creatine [18]. This level remains high for a few weeks after supplement loading, and individuals who consume vegetarian diets show the greatest increase in muscle creatine levels.

There is evidence that the ingestion of creatine with a sugar-containing drink increases creatine uptake and storage in the muscle [19]. Short-term caffeine ingestion, on the other hand, blunts the ergogenic effects of creatine. The mechanisms by which caffeine and creatine counteract are not yet fully elucidated [20]. There is also evidence that creatine supplementation enhances the rate of phosphocreatine resynthesis following intense exercise [21].

Many studies have investigated the effect of creatine supplement on exercise performance, and the results vary according to the subjects, the mode of exercise and the administration of creatine [22]. Most [23] but not all [24] studies indicate that short-term creatine significantly enhances the ability to produce higher muscular force and/or power output during short bouts of exercise in young healthy adults. Creatine supplementation increases total body mass, work performed during multiple sets of maximal effort muscle contractions, and single and/or repetitive sprint capacity. In addition, long-term creatine supplementation during training has been reported to promote greater gains in strength, fat-free mass, and sprint performance [25].

Creatine has not been shown to improve aerobic performance. In healthy people, it is unlikely that creatine supplementation is required during aerobic activity since normal phosphorylated creatine levels are sufficient to maintain adequate ATP production. It is only in activities that require high-energy outputs in short bursts that supplementing creatine might be useful.

There has been only anecdotal evidence of adverse events from short-term use of creatine; these include mainly gastrointestinal side effects (nausea, diarrhea and vomiting), headaches and muscle cramps [26]. Since the majority of creatine (>90%) and its metabolite creatinine are removed by the kidney and excreted in the urine, attention has been paid to possible renal impairments following creatine supplementation. Most studies agree that creatine does not alter renal function in healthy subjects [27]; this would probably not be the case if used by people with impaired

renal function. Limited data are available on the effects of chronic creatine use on the kidney. Creatine supplementation while using non-steroidal anti-inflammatory drugs may lead to a transient impairment in renal function [28]; the long-term effect of this combination are yet unknown. Caution should be taken until long-term and large population studies are available.

Glutamine

Glutamine is a non-essential amino acid. It appears to have many regulatory functions in the body, one of which is to augment protein synthesis and to provide an anti-catabolic effect [29]. Glutamine supplementation has been shown to increase protein synthesis in rats and to decrease muscle protein degradation in both animals and humans [30]. This may be advantageous to resistance-training athletes who are seeking to enhance muscle hypertrophy.

Although dietary protein supplementation is commonly used by both athletes and people engaged in recreational sports, there are limited data to support its wide use

Glutamine plays an important role in the normal immune function. It is an important fuel for white blood cells, particularly for lymphocyte-activated natural killer activity, lymphocyte proliferation, and macrophage phagocytosis. Therefore, reduction in blood glutamine concentration following intense exercise is thought to contribute to immune suppression in overtrained athletes [31]. Preliminary studies indicate that supplementation with glutamine (4–12 g/day) can prevent the decline or even increase glutamine concentration during exercise. Castell and co-workers [32] demonstrated that glutamine supplement reduces the self-reported increased susceptibility of upper respiratory infections following exhaustive exercise. However, this change was not attributed to the effect of glutamine on lymphocyte function. Furthermore, recent data indicate that increased glutamine availability by pre-exercise supplementation had little or no effect on immune status [33], even when the post-exercise reduction in glutamine was prevented.

Currently, the data suggest that glutamine supplementation is of benefit only for athletes with true glutamine deficiency [8], and that this problem is not as common as once thought.

β-Hydroxy β-methylbutyrate

β-hydroxy-β-methylbutyric acid is a bioactive metabolite formed from breakdown of the essential branched amino acid leucine. HMB has recently become a popular dietary supplement purported to promote gains in fat-free mass and strength during resistance training [34]. Leucine and its metabolite α-ketoisocaproate appear to inhibit protein degradation, and this anti-proteolytic effect is believed to be mediated by HMB. The body synthesizes approxi-

HMB = β-hydroxy-β-methylbutyrate

mately 0.3–1.0 g of HMB daily, depending mainly on the amount of HMB contained in food such as grapefruit, some fish, and breast milk. Animal studies indicate that approximately 5% of oxidized leucine is converted to HMB via α-ketoisocaproate [35]. A markedly decreased protein muscle breakdown and a slight increase in protein synthesis occurred in animal muscle tissue exposed *in vitro* to HMB. Supplementing with leucine and/or HMB may therefore inhibit protein degradation during periods associated with increased proteolysis, such as resistance training [36].

Leucine infusion appears to decrease protein degradation in humans [37]. HMB supplementation during 3–8 weeks of training has been reported by Nissen and colleagues [34] to promote significantly greater gains of fat-free mass and strength in untrained men and women initiating resistance training. It is yet unclear whether HMB affects the bone, muscle or water components of free fat mass. In some instances, these gains were associated with signs of significantly less muscle damage (efflux of muscle enzymes and urinary 3-methylhistidine excretion). Recently, in a double-blind placebo-controlled study, Thomson [38] demonstrated that 9 weeks of HMB supplementation in trained men led to increased muscle strength with no change in body composition. Although these findings suggest that HMB supplementation during training may enhance training adaptations in trained and untrained individuals, others report no significant effects of HMB supplementation [39]. The available literature on HMB supplementation in humans is still preliminary in nature and should be considered with reservation [40]. The long-term effects of HMB both on performance and on health and safety require further evaluation.

Summary

Although dietary protein supplementation is commonly used by both athletes and people engaged in recreational sports, the data supporting its wide use are still limited. Some evidence supports the use of creatine and possibly HMB as ergogenic aids in specific situations [8], however this is also based on limited data. The use of supplements for the healthy, non-competitive adult engaged in recreational sports is usually not warranted.

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