2017

Metformin and Vitamin B12 Deficiency: Consequences and Patient Monitoring

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From 1980 through 2014, the number of people diagnosed with type 2 diabetes has increased from 6.5 to 22 million (Centers for Disease Control and Prevention, 2014). Of these, 90-95% have type 2 diabetes mellitus.

Most global guidelines recommend starting metformin in patients with no contraindications at the time of diagnosis due to its efficacy, safety, and cost. There have been numerous studies that have suggested a relationship between metformin use and decreased vitamin B12 levels at a rate of 5.82-22% (de Groot-Kampius et al., 2013). While not fully understood, it is hypothesized that this could be occurring due to an impaired calcium dependent absorption of intrinsic factor and vitamin B12 in the ileum, an altered motility of the small intestine, a decrease in the acidity of the stomach, or an alteration in the normal flora of the gut (Kibride & Wmebaze, 2013). The purpose of this scholarly project is to establish a link between metformin use in type 2 diabetes and vitamin B12 deficiency, explore the consequences of such a deficiency, and make recommendations as to who should be screened.

Statement of the Problem

While the link between metformin and decreased vitamin B12 levels has been well established in literature, there are no clinical guidelines addressing routine evaluation for this condition in type 2 diabetes taking this medication. In addition, the effects of such a deficiency in the patient population has not been well established.

Research Questions

In adult patients with type 2 diabetes taking metformin, does a vitamin B12 deficiency cause adverse effects?

In this same population, should routine screening for a vitamin B12 deficiency be performed?

Effects of a Metformin Induced Vitamin B12 Deficiency on Patients

Adakalakotawarn, et al. (2014) found triglycerides and cholesterol/HDL ratios were inversely related to vitamin B12 levels but did not find a relationship between B12 levels and other diabetes co-morbidities such as retinopathy, neuropathy, cerebrovascular accident, and peripheral vascular disease.

Hansen, et al. (2016) found vitamin B12 levels to be inversely related to cardiovascular disease.

Aroda, et al. (2016) found that homocysteine levels were increased in those with low or borderline low vitamin B12 levels. At year 9 of the study, anemia in the metformin group was slightly increased in those with lower B12 levels but was not significant (p=0.25).

Chen, et al. (2012) used multiple methods to assess for neuropathy and were unable to find a significant relationship between peripheral neuropathy and vitamin B12 levels.

Singh, et al. (2013) found the duration of metformin use to be positively related to neuropathy score (95% CI 0.35-0.65, p<0.001).

Current Vitamin B12 Monitoring in Type 2 Diabetes taking Metformin

Pierce, Chung, & Black (2012) looked at subjects taking metformin. Only 40% of the total subjects had a vitamin B12 measured and 46% of patients who had been on high dose metformin for more than 10 years had never had one assessed. 29% with newly diagnosed anemia and 42% with newly documented neuropathy did not have a vitamin B12 level measured.

Farland, et al. (2015) found those with symptoms or a diagnosis of macrocytic anemia or peripheral neuropathy were at least 10 times more likely to have a vitamin B12 level measured.


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