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Arginine: L-arginine (2-amino-5-guanidinovaleric acid)

Common Indications:

- Hypertension - as it increases nitric oxide production
- Improves endothelial dysfunction in hypercholesterolemia and atherosclerosis
- Erectile dysfunction, improving blood flow
- Burn care and wound healing – increase blood delivery
- Growth hormone production

General Comments:

L-Arginine (2-amino-5-guanidinovaleric acid) is the precursor of nitric oxide, which impacts multiple physiological effects upon the endothelium. In humans with lipid disorders and atherosclerosis, arginine improves vasodilatation via its conversion to nitric oxide, the chemical entity shown to be identical with endothelium-derived relaxing factor. Arginine also provides endocrine effects at higher doses and has been shown to increase growth hormone levels.

Our endogenous production of this semi-essential amino acid occurs primarily in the kidney, taking L-citrulline from the small intestines. Our liver also produces arginine but is used within the liver and does not contribute to the systemic circulation. Other cells such as macrophages that contain inducible NOS can also produce arginine and thus nitric oxide for its own purposes. Each gram of dietary protein supplies about 54 mg of L-arginine. Average L-arginine intake can therefore be assumed to be on the order of 4–5 g/day but varies greatly based on personal dietary intake. Supplementation with this semi-essential amino acid is therefore therapeutic in many clinical issues. L-arginine is required for the synthesis of creatine, which is an essential energy source for muscle contraction, and is then degraded to produce creatinine.

Benefits & Mechanism of Action:

Vascular Effects

Endothelial cells do synthesize L-arginine from L-citrulline. Endothelial production of nitric oxide synthase (eNOS) results in low level nitric oxide (NO). NO acts as a paracrine-signaling molecule and has the following effects:

- Mediates vasodilation
- Inhibition of platelet activation
- Inhibition of monocyte and leukocyte adhesion
- Inhibition of smooth muscle cell proliferation
- Controlling vascular oxidative stress and the expression of redox-regulated genes
- Protection against oxidative damage.

In disease states such as the presence of atherosclerotic disease, hypertension, diabetes and hyperlipidemia where oxidative tension is high, there is a reduced ability of eNOS to function and increased oxidative inactivation of NO. In this setting there is enhanced formation of vasoconstrictor mediators like endothelin-1 and thromboxane A2. NOS is inhibited by L-arginine analogs that are substituted at the guanidino nitrogen atom, like NG-monomethyl-L-arginine or NG-nitro-L-arginine. This is a competitive inhibition and these inhibitory actions can be overcome by excess L-arginine. Reduced activity of endothelial cell NOS was also shown to occur in the presence of LDL cholesterol and can be overcome by excess L-arginine. So under certain conditions, L-arginine availability regulates endothelial cell NOS activity. Long-term oral administration of L-arginine has been associated with a significant improvement in NO-dependent vasodilation in cholesterol-fed rabbits.

Animal studies, especially rabbit studies should always be viewed with caution as the physiology does not reflect that of omnivorous humans. With that said there is strong evidence in rabbit studies that use of oral arginine may slow development of intimal plaque in carotid arteries and reduction of aortic atherosclerotic lesions.

Hypertensive patients refractory to enalapril and hydrochlorothiazide demonstrated a good response to oral arginine (2 g three times daily). Oral arginine significantly lowers blood pressure in healthy volunteers.

Congestive Heart Failure patients demonstrate improvement with oral arginine at a dose of 5 to 12 grams per day. Physiologic improvements included significantly improved blood flow, arterial compliance, and functional status, compared to placebo, in a randomized, double-blind trial. A second trial using 5 grams of arginine three time per day in patients with CHF improved renal function.

Immune Modulation

Arginine at high doses can up-regulate killer cell function and impact infectious process. It has been shown to reduce pro-inflammatory cytokine levels and enhance lymphocyte mitogenic reactivity.

Arginine was shown to increase natural killer cell activity in individuals with HIV/AIDS. A small pilot study of 11 HIV patients, arginine supplementation was given at a dose of

19.6 g/day arginine or placebo for 14 days. Natural Killer cell cytotoxicity increased 18.9 lytic units, compared to an increase of 0.3 lytic units with placebo.

Endocrine

Arginine has significant effects on endocrine function, particularly adrenal and pituitary secretion, in humans and animals. Arginine administration can stimulate the release of catecholamines, insulin and glucagon, prolactin, and growth hormone however, little is known about the specific mechanisms by which arginine exerts these effects.

Growth Hormone Secretion and Athletic Performance

In rats, nitric oxide (N.O.) stimulates secretion of GH-releasing hormone (GHRH), thereby increasing secretion of GH. However, GHRH then increases production of N.O. in somatotroph cells, which subsequently inhibits GH secretion. In humans, arginine stimulates release of GH from the pituitary gland in some populations, but the mechanism is not well understood. Most studies suggest inhibition of somatostatin secretion is responsible for the effect. At high doses (approximately 250 mg/kg body weight), arginine aspartate increased GH secretion, an effect of interest to body builders wishing to take advantage of the anabolic properties of the hormone. In a controlled clinical trial, arginine and ornithine (500 mg of each, twice daily, five times per week) produced a significant decrease in body fat when combined with exercise.

Acute dosing of arginine (5 g taken 30 minutes before exercise) did not increase GH secretion, and may have impaired release of GH in young adults. Longer-term, low dose supplementation of arginine and ornithine (1g each, five days per week for five weeks) resulted in higher gains in strength and enhancement of lean body mass, compared with controls receiving vitamin C and calcium.

Symptoms of Depletion:
Symptoms of arginine deficiency include hair loss, poor wound healing, rash, constipation, and liver abnormalities.

Food Sources: The best dietary sources of arginine are meat, nuts, eggs, milk and cheese.

Dose:

- 500mg – 6gm daily in divided doses
- 1 gm sustained-release (2 x 500mg capsules) 2 times daily

Cautions & Side Effects:

- L-arginine dose is metabolized to ornithine and urea. Increases in blood nitrogen urea and urea may occur in patients with renal function impairment owing to their limited capacity to eliminate urea.
- Oral L-arginine may cause nausea and vomiting, occurrence is roughly 3%.
- Abdominal cramps and bloating have been observed in patients with cystic fibrosis receiving oral L-arginine.
- Use with caution in pregnancy and lactation.
- If you are taking prescription or non-prescription medications, have a pre-existing medical condition, or are pregnant and/or breastfeeding, talk with your healthcare provider before taking any dietary supplement.
- Do not take if there is an allergy to any component of this dietary supplement.

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