

Research Abstracts

Vitamin B12 & Folic Acid

Effect of folic acid and antioxidant vitamins on endothelial dysfunction in patients with coronary artery disease

OBJECTIVES: The purpose of this study was to determine whether lowering homocysteine levels with folic acid, with or without antioxidants, will improve endothelial dysfunction in patients with coronary artery disease (CAD). **BACKGROUND:** Elevated plasma homocysteine levels are a risk factor for atherosclerosis. Homocysteine may promote atherogenesis through endothelial dysfunction and oxidative stress. **METHODS:** In a double-blind, placebo-controlled, randomized trial, we used vascular ultrasound to assess the effect of folic acid alone or with antioxidants on brachial artery endothelium-dependent flow-mediated dilation (FMD). Seventy-five patients with CAD (screening homocysteine level ≥ 9 micromol/liter) were randomized equally to one of three groups: placebo, folic acid alone or folic acid plus antioxidant vitamins C and E. Patients were treated for four months. Plasma folate, homocysteine, FMD and nitroglycerin-mediated dilation were measured before and after four months of treatment. **RESULTS:** Plasma folate, homocysteine and FMD were unchanged in the placebo group. Compared with placebo, folic acid alone increased plasma folate by 475% ($p < 0.001$), reduced plasma homocysteine by 11% ($p = 0.23$) and significantly improved FMD from $3.2 \pm 3.6\%$ to $5.2 \pm 3.9\%$ ($p = 0.04$). The improvement in FMD correlated with the reduction in homocysteine ($r = 0.5$, $p = 0.01$). Folic acid plus antioxidants increased plasma folate by 438% ($p < 0.001$), reduced plasma homocysteine by 9% ($p = 0.56$) and insignificantly improved FMD from $2.6 \pm 2.4\%$ to $4.0 \pm 3.7\%$ ($p = 0.45$), as compared with placebo. Nitroglycerin-mediated dilation did not change significantly in any group. **CONCLUSIONS:** Folic acid supplementation significantly improved endothelial dysfunction in patients with coronary atherosclerosis. Further clinical trials are required to determine whether folic acid supplementation may reduce cardiovascular events. Title LM, Cummings PM, Giddens K, Genest JJ Jr, Nassar BA. *J Am Coll Cardiol* 2000 Sep;36(3):758-65.

Randomized trial of folic acid supplementation and serum homocysteine levels

BACKGROUND: Lowering serum homocysteine levels with folic acid is expected to reduce mortality from ischemic heart disease. Homocysteine reduction is known to be maximal at a folic acid dosage of 1 mg/d, but the effect of lower doses (relevant to food fortification) is unclear. **METHODS:** We randomized 151 patients with ischemic heart disease to 1 of 5 dosages of folic acid (0.2, 0.4, 0.6, 0.8, and 1.0 mg/d) or placebo. Fasting blood samples for serum homocysteine and serum folate analysis were taken initially, after 3 months of supplementation, and 3 months after folic acid use was discontinued. **RESULTS:** Median serum homocysteine level decreased with increasing folic acid dosage, to a maximum at 0.8 mg of folic acid per day, when the homocysteine reduction (placebo adjusted) was 2.7 micromol/L (23%), similar to the known effect of folic acid dosages of 1 mg/d and above. The higher a person's initial serum homocysteine level, the greater was the response to folic acid, but there were statistically significant reductions regardless of the initial level. Serum folate level increased approximately linearly (5.5 nmol/L for every 0.1 mg of folic acid). Within-person fluctuations over time in serum homocysteine levels, measured in the placebo group, were large compared with the effect of folic acid, indicating that monitoring of the reduction in an individual is impractical. **CONCLUSIONS:** A dosage of folic acid of 0.8 mg/d appears necessary to achieve the maximum reduction in serum homocysteine level across the range of homocysteine levels in the population. Current US food fortification levels will achieve only a small proportion of the achievable homocysteine reduction. Wald DS, Bishop L, Wald NJ, Law M, Hennessy E, Weir D, McPartlin J, Scott J. *Arch Intern Med* 2001 Mar 12;161(5):695-700.

Effects of a vitamin B complex on functional recovery after nerve injury

Functional recovery after nerve crushing was investigated in the following manner: Under pentobarbital anesthesia the sciatic nerve of the rat was crushed at the level of the hip (proximal crush) or the thigh (distal crush). The recovery processes after the nerve crushing were followed by measuring distances between the first and fifth digits (DBD.1 approximately 5) and between the second and fourth digits (DBD.2 approximately 4) of the hind paw, and by observing changes in "behavior" scored on a scale of 10 according to the degree of behavioral disorder of the hind paw and leg. Results obtained by these methods showed good reproducibility. The DBD values and the scores for behavior recovered significantly faster after weak nerve crushing than after strong crushing, and after distal rather than after proximal crushing. When a segment of the sciatic nerve was resected, there was no recovery. These results suggest that DBD.1 approximately 5, DBD.2 approximately 4, and the behavior observed in these experiments serve as good indices for evaluating the degree of functional recovery after nerve injury in unanesthetized and unrestrained animals. Effects of a preparation of vitamins B₁, B₆, and B₁₂ (B complex) on these three parameters and on weights of 9 muscles of the hind leg were also studied. These studies showed that the B complex facilitated functional recovery from nerve injury faster than its components, and that on muscle atrophy the B complex had its most effects on the soleus. It was also shown that B₁ and B₁₂ by themselves had significant facilitating effects on the functional recovery. Hasegawa K, Mikuni N, Sakai Y. *Nippon Yakurigaku Zasshi* 1978 Sep;74(6):721-34.