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Diabetic Neuropathy Patients with Vitamin B12 Deficiency

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Abstract: **Many human deficiencies may be traced back to insufficient levels of vitamin B12, which is soluble in water. Levels of B12 in the blood and a revised demographic study disprove the former hypothesis. Weight, blood levels, and dietary consumption of vitamin B12 were all studied in connection to one another in persons with Type 2 diabetes and diabetic neuropathy. Thirty volunteers were selected from the medical student bodies at the Universities of Kansas and Utah. Initial measurements of height, weight, body mass index, medicines, supplements, age, blood levels of vitamin B12, and dietary intake were collected for a randomised exercise intervention study (Activity for Diabetic Polyneuropathy: ADAPT Study). Nutrition data was entered into a software programme to identify the types and quantities of vitamin B12 ingested during a 3-day period (NDSR), and descriptive statistics were used to profile the individuals. The effects of metformin on patients were compared to those of non-metformin patients using analysis of variance. Blood B12 levels were correlated with demographic variables including age, body mass index, supplement use, and diet by regression analysis. For each set of independent variables at any given moment, a pairwise correlation matrix was compiled. Humans used up an average of 4.3 g of vitamin B12 daily. Taking metformin was not significantly linked to lower blood B12 levels. There was no correlation between age, body mass index, or obesity and vitamin B12 levels in the blood. Vitamin B12 supplementation was linked to increased vitamin B12 levels in the blood regardless of dosage (p =.031). Individuals concerned they may be vitamin B12 deficient can take heart from these findings. Similar to how there was no drop in blood B12 levels associated with ageing, this phenomenon was not observed in the investigations. age and blood B12 levels are related; so, screening for deficiencies should begin earlier in life.**

Key words: diabetic neuropathy, vitamin B12, diabetes mellitus, autonomic neuropathy, painful neuropathy

Full Bibliographic References

Whether published in academic publications or presented at research academies, the papers and theses studied here were all produced by respected academics and medical professionals and given to medical students by reputable organizations. Their primary goal is to spread knowledge about vitamin B12 deficiency among those who suffer from Neuropathy diabetes. In addition, the investigations focus on the management and treatment of such efficiency to lessen and prevent its effects in patients with diabetic neuropathy.

Objective of the articles

Metformin medication, vitamin B12 supplements, and biochemical B12 insufficiency in patients with Type 2 diabetes and diabetic neuropathy, as well as these patients' weight, blood vitamin B12 levels, and vitamin B12 food consumption, were the primary foci of the evaluated papers [*Atlanta et al., 2014*].

I. INTRODUCTION

Statistics from the Centers for Disease Control and Prevention show that 29 million Americans suffer from diabetes mellitus (Atlanta *et al.*, 2014). Most persons with Type 2 diabetes are overweight or obese, per the World Health Organization (NIH, 2019). Sixty percent to seventy percent of the 27.5 million persons with type 2 diabetes (Singh *et al.*,2013). have PN, and twenty two percent have vitamin B12 deficiency. Patients undergoing DPN testing should first rule out vitamin B12 insufficiency because the symptoms are similar. The incidence of vitamin B12 deficiency was 74% (Andrès *et al.*,2004). higher in people on the diabetes treatment metformin compared to those taking insulin or other biguanides. Age, poor nutrition, malabsorption, and some medications are all contributors to vitamin B12 deficiency (Andrès *et al.*, 2004). There have been a number of studies looking at how ageing and metformin usage affect vitamin B12 levels.

Diabetic neuropathy (DN) can be diagnosed after all other possible causes of neuropathy in a diabetic patient have been ruled out. Seventy-five percent of all occurrences of DN are due to distal symmetrical neuropathy, making it the most common kind of DN. Acute asymmetrical neuropathies may affect the cranial, thoracic, or leg nerves and are usually the result of an ischemic infarction of the vasa nervosa. Diabetic patients with asymmetric neuropathies should be evaluated for entrapment neuropathy. Previously thought to be caused

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by metabolic problems and then by ischemia, amyotrophy in persons with diabetes is now thought to be caused by alterations in the immune system. Observation of symptoms and signs, quantitative sensory testing, nerve conduction investigations, and autonomic testing are all useful in the clinical diagnosis of DN, although only two of these modalities are necessary. Lipoic acid and L-carnitine are used to lower blood sugar and other cardiovascular risk factors. Symptoms and indicators, quantitative sensory testing, a nerve conduction study, and autonomic testing are all recommended for clinical diagnosis of DN. Supplementation with lipoic acid and L carnitine, management of hyperglycemia, and management of other cardiovascular risk factors are all components of therapy for people with DN. Analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants, and anticonvulsants (both conventional and alternative) are all used to alleviate the discomfort associated with neuropathy. Those with autonomic neuropathy might find relief from their symptoms.

Analysis of vitamin B12 insufficiency in the elderly conducted in Framingham in 1994. [International Diabetes Federation], results showed that whereas 40% of those over 65 were inadequate, just 17.9% of those between the ages of 22 and 63 were. Nutritional cobalamin insufficiency due to inadequate oral vitamin B12 consumption was detected in 12% of the population aged 64 and older (Couderc *et a*l., 57.6%) (Couderc AL *et al.*,2015), serum B12 levels were found to be considerably lower in people aged 70 and higher compared to those aged 60-69, as reported by Solomon *et a*l (Solomon *et a*l., 2011). According to research by El-Khateeb (2014), Jordanians aged 19 to 30 had the highest prevalence of vitamin B12 insufficiency. Many previous research with similar findings are cited in this one (El-Khateeb *et al*.,2014). Yajnik found that 67% of rural Indian men between the ages of 30 and 50 had deficient levels of vitamin B12 in his cross-sectional investigation (Yajnik CS *et al.*,2006). Metformin use and other possible vitamin B12 insufficiency causes are inconsistent in similar ways.

Pre-diabetes and type 2 diabetes patients take metformin more than any other medication [Baltrusch S et al.,2021 - de Jager J et al.,2010]. Most studies show that those who use metformin have a 10%-30% higher risk of vitamin B12 insufficiency, albeit the timing varies widely (Singh *et al*.,2021, de Jager *et al*.,2010). Researchers found that after 12-15 years of inadequate vitamin B12 consumption, metformin users' blood B12 levels began to exhibit diminished storage (Baltrusch *et al.,* 2021). However, Bauman et al. found in a clinical trial that blood B12 levels dropped after just 3 months of metformin use. Cross-sectional research conducted by the National Health and Examination Survey between 1999 and 2006 found a weak association between metformin usage and an increased risk of vitamin B12 insufficiency (Martin *et al*.,2021). Metformin users with a longer duration of usage (8.1%) had a greater risk than those who had used the drug for a shorter period of time (1.4%). (Reinstatler *et al.* ,2012). Outpatients with Type 2 diabetes were the subjects of a cross-sectional research by Pflipsen et al. Studies have shown that using metformin raises the risk of vitamin B12 insufficiency, and that the dose has no influence on this correlation. They did say that using metformin for an extended period of time raises the chance of insufficiency, but they did not specify how much time. After only one year of treatment, Singh et al. found a 28.5% rise in vitamin B12 insufficiency and a 48.8% increase in peripheral neuropathy among metformin users. (Baltrusch *et al*.,2021). Metformin's effects on the elderly and those taking several drugs are poorly studied, however. The relationship between obesity and a lack of vitamin B12 has not been adequately investigated. As of yet, only two studies have linked vitamin B12 deficiency to being overweight (El-Khateeb *et al*.,2014, Out *et al*.,2018). Population research found that 35.5% of those over 60 who were overweight or obese were vitamin B12 deficient, while 34.4% of those over 60 who were obese were deficient. Prospective descriptive studies found that children who were overweight had blood B12 levels that were 130 pg/mL lower than their leaner peers. Ten percent of kids who are overweight had low blood B12 levels, but just 2.2% of kids who were slim had poor B12 levels (Out *et al.,* 2018). Neither investigation considered obesity to be a separate factor in vitamin B12 insufficiency.

When used to treat vitamin B12 deficiency and DPN, supplements have shown mixed effectiveness. Metformin did not have an association with a reduced frequency of vitamin B12 deficiency in the National Health and Nutrition Examination Survey (NHANES). 14.1% of those who took less than 6 g/day were deficient, whereas 1.8% of those who took more than 6 g/day were deficient. Vitamin B12 from both plants and animals was investigated in the Framingham Offspring Prospective Cohort research of healthy adults aged 26 and above. (Tucker *et al.,* 2000). Those who consumed fortified cereals less often (less than four times per week) were shown to be 23% more likely to become deficient than those who consumed fortified cereals more regularly. Researchers found that fortified foods may be easier to digest than meat and other protein sources.

A. Research Questions

Through most of the reviewed articles there were some repeated articles like:

A. What is the average daily intake of vitamin B12 for people with diabetes who have peripheral neuropathy?

B. Do people who use metformin have lower vitamin B12 levels in their blood than those who don't?

c. Is there a correlation between vitamin B12 intake and blood levels of this vitamin?

d. Is there a relationship between BMI and B12 in the blood?

e. How does ageing affect serum B12 concentration?

B. Time frame of the analyzed researches

Up to six years may pass before vitamin B12 insufficiency is detected in the blood (Chatthanawaree, 2011). Longitudinal research examined how long it takes to develop vitamin B12 deficiency. Similarly, Flippen et al. demonstrated that a patient's risk of vitamin B12 insufficiency increased with the duration of their diabetes diagnosis and metformin use (Pflipsen.,2009). Kumar discovered that after one year of exposure to metformin, vitamin B12 deficiency increased (Singh, 2013). Researchers discovered no change in the dosage of metformin supplied (Golay *et al.,* 2005).

(Lindenbaum, 1994) Jager et al. discovered that vitamin B12 insufficiency is a progressive illness that worsens with time.

C. Stated problems:

Peripheral-neuropathy is a common symptom of vitamin B12 deficiency. Retrospective research (Roglic G.,2011) found that neuropathy affected 62% of diabetes patients with vitamin B12 deficiency seen in a primary care clinic. Sixty percent of patients with insulin-dependent diabetes (Roglic, 2016) and 59 percent of patients with non-insulin-dependent diabetes (NID., 2016) reported neuropathy while using the treatment, compared to 46 % percent of those who were not taking the drug. When comparing the sexes, the difference was more pronounced in women. Only around 20% of all patients suffered from neuropathy. Non-insulin-dependent diabetics with poor control of their blood sugar often get neuropathy (NID DK, 2016).

II. METHODS

The significant majority of research conducted up to this point support this. People with idiopathic B12 deficiency who were either using metformin or were in the control group were examined using cross-sectional analysis.

Diabetic neuropathy was identified using the medical history, nerve conduction tests, and the Michigan test. As a result of the efforts made, a lot of information, including demographic data, was acquired.

Using a linear regression model, the variables affecting vitamin B12 and diabetic neuropathy were investigated.

T2DM in accordance with recommendations from the ADA (American Diabetes Association) (Edelman, 2004). Peripheral neuropathy must be present, and the patient must be receiving care from a primary care physician who satisfies the requirements established by the Toronto Diabetic Neuropathy Expert Group (Tesfaye S., 2010).

C. Proposed solutions:

The following are some (measures to prevent a lack of V B12):

1. supplements of vitamin B12

Intramuscular cyanocobalamin, oral cyanocobalamin (Couderc *et al*.,2015, Reinstatler *et al*.,2011, Reinstatle *et al*., 2012, Jayabalan *et al*,.2016) and oral methyl cobalamin are the three distinct forms of vitamin B1. The descendants of the Framingham Cohort study were used in a prospective cohort study by Tucker et al. Participants must come from a healthy demographic and be at least 26 years old. The study examined oral and intramuscular vitamin B12 supplementation. Cyanocobalamin was given orally in amounts ranging from 1000g daily to 1000g monthly. From 1000g per day for a week to 1000g per month, the intramuscular dose was used. According to the study, comparing supplement users to non-users, the likelihood of developing a deficit was 8% versus 20%. Despite the fact that both oral and intramuscular treatments significantly increased blood B12 levels, the study suggests intramuscular injection therapy for the quickest results if serum B12 levels are 149pg/mL or above. In persons over 50 who take metformin, NHANES found no association between vitamin B12 supplementation and a risk of vitamin B12 deficiency. People who ingested up to 6g of vitamin B12 had a 14.1% chance of becoming deficient, while people who consumed more than 6g had a 1.8% chance. Finally, a thorough assessment of vitamin B12 supplementation for diabetic peripheral neuropathy came to the conclusion that it was unlikely that any vitamin B12 (Reinstatler .,2012).

Therefore, there is insufficient evidence from the few studies that have been done to say that taking calcium or vitamin B12 supplements lowers the chance of developing vitamin B12 deficiency (Tucker ,2000).

2.Adding vitamin B12 to fortified foods Vitamin B12 deficiency has been shown to be prevented by increasing the intake of foods high in the vitamin as well as by using fortified foods. The Framingham A research on children examined fortified foods. Users of fortified cereal had a 14% likelihood of developing a deficiency, compared to 23% for non-users. Four servings or more of fortified cereal per week was the standard for intake. Additionally, the researchers discovered that fortified meals, like cereal, may help people absorb protein more quickly than meats and other sources. sources like beef and others (Tucker,2000).

3. Supplementing calcium

Due to calcium's role in vitamin B12 absorption, it has been attempted in conjunction with oral vitamin B12 supplements and fortified foods to treat or prevent vitamin B12 deficiency. Patients using metformin were enrolled in a randomized controlled trial of calcium carbonate for vitamin B12 deficiency. After three months of metformin treatment, the participants began taking a calcium carbonate (1.2g) tablet once a day. One research found that calcium carbonate increased serum transcobalamin II holoTCII levels but had no effect on serum B12 levels in patients on proton pump inhibitors (PPIs) (Couderc 2015- Presse., 2016). A cross-sectional study was conducted using data collected from a geriatric hospital where patients were given calcium carbonate supplements ranging in dosage from 250 milligrams per day to 1,500 milligrams per day. The study found that those who used PPIs without also taking calcium supplements were at a higher risk of vitamin B12 deficiency. Combining calcium supplements with PPI usage significantly reduced the incidence of vitamin B12 deficiency, the study found. Results from studies on the use of calcium supplements to prevent vitamin B12 insufficiency have been mixed (Presse *et al.,* 2016), calling for more investigation into this topic.

III. RESULTS AND DISCUSSION

The intake of vitamin B12 was the subject of this study. to compare the vitamin B12 blood levels of persons with diabetic peripheral neuropathy who took metformin to those who did not. [Dali-Youcef N et al., 2009] Also considered were the effects of age (6-8), body mass index, and blood B12 levels.

Studies included in the meta-analysis (Harrington *et a*l., 2016) reported a wide variety of blood B12 levels, from an average of 222 pmol/L to well over 2000 pmol/L.

Seventy percent of individuals on metformin in one study also took a vitamin B12 supplement, compared to just 37% of those on the placebo. Age, body mass index, supplement use, and serum B12 levels were similar between people who used metformin and those who didn't.

After keeping track of everything I ate for three days, I found that I consumed an average of 1,728 calories each day. A median of 37% fat, 17% protein, and 42% carbohydrates was found. There was an average daily intake of 4.3 g of vitamin B12. Fortified foods accounted for 20% of calories, whereas animal products accounted for 14% (and 43% of the total dietary vitamin B12). Only 48% of people who responded indicated they ate vitamin B12 fortified meals, and 1 individual identified as a vegetarian. Protein intake was lower among people on metformin (16.1% versus 19.6%) compared to those not taking the drug. No further material differences were found between the groups (Atlanta *et al.*, 2014). Serum B12 levels did not change significantly between metformin users and nonusers (p=0.182). Lack of a correlation between vitamin B12 consumption and serum levels was observed (p= 0.17). Although supplement use was linked to higher levels of vitamin B12 in the blood, this correlation was not statistically significant (p=0.031). There was no association between vitamin B12 levels in the blood and either age, BMI, or obesity status (Atlanta.,2014).

A pairwise correlation matrix was widely utilised in experiments and analysis to approximate the strength of association between each independent variable. Fortified meals and animal products are both associated with vitamin B12 intake. There was a statistically significant correlation between eating fortified foods and getting enough vitamin B12 (p=0.00) (Dyck *et al*., 1993- El-Khateeb, 2014).

Finally, diabetics often worry about nerve damage, which can be caused by a lack of vitamin B12. One study found a correlation between diabetic neuropathy and vitamin B12 deficiency in the blood plasma. Supplemental vitamin B12 intake should be considered when using metformin.

Blood B12 concentrations have not been studied in relation to age, body mass index, medication usage, or the use of dietary supplements (Tucker, 2000). In addition, studies examining blood B12 levels in people with diabetic peripheral neuropathy are few. The distribution of macro and micronutrient intake among individuals has never been studied using 3-day meal diaries. Supplements have been shown to be more helpful than either conventional treatment or demographic factors in a number of studies (Reinstatler.,2012). No correlation between age and B12 levels in the blood was found in the most recent study [El-Khateeb M.,2014]. Blood B12 levels are associated with body mass index (BMI) (El-Khateeb.,2014). However, more research is needed to draw firm conclusions, as this study did not find a correlation between BMI and blood B12 levels.

VI. Evaluation of the Quality of the Studies

In the first place, it explains why Vitamin B12 is essential to our bodies and what happens when we don't get enough of it. Also, the link between diabetes and neuropathy is broken out here. These two areas form the backbone of the field's foundational research. Primary research question is implicit in the title.

The abstracts together demonstrate that this is not a simple issue. A future study should investigate whether or not age and blood B12 levels are connected, as doing so makes it more challenging for the reader to understand and identify the direction of the essay or thesis. They did an excellent job of describing both areas in detail, beginning with Vitamin B12 and its effects on the body and outlining the types of deficiencies, then moving on to Diabetes and a general understanding of it, and finally concluding that Vitamin B12 supplements and metformin therapy are associated with biochemical B12 deficiency. Each author on average referred to seven other research and scholarly journals for their work. They weren't only honest; they also offered sharp analysis. Personally, I think the inclusion of such excellent, widely recognized authors and examples does a lot to strengthen the text's legitimacy. Unless you read the introduction, you probably won't understand where anything belongs. To pique the attention of more readers and encourage them to continue reading, the opening must be modified to be shorter and catchier. It's likely that the reader will have already read quite a few of the articles in the collection by the time they get to the part with the genuinely good examples that belong to the regular workday of a public administrator. The work as a whole is strong and well-written, and it gets across an important point to business and government organizations. As a whole, the work is interesting and engaging, but it drags in the beginning and doesn't offer a satisfying conclusion to the problem it's addressing.

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