

Abstract

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Effect of B-vitamin therapy on progression of diabetic nephropathy: a randomized controlled trial.

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CONTEXT: Hyperhomocysteinemia is frequently observed in patients with diabetic nephropathy. B-vitamin therapy (folic acid, vitamin B(6), and vitamin B(12)) has been shown to lower the plasma concentration of homocysteine.

OBJECTIVE: To determine whether B-vitamin therapy can slow progression of diabetic nephropathy and prevent vascular complications.

DESIGN, SETTING, AND PARTICIPANTS: A multicenter, randomized, double-blind, placebo-controlled trial (Diabetic Intervention with Vitamins to Improve Nephropathy [DIVINe]) at 5 university medical centers in Canada conducted between May 2001 and July 2007 of 238 participants who had type 1 or 2 diabetes and a clinical diagnosis of diabetic nephropathy.

INTERVENTION: Single tablet of B vitamins containing folic acid (2.5 mg/d), vitamin B(6) (25 mg/d), and vitamin B(12) (1 mg/d), or matching placebo.

MAIN OUTCOME MEASURES: Change in radionuclide **glomerular filtration rate (GFR)** between baseline and 36 months. Secondary outcomes were dialysis and a composite of myocardial infarction, stroke, revascularization, and all-cause mortality. Plasma total homocysteine was also measured.

RESULTS: The mean (SD) follow-up during the trial was 31.9 (14.4) months. At 36 months, radionuclide GFR decreased by a mean (SE) of 16.5 (1.7) mL/min/1.73 m² in the B-vitamin group compared with 10.7 (1.7) mL/min/1.73 m² in the placebo group (mean difference, -5.8; 95% confidence interval [CI], -10.6 to -1.1; P = .02). There was no difference in requirement of dialysis (hazard ratio [HR], 1.1; 95% CI, 0.4-2.6; P = .88). The composite outcome occurred more often in the B-vitamin group (HR, 2.0; 95% CI, 1.0-4.0; P = .04). Plasma total homocysteine decreased by a mean (SE) of 2.2 (0.4) micromol/L at 36 months in the B-vitamin group compared with a mean (SE) increase of 2.6 (0.4) micromol/L in the placebo group (mean difference, -4.8; 95% CI, -6.1 to -3.7; P < .001, in favor of B vitamins).

CONCLUSION: **Among patients with diabetic nephropathy, high doses of B vitamins compared with placebo resulted in a greater decrease in GFR and an increase in vascular events.**

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