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Effect of metformin on serum vitamin B12 and blood homocysteine levels in patients with type 2 diabetes mellitus and role of vitamin B12 supplementation

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Background: Vitamin B12 (B12) deficiency is a side effect of metformin use in diabetic patients together with associated increase in plasma homocysteine levels. It is easy to diagnose vitamin B12 deficiency by its hematological and neurological manifestations however they are often unnoticed and ascribed to diabetic complications among diabetic patients. This work was to investigate B12 level in patients with type 2 diabetes mellitus (T2DM) on metformin therapy, and correlation of its level with the prevalence of peripheral neuropathy and/or anemia in these patients. Also, this study investigated blood homocysteine levels in these patients and its correlation to vitamin B12 levels.

Methods: Eighty eight patients with T2DM were selected from Fayoum University Hospital outpatient clinics. They were divided into three groups: Group 1: Thirty patients on metformin therapy for more than one year without B12 supplementation, Group 2: Thirty patients on metformin therapy for more than one year on B12 supplementation and Group 3: 28 patients not receiving metformin therapy or B12 supplements (control group). All patients were subjected to complete history taking, including peripheral neuropathy using stocking and glove method, and laboratory investigations such as complete blood count, serum B12 and blood homocysteine levels.

Results: The mean serum B12 level was significantly lower in the metformin group compared to metformin and vitamin supplementation users (216 vs. 629.9 ng/L, $P<0.001$) and 354.6 ng/L in non-metformin users. Homocysteine levels weren't significant within groups. There was significant correlation between metformin dose and B12 levels ($P<0.05$), also between B12 deficiency and hyperhomocysteinemia ($P<0.01$, $r=-0.45$). There was significant relation between homocysteine and macrovascular complications ($r=0.33$, $P<0.01$) and between B12 and peripheral neuropathy ($P<0.01$, $r=-0.303$).

Conclusions: Vitamin B12 deficiency is associated with metformin use in T2DM patients with significant correlation with diabetic peripheral neuropathy (DPN) and hyperhomocysteinemia, whereas vitamin supplementation with metformin could prevent those effects.

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