Pathogenetic aspects of the L-arginine-NO metabolic pathway in arteriosclerosis and possible therapeutic aspects

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L-arginine is the physiological precursor of nitric oxide (NO) which is formed in endothelial cells by the activity of the constitutive NO synthase isoenzyme. NO is tonically released from the endothelium, thus maintaining an active vasodilator tone and inhibiting platelet aggregation, leukocyte adhesion, and vascular smooth muscle cell proliferation. In experimental hypercholesterolemia and atherosclerosis as well as in hypercholesterolemic patients, NO-mediated responses have been shown to be impaired. Whether decreased formation and/or enhanced oxidative inactivation are involved in this process, is still unclear. Chronic dietary administration of L-arginine has been shown to exert anti-atherosclerotic effects in hypercholesterolemic rabbits. Intravenous infusion of L-arginine induces NO-dependent peripheral vasodilatation and inhibits platelet aggregation in healthy humans as well as in patients with severe limb ischemia and generalized atherosclerosis. Whether L-arginine may induce therapeutic effects in peripheral vascular disease, still remains unclear.

Metabolism of nitric oxide (NO) and arginine: significance for male health


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Since the first description of the "endothelium-derived relaxing factor" (EDRF) in 1980 the function of the endothelium has developed into a field of research of its own. The most important endothelial factor is nitric oxide (NO), which is formed from l-arginine with the help of NO synthase (NOS). Disturbances of the endothelial function play an important role in men's health such as atherogenesis and erectile dysfunction and are also followed by morphological vessel changes. Furthermore, NO seems to play an important role in LUTS (lower urinary tract symptoms) and male fertility.

Arginine: Clinical potential of a semi-essential amino.


Appleton J.

Arginine, a semi-essential amino acid, is involved in numerous areas of human biochemistry, including ammonia detoxification, hormone secretion, and immune modulation. Arginine is also well known as a precursor to nitric oxide (NO), a key component of endothelial-derived relaxing factor, an endogenous messenger molecule involved in a variety of endothelium-dependent physiological effects in the cardiovascular system. Because of arginine's NO-stimulating effects, it can be utilized in therapeutic regimens for angina pectoris, congestive heart failure, hypertension, coronary heart disease, preeclampsia, intermittent claudication, and erectile dysfunction. In addition, arginine has been studied in the treatment of HIV/AIDS, athletic performance,
burns and trauma, cancer, diabetes and syndrome X, gastrointestinal diseases, male and female infertility, interstitial cystitis, immunomodulation, and senile dementia. Toxicity, dosage considerations, and contraindications are also reviewed.

Clinical assessment of a supplement of Pycnogenol and L-arginine in Japanese patients with mild to moderate erectile dysfunction.

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A double-blind parallel group comparison design clinical study was conducted in Japanese patients with mild to moderate erectile dysfunction to investigate the efficacy of a supplement containing Pycnogenol and L-arginine. Subjects were instructed to take a supplement (Pycnogenol 60vmg/day, L-arginine 690vmg/day and aspartic acid 552vmg/day) or an identical placebo for 8 weeks, and the results were assessed using the five-item erectile domain (IIEF-5) of the International Index of Erectile Function. Additionally, blood biochemistry, urinalysis and salivary testosterone were measured. Eight weeks of supplement intake improved the total score of the IIEF-5. In particular, a marked improvement was observed in 'hardness of erection' and 'satisfaction with sexual intercourse'. A decrease in blood pressure, aspartate transaminase and (sup)-glutamyl transpeptidase ((sup)-GTP), and a slight increase in salivary testosterone were observed in the supplement group. No adverse reactions were observed during the study period. In conclusion, Pycnogenol in combination with L-arginine as a dietary supplement is effective and safe in Japanese patients with mild to moderate erectile dysfunction.

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Effect of niacin on erectile function in men suffering erectile dysfunction and dyslipidemia.

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INTRODUCTION: Dyslipidemia is closely related to erectile dysfunction (ED). Evidence has shown that the lipid-lowering agent, 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitor (statins), can improve erectile function. However, information about the potential role of another class of lipid-lowering agent, niacin, is unknown. AIM: To assess the effect of niacin alone on erectile function in patients suffering from both ED and dyslipidemia. METHODS: A single center prospective randomized placebo-controlled parallel-group trial was conducted. One hundred sixty male patients with ED and dyslipidemia were randomized in a one-to-one ratio to receive up to 1,500 mg oral niacin daily or placebo for 12 weeks. MAIN OUTCOME MEASURES: The primary outcome measure was the improvement in erectile function as assessed by question 3 and question 4 of the International Index of Erectile Function (IIEF Q3 and Q4). Secondary outcome measurements included the total IIEF score, IIEF-erectile function domain, and
Sexual Health Inventory for Men (SHIM) score. RESULTS: From the overall analysis, the niacin group showed a significant increase in both IIEF-Q3 scores (0.53 1.18, P < 0.001) and IIEF-Q4 scores (0.35 1.17, P = 0.013) compared with baseline values. The placebo group also showed a significant increase in IIEF-Q3 scores (0.30 1.16, P = 0.040) but not IIEF-Q4 scores (0.24 1.13, P = 0.084). However, when patients were stratified according to the baseline severity of ED, the patients with moderate and severe ED who received niacin showed a significant improvement in IIEF-Q3 scores (0.56 0.96 [P = 0.037] and 1.03 1.20 [P < 0.001], respectively) and IIEF-Q4 scores (0.56 1.03 [P = 0.048] and 0.84 1.05 [P < 0.001], respectively) compared with baseline values, but not for the placebo group. The improvement in IIEF-EF domain score for severe and moderate ED patients in the niacin group were 5.28 5.94 (P < 0.001) and 3.31 4.54 (P = 0.014) and in the placebo group were 2.65 5.63 (P < 0.041) and 2.74 5.59 (P = 0.027), respectively. There was no significant improvement in erectile function for patients with mild and mild-to-moderate ED for both groups. For patients not receiving statins treatment, there was a significant improvement in IIEF-Q3 scores (0.47 1.16 [P = 0.004]) for the niacin group, but not for the placebo group. CONCLUSIONS: Niacin alone can improve the erectile function in patients suffering from moderate to severe ED and dyslipidemia. [ 2011 International Society for Sexual Medicine.]

Propionyl-L-carnitine, L-arginine and niacin in sexual medicine: a nutraceutical approach to erectile dysfunction.

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Gianfrilli D; Lauretta R; Di Dato C; Graziaido C; Pozza C; De Larichaudy J; Giannetta E; Isidori AM; Lenzi A

The application of nutraceuticals in the field of male sexual function -in particular for erectile dysfunction (ED)--remains relatively underexplored. In a group of 54 unselected men (35-75 years), consecutively presenting to our ED clinic and naive to other ED treatments, we carried out a single-blind, one-arm study to evaluate the effects of a 3-month supplementation with propionyl-L-carnitine, L-arginine and niacin on their sexual performance. All patients had the short-international index of erectile function (IIEF) questionnaire, global assessment questions (GAQs) and routine laboratory testing, at baseline and 3 months afterward. 51 (92%) patients of 54 completed the entire study period. After 3 months of treatment, a small, but statistically significant improvement in total and single items of the IIEF was found (< = 5.7 4.1 P < 0.01). Analyses on GAQs revealed that treatment improved erections in 40% of cases, with a partial response occurring in up to 77% of subjects enrolled. These preliminary findings indicate that the favourable cardiovascular effects of nutraceuticals might also reflect on male sexual function with possible implication in the treatment and prevention of ED. This study documents a considerable patient's interest toward nutritional supplementation--as first-line or adjunctive treatment to PDE5 inhibitors--that goes beyond the measurable increment in penile rigidity. [ 2011 Blackwell Verlag GmbH.]

A meta-analysis of randomized controlled studies on the effects of extended-release niacin in women.
Goldberg AC

The present meta-analysis pooled data from 5 double-blind, placebo-controlled studies in 432 patients with dyslipidemia treated with various doses of extended-release niacin. Data were analyzed for possible gender differences in response to treatment. At all doses, mean decreases in low-density lipoprotein cholesterol were greater in women than in men; differences were significant at doses of 1,000 mg (6.8% vs 0.2%, p = 0.006), 1,500 mg (11.3% vs 5.6%, p = 0.013), 2,000 mg (14.8% vs 6.9%, p = 0.010), and 3,000 mg (28.7% vs 17.7%, p = 0.006). Decreases in triglyceride levels also tended to be greater in women than in men but reached significance only at the 1,500-mg dose (28.6% vs 20.4%, p = 0.040). No similar trends or significant gender differences were noted in levels of lipoprotein(a) and high-density lipoprotein cholesterol. This meta-analysis confirms that women respond as well as men, and possibly slightly better, to treatment with extended-release niacin and that it is a safe and effective treatment option for women with dyslipidemia.