

## Metformin for type 2 diabetes

JANUARY 2019

**TO THE EDITOR:** I enjoyed reading “Should metformin be used in every patient with type 2 diabetes” by Makin and Lansang in the January 2019 issue.<sup>1</sup>

I just wanted to point out that metformin is a frequent cause of low serum vitamin B<sub>12</sub> levels, and serum vitamin B<sub>12</sub> levels should be monitored intermittently in patients using metformin.

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#### ■ REFERENCE

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doi:10.3949/ccjm.86c.04003

**IN REPLY:** We thank Dr. Moskowitz for his kind comments. We agree about the need for assessing vitamin B<sub>12</sub> levels during chronic metformin use.

Secondary analysis of patients in the Diabetes Prevention Program Outcomes Study showed a higher incidence of combined low and low-normal vitamin B<sub>12</sub> deficiency in users assigned to the metformin group compared with those assigned to the placebo group at the 5-year and 13-year marks after randomization.<sup>1</sup> Post hoc analysis of patients in the Hyperinsulinemia: the Outcome of Its Metabolic Effects trial also showed lower levels of vitamin B<sub>12</sub> and higher levels of methylmalonic acid associated with significant

worsening of a validated neuropathy score in metformin users.<sup>2</sup>

The mechanism behind the development of vitamin B<sub>12</sub> deficiency is not completely understood but could possibly be alterations in intestinal mobility, bacterial overgrowth, or calcium-dependent uptake by ileal cells of the vitamin B<sub>12</sub>-intrinsic factor complex.<sup>3</sup>

Our electronic medical record has a built-in tool that suggests checking vitamin B<sub>12</sub> whenever a patient requests metformin refills. There are no current guidelines on the need for baseline testing of the vitamin B<sub>12</sub> level. The American Diabetes Association recommends periodic measurement of vitamin B<sub>12</sub> levels, possibly yearly, in metformin users and more often if there are symptoms indicative of deficiency.<sup>4</sup>

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