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A Study on Vitamin B12 Levels in Metformin Therapy

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Abstract
Metformin is a widely prescribed medication for the management of type 2 diabetes, known for its efficacy and safety profile. It is generally acknowledged that it enhances insulin signalling, primarily in muscle, liver and adipose tissue and inhibits the synthesis of glucose by the liver. However, concerns have arisen regarding its potential impact on vitamin B12 levels. Vitamin B12 deficiency can lead to various health complications, including anemia and neuropathy. This study aims to investigate the relationship between metformin therapy and vitamin B12 levels in patients with type 2 diabetes. This cross-sectional study was carried out with 60 patients of type 2 diabetes mellitus of both sexes. They were split into two groups: group A consisted of 30 type 2 diabetes mellitus patients who had been receiving metformin therapy for more than a year and group B included 30 type 2 diabetic patients who had either ceased taking metformin six months prior or were not on it. A chemiluminescence approach was used to assess the amounts of serum vitamin B12. Data was examined statistically. Our findings indicate a statistically significant decrease in vitamin B12 levels among patients receiving metformin therapy when compared to the control group ($p<0.002$). The reduction in vitamin B12 levels was associated with the duration of metformin therapy and increased metformin dosage. Notably, we observed that patients who had been using metformin for more than two years had a higher risk of developing vitamin B12 deficiency. There is a correlation between metformin and a drop in serum vitamin B12. It is advised that individuals with type 2 diabetes mellitus who are receiving greater dosages or a longer period of metformin medication have an annual evaluation of their serum vitamin B12.

INTRODUCTION

Metformin, a widely prescribed first-line treatment for type 2 diabetes mellitus, has garnered recognition for its role in improving glycemic control and reducing the risk of diabetes-related complications[1]. Its efficacy, safety profile and cost-effectiveness have solidified its place in diabetes management. However, in recent years, concerns have arisen about the potential impact of metformin therapy on vitamin B12 status[2].

Vitamin B12, also known as cobalamin, is an essential water-soluble vitamin with critical roles in hematopoiesis, neurologic function and DNA synthesis[3]. Its deficiency has been associated with megaloblastic anemia, neuropathy and a range of neuropsychiatric symptoms[4]. As such, any factor that may compromise vitamin B12 status warrants careful consideration.

Metformin's impact on vitamin B12 levels stems from its potential interference with the absorption of this vital nutrient in the gastrointestinal tract[5]. Despite its popularity in diabetes management, metformin's precise mechanisms of vitamin B12 disruption remain incompletely understood[2]. The concerns surrounding vitamin B12 deficiency in metformin-treated individuals are particularly significant given the already elevated risk of comorbidities among patients with type 2 diabetes, including cardiovascular disease, neuropathy and retinopathy[6].

The use of metformin in the early stages of type 2 diabetes, often necessitating long-term therapy, highlights the importance of understanding the relationship between metformin and vitamin B12. Consequently, this study aims to comprehensively investigate the effect of metformin therapy on vitamin B12 levels in individuals with type 2 diabetes. We seek to determine whether metformin use is associated with reduced serum vitamin B12 levels, the extent of this potential influence and its clinical significance. By addressing these questions, our research intends to provide insights that can guide clinical practice by informing monitoring and supplementation strategies for patients with type 2 diabetes.

MATERIALS AND METHODS

Setting: The study was conducted Diabetic patients attending OPD or admitted in the inpatient Medicine department of CMR Medical College .

Type of Study: Hospital based observational cross-sectional comparative study.

Sampling Method: Random sampling was done among the patients attending OPD and admitted in wards. The study population consisted of 30 diabetic (type 2) patients. All the patients in the diabetic group were newly confirmed diabetics or were already receiving treatment for DM.

Inclusion Criteria: Patients with type 2 diabetes mellitus aged between 20-60 years. A detailed history was taken regarding duration of diabetes, dose and duration of metformin therapy, co-morbid conditions and symptoms of peripheral neuropathy (tingling sensation, pricking sensation and paresthesia). Patients were also examined for body weight and height.

Exclusion Criteria: Diabetes in pregnancy, chronic alcohol abuse, chronic renal failure, malabsorption, chronic diarrhea, critical illness, pernicious anemia, gastrointestinal surgery, Crohns disease, autoimmune thyroid disease, chronic hepatitis and the use of oral/ parenteral Vitamin B12 or multivitamin supplements.

Vitamin B12 levels were estimated by electro chemiluminescence. The hospital records, patient's prescriptions and medicines were searched for prescription of any Vitamin B12-containing supplements and patients were shown a list of commonly available multivitamins containing Vitamin B12 and were asked about their use at any time in the past.

Data Analysis: Data were all entered into MS excel and subjected to appropriate statistical tests like descriptive and inferential statistical analysis. Results on continuous measurements are presented as Mean±SD and results on categorical measurements are presented in Number (%). In this study, levels of vitamin B12 are interpreted as

- <200 pg/m/ml-low vitamin B12 levels
- >300 pg/ml-normal vitamin B12 levels

RESULTS AND DISCUSSIONS

This cross-sectional comparative study included 60 patients equally divided into two groups,
Group M-Patients with type 2 diabetes who took metformin for at least 6 months.
Group N-Patients with type 2 diabetes who do not take Metformin.

In Group M, 40% of patients were male and 60% were female (Table 1) with the age group ranging 20-40 years (30%) and 41-60 years(70%).
In Group N, 33% were males in the age group of 20-40 years and 67% were females in the age group of 41-60 years (Table 2).

The mean serum vitamin B12 in group M was 198.02±90.66 and in the group N was 566.72±230.19. The difference in mean serum Vitamin B12 levels of the two groups was statistically significant (p value = 0.002). The metformin users had significant reduction in the serum vitamin B12 levels as shown in (Table 3).

For most individuals with type 2 diabetes mellitus, metformin medication along with lifestyle change is advised as the initial course of treatment. Vitamin B12 insufficiency is one of the recently reported negative effects of metformin medication.

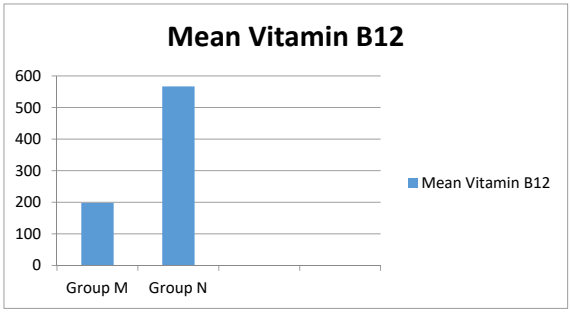

Fig. 1 Mean Vitamin B12 between cases and controls

Table No. 1 Gender distribution

Gender	Group M	Group N
Male	12(40%)	10(33%)
Female	18(60%)	20(67%)

Table No. 2 Age distribution

Age Group	Group M	Group N
20-40 Years	9(30%)	10(33%)
41-60 Years	21(70%)	20(67%)

Table No. 3 Mean vitamin B12

Group	Mean Vitamin B12
Group M	198.29±90.66
Group N	566.72±230.19

The study group had mean vitamin B12 levels of 190.02±90.75, while the control group had mean values of 586.9±243.69. The two groups' differences in vitamin B12 were statistically significant (p value = 0.002). In their investigation, Reinstatler *et al.*, discovered that among type 2 diabetics on metformin, the geometric mean blood B12 concentration was 317.5 pmol/L. This was much less than the geometric mean concentration in people without diabetes (350.8 pmol/L., p = 0.0011) and those with type 2 diabetes who were not taking metformin (386.7 pmol/L., p = 0.0116)[7]. Moreover, cross-sectional studies detail a broad range of prevalence-from 5.8% to as high as 30%-of biochemical vitamin B12 deficiency associated with metformin consumption[8,9-12].

This study's primary strength was that we separated metformin use based on dosage and duration of use, unlike many other studies that only looked at one factor-dosage or duration. This study differentiated metformin use based on two parameters: daily dosage and duration of use and compared the prevalence of vitamin B12 deficiency in users and non-users. It was feasible to examine the prevalence of vitamin B12 deficiency with a comparable population that was not using metformin because a control group was present.

CONCLUSION

Metformin at = 1500 mg/d may play a significant role in vitamin B12 insufficiency, whereas concomitant multivitamin administration may help prevent the shortfall. This study provides evidence of a significant association between metformin therapy and reduced vitamin B12 levels in patients with type 2 diabetes. Healthcare providers should be vigilant in monitoring vitamin B12 status in individuals on long-term metformin treatment. Routine screening, early detection and appropriate supplementation may be warranted to prevent the development of vitamin B12 deficiency-related complications. Further research is needed to explore the clinical significance of these findings and to inform guidelines for the management of type 2 diabetes in patients on metformin therapy.

REFERENCES

1. Nathan, D.M., J.B. Buse, M.B. Davidson, E. Ferrannini, R.R. Holman, R. Sherwin and B. Zinman, 2009. Medical management of hyperglycemia in type 2 diabetes: A consensus algorithm for the initiation and adjustment of therapy. Diabetes Care, 32: 193-203.
2. Bailey, C.J., C. Wilcock, J.H. Scarpello and S.J. Yeaman, 2014. Metformin and the intestine. Diabetologia, 57: 1434-1445.
3. Stabler, S.P., 2013. Clinical practice. Vitamin B12 deficiency. New Engl. J. Med., 368: 149-160.
4. Aroda, V.R., S.L. Edelstein, R.B. Goldberg, W.C. Knowler and S.M. Marcovina *et al.*, 2016. Long-term metformin use and vitamin B12 deficiency in the diabetes prevention program outcomes study. J. Clin. Endocrinol. Metab., 101: 1754-1761.
5. Adake, R. and A. De, 2017. Metformin and vitamin B12 deficiency: A review. Canad. J. Physiol. Pharmacol., 95: 455-459.
6. Draznin, B., 2016. Mechanism of disease: The pathogenesis of insulin resistance: A small islet hormone with big actions. Ann. Internal Med., 145: 137-139.
7. Reinstatler, L., Y.P. Qi, R.S. Williamson, J.V. Garn and G.P. Oakley, 2012. Association of biochemical B12 deficiency with metformin therapy and vitamin B12 supplements. Diabetes Care, 35: 327-333.
8. Tomkin, G.H., D.R. Hadden, J.A. Weaver and D.A.D. Montgomery, 1971. Vitamin-b12 status of patients on long-term metformin therapy. BMJ, 2: 685-687.
9. Nervo, M., A. Lubini, F.V. Raimundo, G.A.M. Faulhaber, C. Leite, L.M. Fischer and T.W. Furlanetto, 2011. Vitamin B12 in metformin-treated diabetic patients: a cross-sectional study in Brazil. Rev. Assoc. Med. Bras., 57: 46-49.
10. Pflipsen, M.C., R.C. Oh, A. Saguil, D.A. Seehusen, D. Seaquist and R. Topolski, 2009. The prevalence of vitamin b12 deficiency in patients with type 2 diabetes: A cross-sectional study. J. Am. Board Family Med., 22: 528-534.
11. Romero, J.M.C. and J.M.R. Lozano, 2012. Vitamina b12 en pacientes diabéticos tipo 2 en tratamiento con metformina. Endocrinol. Nutr., 59: 487-490.

12. Pongchaidecha, M., V. Srikusalanukul, A. Chattananon and S. Tanjariyaporn, 2004. Effect of metformin on plasma homocysteine, vitamin B12 and folic acid: A cross-sectional study in patients with type 2 diabetes mellitus. J. Med. Assoc. Thai., 87: 780-787.