Glutamine: An Effective Anti-Aging Therapeutic and Immune-Modifying Amino Acid Supplement

By James P. Meschino, DC, MS

L-glutamine is the most abundant amino acid in the bloodstream and in the body. It’s involved in more metabolic processes than any other amino acid, fulfilling a number of biochemical needs. It operates as a nitrogen shuttle, taking up excess ammonia and forming urea. Ammonia, a byproduct of certain normal biochemical reactions in the body (including the brain), is toxic to the human body, and thus glutamine serves an important function in helping to convert ammonia into urea, a nontoxic end-product, which the body can easily eliminate.

L-glutamine can contribute to the production of other amino acids, glucose, nucleotides, protein and glutathione. It’s the principal metabolic fuel for the epithelial cells that line the small intestine (enterocytes) and for certain immune cells, namely lymphocytes, macrophages and fibroblasts. Glutamine is a non-essential amino acid, in that the body can synthesize it from the amino acid glutamic via the glutamine synthase enzyme.

Glutamine intake has been shown to enhance glutathione stores in conjunction with N-acetylcysteine, which may forestall the progression of HIV infection to AIDS in afflicted patients. Glutamine supplementation has been shown to help protect the gastrointestinal tract from damage by certain chemotherapy drugs (e.g., fluorouracil [Adrucil]) and also prevents the diarrhea these drugs are known to produce.

Glutamine supplementation has been shown to enhance immune system function and result in a lower level of infection and a shorter hospital stay following surgery, radiation treatment, bone marrow transplantation and injury, compared with patients receiving glutamine-free parenteral nutrition. However, during periods of fasting, starvation, critical illness, cancer or AIDS; following trauma, radiation treatment, surgery or bone marrow transplantation; or in patients with a weakened immune system or catabolic stress, extra glutamine replenishment has been shown to be beneficial to re-establish homeostatis.

Glutamine also is a main anti-catabolic agent in muscle, which might help preserve muscle tissue (preventing its breakdown) during and after exercise. The heavier one trains, the greater the stress on the
muscle and therefore the greater the use of glutamine.8

Glutamine May Help Athletes Reduce Exercise-Induced Muscle Catabolism

During and following exercise or trauma, large amounts of alanine and glutamine are released from muscle. They then travel through the bloodstream to the liver, where they can be used to form glucose and glycogen. The total loss of alanine and glutamine induced by exercise is above the amount available in muscle. This represents more than 50 percent of the total loss of muscle amino acids and nitrogen loss from muscle tissue during exercise. Studies show that during exercise, other muscle amino acids (branched-chain amino acids) donate their carbon skeletons to make alanine.

Certain alpha-ketoacids and amino acids, such as alpha-ketoglutarate and glutamic acid, are converted within the muscle to glutamine. Most notably, the branched-chain amino acids leucine, isoleucine and valine serve as a substrate for alanine synthesis. However, higher levels of intramuscular glutamine (via supplementation) might help stop the catabolism of branched-chain amino acids, as glutamine can diffuse from the muscle and become a source of glucose in the liver to help maintain blood glucose and liver glycogen levels during periods of stress (e.g., exercise).8,9,10 This also is the role played by alanine, and thus, higher glutamine concentrations might reduce the requirement for alanine synthesis in the muscle and spare the breakdown of muscle tissue (branched-chain amino acid catabolism) during exercise and other periods of catabolic stress (burn victims, infection, post-surgery, etc).8,9,10

Supplementation Studies and Clinical Applications

HIV infection: Glutamine supplementation plus N-acetylcysteine supplementation enhances glutathione levels in HIV patients. Higher glutathione status correlates with a slowing of the progression of HIV to AIDS. Glutathione depletion is common in these patients due to increased free-radical production. Glutathione is a first-line antioxidant in the quenching of free radicals and participates in phase I and phase II liver detoxification functions.2

Anti-catabolic effect with exercise: Oral glutamine has been shown to maintain muscle mass in catabolic patients.11 However, glutamine supplementation might increase ammonia levels and add to the ammonia burden of certain patients and athletes, jeopardizing recovery or performance, respectively.8 To overcome this burden, the use of alpha-ketoglutarate has been shown to act as a glutamine precursor, without contributing to ammonia buildup. However, L-glutamine at doses of up to 2,000 mg to 5,000 mg per day
appears to be safe. Oral ornithine alpha-ketoglutarate reduces muscle catabolism in burn and surgery patients and is known to increase muscle glutamine levels. Ornithine alpha-ketoglutarate also stimulates the release of growth hormone and also might provide an anti-catabolic and indirect anabolic effect on muscle tissue and lean mass, in general. A daily dosage of 2 mg to 4 mg per day of ornithine alpha-ketoglutarate is required to increase growth hormone levels.\(^\text{12-14}\)

**Prevention of infections in athletes:** Glutamine supplementation in endurance athletes has been shown to reduce the incidence of infections in this population, who are known to have their immune systems suppressed by excess training. A double-blind, placebo-controlled study showed that 5 gm glutamine supplementation, taken after the end of exercise in 151 endurance athletes, resulted in a significantly lower incidence of infections (19 percent) compared to the placebo group (51 percent) during the study period.\(^\text{23}\) It has been suggested that the immune system suppression associated with endurance exercise might be due to reduction in glutamine that results from intensive training.\(^\text{23}\) Another study, using the same protocol, demonstrated that 81 percent of athletes taking glutamine had no subsequent infection during the study period, compared to 49 percent in the placebo group.\(^\text{22}\)

**Dosage Ranges**

As oral glutamine supplementation can potentially produce undesirable levels of ammonia in the body, it is unclear as to what levels of intake are safe (as a supplement). As an alternative, oral ornithine alpha-ketoglutarate has been used to elevate glutamine status without ammonia buildup when taken orally.

HIV-infection: 7 gm twice daily, with 7 gm of L-arginine twice daily.\(^\text{21}\) Recovering from illness (in the elderly), surgery, burn or wound healing: 10 gm to 30 gm per day of ornithine alpha-ketoglutarate, in divided doses.\(^\text{15,16}\) Muscle anti-catabolic-anabolic effect with exercise training: 2 gm to 4 gm, three times daily with meals (ornithine alpha-ketoglutarate) or 2,000 mg per day of L-glutamine.\(^\text{17}\) Prevention of infections in athletes: 5,000 mg per day of L-glutamine post-exercise.\(^\text{22,23}\)

**Side Effects and Toxicity**

L-glutamine supplementation might increase the ammonia load on the body. Thus, medical supervision should accompany high-dose supplementation of L-glutamine (above 2,000 mg to 5,000 mg per day).\(^\text{8}\) Ornithine alpha-ketoglutarate supplementation is not associated with any side effects to date.\(^\text{18,19}\) Glutamine might trigger seizures in epileptic patients.\(^\text{24}\) Mania symptoms might develop at doses above
2,000 mg per day. These symptoms might develop in the absence of prior bipolar disease.\textsuperscript{24}

**Drug-Nutrient Interactions**

Supplementation with L-glutamine has been shown to reduce side effects associated with the use of methotrexate, paclitaxel and chemotherapy drugs. It also might improve the efficacy of some chemotherapy drugs. Use of glutamine in these applications should be implemented in collaboration with the attending medical physician.\textsuperscript{20} There are no well-known drug interactions with ornithine alpha-ketoglutarate.\textsuperscript{20} For more information on this or other related topics, visit [www.renaisante.com](http://www.renaisante.com).

**References**


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