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Metformin and Vitamin B_{12} Deficiency

Evidence suggests that metformin lowers vitamin B_{12} levels in patients with diabetes.

Observational studies have suggested that metformin causes vitamin B_{12} deficiency in some patients; researchers have proposed several possible mechanisms whereby metformin might interfere with B_{12} absorption. Understanding this interaction is important, because B_{12} deficiency could exacerbate neuropathic symptoms in patients with diabetes.

In this prospective case-control study, Canadian investigators identified 122 type 2 diabetic patients with peripheral neuropathy: Half had taken metformin for at least 6 months, and half had never received metformin. Otherwise, clinical characteristics of the groups were similar.

Median serum B_{12} level was significantly lower in the metformin group than in the no-metformin group (231 vs. 486 pmol/L). Metformin recipients also had significantly higher levels of homocysteine and methylmalonic acid (markers of B_{12} deficiency) and significantly worse scores on standardized clinical assessments of severity of neuropathy. In multivariate analyses controlled for age, duration of diabetes, and glycosylated hemoglobin (HbA_{1c}) level, metformin therapy was associated independently with worse neuropathic symptoms.

Comment: This study strengthens the case for an effect of metformin therapy on vitamin B_{12} levels. The analysis also suggests that this interaction worsens neuropathy, but confounding by unknown factors could be responsible for this observation. In one randomized placebo-controlled trial, metformin lowered B_{12} levels (J Intern Med 2003; 254:455); now, we need a trial to determine whether B_{12} supplementation is beneficial for diabetic patients who take metformin.

— ***Allan S. Brett, MD***

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Wile DJ and Toth C. Association of metformin, elevated homocysteine, and methylmalonic acid levels and clinically worsened diabetic peripheral neuropathy. *Diabetes Care* 2010 Jan; 33:156.

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