REVIEW ARTICLE

A Review on Vitamin B12 and Diabetic Neuropathy

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ABSTRACT:
Vitamin B12, also called cobalamin, is a vitamin that is important for several biological functions. It is acted as a neurotrophic factor with an affinity for neuronal tissues and has been showing to be essential in preserving and regenerating peripheral nerves. It is important in supporting the process of myelination, participating to functional restoration. Diabetic neuropathy mentions to various types of nerve damage linked to diabetes mellitus. These conditions are microvascular complications of diabetes mellitus including small blood vessels that provide nerves. Relatively, third, fourth, or sixth cranial nerve palsy are common conditions that may be linked with diabetic neuropathy. Interestingly, a significant correlation was found between lower vitamin B12 concentrations and possessing a positive diagnosis of diabetic neuropathy.

KEYWORDS: VitaminB12,diabetic neuropathy.

INTRODUCTION:

Vitamin B12:

Vitamin B12, also called cobalamin, is a vitamin which is important for several biological functions. It is acted as a neurotrophic factor with an affinity for neuronal tissues and has been showing to be essential in preserving and regenerating peripheral nerves [1]. It is important in supporting process of myelination, participating in functional restoration [2]. Also, it has been shown that vitamin B12 could affect nerve regeneration via regulation of gene transcription [2]. Vitamin B12 may diminish ectopic nerve firing, which could demonstrate why it participate in relieving painful symptoms [3].

Diabetic neuropathy:

Diabetic neuropathy mentions various types of nerve damage linked to diabetes mellitus. These conditions are microvascular complications of diabetes mellitus including small blood vessels that provide nerves. Relatively, third, fourth, or sixth cranial nerve palsy are common conditions which may be linked with diabetic neuropathy [4]. Diabetic neuropathy influences all peripheral nerves involving sensory neurons, motor neurons as well as autonomic nervous system. Thus, diabetic neuropathy can influence all body organs and systems, as all are innervated. High glucose levels lead to a non-enzymatic covalent bonding with proteins, and these glycated proteins have been involved in the pathogenesis of diabetic neuropathy and other long-term (chronic) complications of diabetes mellitus. In addition, in the presence of hyperglycaemia high glucose is metabolized via the polyol pathway which converts glucose into sugar alcohols (polyols). This pathway seems to be involved in diabetic complications, especially in microvascular damage to the retina, renal, and nerves [5]. Interestingly, a significant correlation was found between lower vitamin B12 concentrations and possessing a positive diagnosis of diabetic neuropathy [6]. So, this review was performed by using PubMed and Google Scholar to identify the related articles involved vitamin B12 deficiency and diabetic neuropathy. Further related articles were identified from revieweing the referenced citations.

The link between vitamin B12 deficiency and diabetic neuropathy:

Neuropathy, being a relative health abnormality occurring owing to vitamin B12 deficiency affects about 30% of diabetic patients who are over forty years of age and state around having a decreased sensory perception in their feet [7]. Unfortunately, signs and symptoms of diabetic neuropathy and paraesthesia are somewhat identical, decreased vibration sense and reduced proprioception related to vitamin B12 deficiency [8]. Diabetic neuropathy symptoms overlap with deteriorated vibration sensation and proprioception, and also paraesthesia, which has also been showed to be linked with vitamin B12 deficiency [8].

Recent studies showed the high prevalence of vitamin B12 deficiency from 28 to 41% of diabetic patients [9, 10, 11, 12]. However, a study by Alvarez et al revealed that the prevalence of vitamin B12 deficiency in diabetic patients with neuropathy was 17%. Also, they found inverse correlation between diabetic neuropathy and vitamin B12 levels and a significant difference in

vitamin B12 concentrations in males than females. This finding considered that diabetic neuropathy is more prevalent in men. However, most researches did not find the differences in vitamin B12 deficiency according to sex. But, a study by Alharbi et al showed a higher prevalence of vitamin B12 deficiency in females [13]. Furthermore, Ahmed et al showed that black people less prone to vitamin B12 deficiency than another ethnic group [12].

Since diabetes mellitus is a common disease and the first line of treatment is metformin. So, several studies investigated the side effects of this treatment on vitamin B 12 amounts. A meta-analysis study showed that the use of metformin is a risk factor for vitamin B12 deficiency in patients with diabetes mellitus [14].

Moreover, Alvarez et al noticed that the patients on high doses of metformin and diabetic patient with neuropathy have significantly lower vitamin B12 concentrations [6]. Other studies found higher dose of metformin was linked with lower concentrations of vitamin B12 [15,16]. Furthermore, a study by Zinman et al reported that metformin treatment is linked with vitamin B12 deficiency and leads to neuropathy, ranging from paraesthesia and reduced peripheral sensation to alters in mental status [17]. However, Gupta et al suggested that a cumulative dose of metformin is linked with a decrease in B12 amounts and worsening neuropathy [18].

Recent research by Gupta et al. [19] revealed a positive correlation between time of metformin intake and diabetic neuropathy as well as a negative correlation between time of metformin intake and vitamin B12 concentrations. A systemic review by Sun et al. [20] showed that taking vitamin B12 supplement had good outcomes on symptoms of neuropathy such as pain and paraesthesia. While, a study by Jayabalan and Low found no significant effect of vitamin B12 supplement on improvement of neuropathy symptoms [21].

Several studies performed to find the possible association between long term use of metformin and vitamin B12 deficiency related peripheral neuropathy. Bauman et al reported that metformin treatment leads to decrease vitamin B12 uptake in the terminal ileum [22]. Additionally, Ting et al showed that long time use of metformin causes malabsorption of vitamin B12, with a reduce in the vitamin B12 levels about 30% [23]. This observation has been attributed to change in small bowel motility (which enhances bacterial overgrowth with subsequent vitamin B12 deficiency), modification in intrinsic factor levels, and suppression of the calcium dependent absorption of cobalamin -intrinsic factor complex at the terminal ileum [24]. According to this mechanism, some of the patients with metformin-associated vitamin B12 deficiency have been treated by calcium supplement as well [25].

CONCLUSION:

In view of current evidence, high prevalence of vitamin B12 deficiency, especially in diabetic patients with neuropathy. Also, high risk of vitamin B12 deficiency induced by metformin treatment. So, screening for vitamin B12 levels is important, especially in patients with diabetic neuropathy and those on high doses or long-term use of metformin.

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