

Issue 96

In a nutshell

Arginine is a precursor of nitrous oxide, which appears to have beneficial effect on vascular endothelial function and produces vasodilation.

A number of small trials have shown positive outcomes in heart disease, but confirmatory and larger trials are required.

Arginine in heart disease

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LIVE LINKS

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NUTRITION RESEARCH REVIEW

Study one: Pulmonary hypertension

Supplemental arginine reduces pulmonary resistance and blood pressure, as well as improving the ventilatory response to carbon dioxide production, according to results from a recent Japanese study.

Subjects: 19 patients with pulmonary hypertension.

Method: Controlled trial of 1 week of placebo or arginine supplementation (1.5 g/10 kg body weight/day).

Results: Supplementation produced a 9% decrease in mean pulmonary arterial pressure and a 16% decrease in pulmonary vascular resistance ($p < 0.05$ for the change), compared to no significant change for placebo.

L-arginine also improved the ventilatory response to carbon dioxide without producing significant systemic hypotension ($p < 0.05$).

Reference: Nagaya N et al. Short-term oral administration of L-arginine improves hemodynamics and exercise capacity in patients with precapillary pulmonary hypertension. *Am J Respir Crit Care Med* 2001;163:887-91

Study two: Renal function

Arginine supplementation improves renal function in patients with chronic heart failure. This was the finding of a study from another Japanese university.

Subjects: 17 patients with chronic congestive heart failure.

Method: Randomised cross-over trial of 5 days of oral L-arginine (15 g/day) vs placebo.

Results: Arginine supplementation was associated with significant improvements of renal function compared to placebo on several parameters (glomerular filtration rate, natriuresis, and plasma endothelin level, (The absolute level of difference was between 20 and 200% and the statistical significance < 0.05 and in some cases < 0.01 for the various parameters).

Reference: Watanabe G et al. Effects of oral administration of L-arginine on renal function in patients with heart failure. *J Hypertens* 2000;18:229-34

Study three: Exercise tolerance in angina

Polish researchers have found that arginine supplementation increases exercise tolerance in stable coronary artery disease patients.

Subjects: 25 patients with stable coronary artery disease.

Method: Randomized double-blind cross-over trial of 3 days of treatment with placebo vs L-arginine (6 g/day).

Results: Arginine improved exercise duration by 8% ($p < 0.03$), but there were no significant differences between arginine and placebo in relation to exercise-induced changes in the ECG.

Reference: Bednarz B et al. Effects of oral L-arginine supplementation on exercise-induced QT dispersion and exercise tolerance in stable angina pectoris. *Int J Cardiol* 2000;75:205-10

Comments

Vascular endothelial function has been increasingly looked at as a possible common mechanism for many cardiovascular diseases, and the nutritional factors that may favourably affect it include omega-3 fatty acids, folic acid, antioxidant vitamins (especially vitamins E and C) and L-arginine ¹. Elevated homocysteine may exert its apparent negative affect on heart disease via affects on endothelial function.

Arginine is interesting because it is a precursor of nitrous oxide, which appears to have beneficial effect on vascular endothelial function and produces vasodilation. There is also some evidence that arginine availability may be affected by cardiac disease in some situations such as heart failure ² and that phytoestrogens have beneficial effects on endothelial function via the arginine-nitrous oxide pathway ³.

For these reasons quite a few small studies have been carried out in the last several years to assess the clinical impact of arginine supplementation.

The three studies we have summarised above are typical, both in showing promising results and in being small studies that definitely need following up by larger and longer term ones. It is also important to note that other studies using arginine in patients with renal failure and angina have failed to produce the same positive outcomes as these three studies.

Apart from its possible role in cardiovascular disease, arginine supplementation has also been trialled in a wider range of disorders, including chronic interstitial cystitis, asthma, preeclampsia and HIV infection. It is too early to say if these will prove useful indications. Arginine has also been looked at as part of several wider nutrition support regimens, in terms of immune function, for example.

At present, arginine remains an apparently safe and intriguing but not yet proven possible nutritional treatment for cardiovascular and possibly some other diseases.

References:

1. Brown AA, Hu FB. Dietary modulation of endothelial function: implications for cardiovascular disease. *Am J Clin Nutr* 2001;73:673-86
2. Kaye DM et al. In vivo and in vitro evidence for impaired arginine transport in human heart failure. *Circulation* 2000;102:2707-12
3. Walker HA et al. The Phytoestrogen Genistein Produces Acute Nitric Oxide-Dependent Dilation of Human Forearm Vasculature With Similar Potency to 17ss-Estradiol. *Circulation* 2001;103:258-262

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