

Association of Low Vitamin B12 in Trigeminal Neuralgia Patients Visiting Peshawar Dental College

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Abstract

Background: Vitamin B12 is also known as cobalamin and is a hydrophilic vitamin, it is involved in metabolism of every cell of the body. It is a cofactor in DNA synthesis RNA, hormones, proteins, and lipids, and in both fatty acid and amino acid metabolism. Low levels of serum vitamin B12 may trigger pain in patients suffering from trigeminal neuralgia. Methylcobalamin, a form of Vitamin B12, protects against neurological diseases and aging. Mauro showed that high doses of methylcobalamin are needed to regenerate neurons as well as the myelin sheath that protects nerve axons and the peripheral nerves.

Objective: The prime focus of this study was to report the frequency of low serum Vitamin B12 level in Identified Trigeminal Neuralgia patients visiting Peshawar Dental College and Hospital and to find the effect of gender on low serum vitamin B12 levels.

Methods: A total of 90 known trigeminal neuralgia patients seeking treatment at the Department of Oral Medicine, Peshawar Dental College and Hospital were enrolled. All patients were advised to carry out serum Vitamin B12 level in laboratory. Data were analyzed by SPSS version 19. The statistical significance was set up at $p < 0.05$.

Results: Out of 90 known trigeminal neuralgia patients, 58.8% were females and 41.1% were males. 43.3% females and 27.0% males had low serum Vitamin B12 levels. No statistical significant difference between gender and low serum vitamin B12 level was found.

Conclusions: Study confirms that gender has no effect on low serum levels of B12 in trigeminal neuralgia patients and a high proportion of trigeminal neuralgia patients had a low serum vitamin B12 levels.

Key Words: Trigeminal Neuralgia, vitamin B12, Methylcobalamin

Introduction

Trigeminal nerve is a fifth cranial nerve, it can be involved in various disorders, among which the Trigeminal neuralgia (Tic douloureux) is very common. Trigeminal neuralgia can cause episodes of stabbing, intense electric shock like pain in the area around the face which is supplied by the fifth nerve are distributed i.e, lips, nose, scalp, nose, Maxillary jaw, Mandibular jaw, and forehead. This pain lasts from few seconds to few minutes.

According to the International Association for the study of pain (IASP), the trigeminal neuralgia is a sudden, brief, severe, stabbing, recurrent and mostly unilateral pain effecting the

area supplied by the trigeminal nerve.¹ Classically, it is a brief attack of pain, triggered by talking, chewing, shaving and even during teeth brushing, applying makeup or even a slight breeze.

The 1st line of treatment commonly used are anticonvulsant drugs, particularly carbamazepine. After the failure of medications, various surgical procedures like micro surgical rhizotomies, microvascular decompression, radiofrequency ablation and stereotactic radiosurgeries can be applied.

The only surgical procedure effective for long term pain relief is Microvascular decompression (MVD).² In a study conducted by Devor and Rappaport, the biopsy specimen where taken, they found that demyelination occurs during nerve compression. It is broadly believed that the constant compression can de-myelinate sensory axons in the nerve and its root. They believed that MVD provides prolonged relief from pain due to re-myelination of axons.³

The exact etiology for trigeminal neuralgia is not fully known, several theories are present, as some associate a low vitamin

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level with trigeminal neuralgia pain. However, no conclusive evidence is provided. Vitamin B12 (Cobalamin) is hydrophilic. Vitamin B12 (cobalamin) is a hydrophilic vitamin but unlike other water-soluble vitamins it is not excreted swiftly in the urine, rather collects and is stored in the liver, kidney and other body tissues. Therefore, vitamin B12 deficiency may not appear until after five or six years of inadequate diet supply. A large study was conducted at University of Tufts, by the USDA and established the fact, that 39 % of studied group of 3,000, had low values, when using a vitamin B12 concentration of 350 mg/mL which falls in the low criteria.⁴

Many cases of vitamin B12 deficiency have been reported. A pure vegetarian diet may lead to a B12 deficiency, as protein rich diet are only acknowledged as a good source of dietary B12. A lack of B12 intake and incompetent absorption leads to deficiency. Vitamin B12 supplements shall be taken with drugs that lower the stomach acids and disturbs the vitamin B12 absorption.

Conditions like autoimmune diseases, pernicious or unexplained anemia, pancreatic pathologies, ileal resection, Crohn's disease, HIV, gastritis, surgical procedures related to stomach or small intestine, malabsorption syndromes, multiple sclerosis and consumption of histamine2 receptor antagonists or proton pump inhibitors can lead to malabsorption of vitamin B12.

In rats, Cyanocobalamin manifests the reduced spinal nerve ligation induced allodynia and tactile allodynia and thus they might have profound role in humans too.⁵

Vitamin B12 acts as a methyl donor and in combination with folic acid aids in the synthesis of DNA and red blood cells. Therefore, has an effective role in maintaining the health of the myelin sheath that surrounds nerve cells. Methyl cobalamin has recently been projected as a Vitamin B12 which can act as a shield against neurological diseases and aging.^{6,7}

The liver transforms cyanocobalamin into Methyl cobalamin within the body but larger quantity of Methyl cobalamin are needed to correct neurological defects thus regenerating neurons as well as the myelin sheath that protects nerve axons and the peripheral nerves.⁸

Isolated facial neuralgia, independent of trigeminal neuralgia and peripheral neuropathy can be caused by vitamin B12 deficiency according to the research paper presented at the 14th Congress of the International Headache Society. Treatment with B12 injections was found to effective in treating patients with neuropathic pain and also a profound dose can be a remedy for trigeminal neuralgia.⁹

Therefore, the aim of this study is to evaluate the frequency of trigeminal neuralgia patients with serum vitamin B12 deficiency and the effect of gender over the level of serum vitamin B12 in comparison to patients with other facial pain syndrome and if increasing the amount of vitamin B12 will actually improve pain levels in Trigeminal neuralgia in the year 1953 and 1954^{10,11} but since then clinical studies support its use. Table I

Table I: Recommended Dietary Allowance for Vitamin B 12

Age	Male	Female	Pregnancy	Location
0-6 months*	0.4 mcg	0.4 mcg	Pregnancy	Location
7-12 months*	0.5 mcg	0.5 mcg		
1-3 years	0.9 mcg	0.9 mcg		
4-8 years	1.2 mcg	1.2 mcg		
9-13 years	1.8 mcg	1.8 mcg		
14+ years	2.4 mcg	2.4 mcg	2.6 mcg	2.8 mcg
*Adequate Intake				

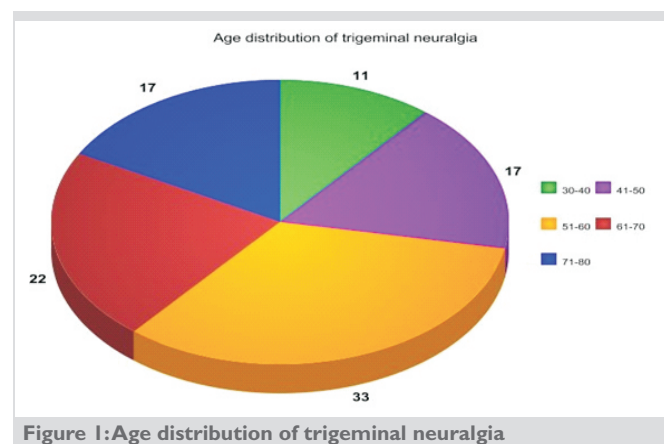
Methodology: The present prospective cross-sectional study was carried out following approval of the Institutional Review Board (IRB) of Peshawar Medical and Dental College Peshawar.

An informed consent was obtained from all the patients. The data were collected from known trigeminal neuralgia (previously diagnosed via IHS criteria) patients who visited Peshawar Dental College and Hospital, between March 2016 and June 2017.

These patients were advised to check their serum vitamin B12 level as a routine laboratory test. Patients who were taken vitamin B12 supplements were not part of the study.

Results: A total of 90 known trigeminal neuralgia patients participated in the study. There were 42.2% males while 57.8% females. Patient in the age range of 30 years to 79 years, Figure 1. The results showed that of the total patients, there were 63 patients (70%) with normal level of serum vitB12 (p-value 0.013) while 27 patients (30%) with deficient vitB12 in their serum (p-value 0.127). Frequency of patients with Trigeminal Neuralgia were significantly higher as compared to other pains, Figure 2.

Amongst male and female participants, % males and % females had normal level of serum vitB12. Similarly 27.0% male and 43.3% females had low serum level of vitB12. The results showed that there is no significant difference between gender and low serum Vitamin B12 levels as shown by (p-value = .5)



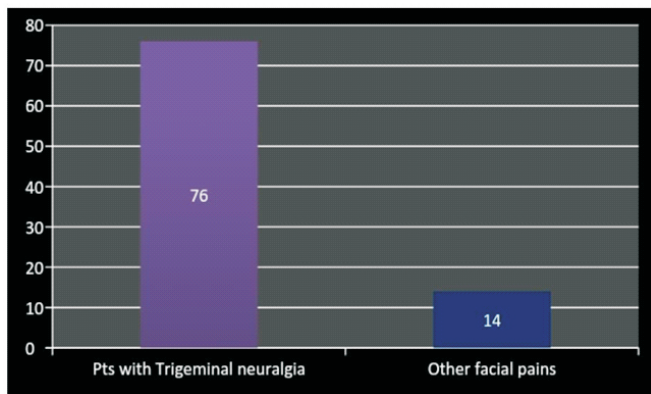


Figure 2: Frequency of trigeminal pain compared to other facial pains

Discussion

This study confirms that patients suffering from trigeminal neuralgia have a low level vitamin B12 in their serum, as 30% patients of trigeminal neuralgia had serum vitamin B12 levels less than the critical value. Similarly, 27.0% males and 43.3% females with trigeminal neuralgia had low serum vitamin B12. But statistically the results were insignificant and no correlation between the gender of the patients and low level of serum vitamin B12 was found.

There are no known adverse effects from taking additional vitamin B12. Methyl cobalamin may even be preventative against neurotoxicity, by enhancing brain cell methylation. In rat cortical neurons it has been shown to prove that Methyl cobalamin protected against glutamate-aspartate and nitroprusside-induced neurotoxicity.⁵

It is quite evident that a nerve that has been continuously damaged cannot be repaired by low levels of vitamin B12. Thus giving us the clarification that trigeminal neuralgia pain is intermittent. When vitamin B12 levels are adequate the recovery of damage neurons is quite good and when the levels are not profound the repair process becomes quite slow, as one Schwann cell can only myelinate 0.2-1.8 mm of cytoplasmic membrane along the length of one axon.¹¹

This study gives us the results and shows that patients with trigeminal neuralgia have a low vitamin B12 syndrome, as 23% of patients with trigeminal neuralgia, in comparison to only 12% of patients with other etiology of facial pain, had serum vitamin B12 levels less than 200 pg/ml. When compared to a cross-sectional, population based study of 1048 aged subjects in which low serum total vitamin B12 (<205 pg/ml) was observed in only 6.1% population controls thus making the results markedly abnormal.¹²

One of the major concerns in this study was that various laboratories uses different measuring units. Most used is picmol (pmol/mL), while other than that picogram (pg/mL) and microgram (µg/mL) are used. Mostly the reports in Australian are on pmol/L while literature worldwide uses pg/ml. Conversion was made for the purpose of comparison.¹³

Conversion of pmol/L to pg/ml-no. $\text{pmol} \times 0.7378 = \text{pg/ml}$
 Molecular weight of B12 = 1355.38 daltons
 Conversion of pg/ml to pmol/L-no. $\text{pg/ml} \times 1.35 = \text{pmol/L}$

In 2018, it became conclusive that vitamin B12 deficiency was unwholesome and there are a number of reasons that can lead to this deficiency.¹⁴ Therefore, it is suggestive that sometimes the oral intake of vitamin B12 is not sufficient and other times the absorption is not good even after enough oral intake of vitamin B12, making this deficiency a common feature especially among the older group of people. It was reckoned by the National Examination Survey that 3.2% of adults approximately over 50 years have a low B12 level, which is a quite a concern and 20% may have their vitamin B12 on borderline. Weight-loss surgery and vegetarian diet are very common practices these days mostly because people are more health conscious but unfortunately it has added to the reasons of vitamin B12 deficiency.

Since animals are the only source of vitamin B12 and plants do not manufacture vitamin B12 therefore, strict vegetarians and vegans commonly develop this deficiency. Also people going through stomach stapling or weight loss surgery can develop this deficiency because the operation intervenes with absorption of the vitamin B12.

Medical conditions like celiac and Crohn's disease and commonly used drugs for heartburn can cause the lower level of acid production. Also, it is common among the old age group because with ascending age, there are lower levels of acid production in the stomach thus conciliates with Vitamin B12 absorption.

Vitamin B12 deficiency symptoms appear gradually but strengthen over a period of time. Symptoms may include strange sensation, numbness and tingling in the hands and feet. Strain while walking accompanied with balance issues. Loss of orientation and inability to reason. With such deficiencies we can also observe anemia, weakness and fatigue.

Though an expert physician will always make the right judgement with the help of clinical history and physical examination of the patient, yet a mere blood test is needed to authenticate the observation.

It is always good to be self-conscious and keep a close check on one's Vitamin B12 levels in case one is a vegetarian, vegan or had a weight-loss surgery because deficiencies can lead to irreversible neurological damage.¹⁵

Since Vitamin B12 has a key role in the formation of myelin, it is commonly used in the treatment of TN and neuropathic facial pain. A very common procedure used by the neurosurgeons is to treat the myelin in the heart of trigeminal nerve which leads to short circuiting pain, is by moving the blood vessel away from where it is in close proximity of the nerve.¹⁶

Conclusion:

Vitamin B12 supplements have no side effects or harm, coherent in use and low priced drugs that makes them feasible for everyone. Absorption of Vitamin B12 is what is the major concern as taking 500mg of cyanocobalamin can lead to only 1.8mg of absorption which is a very scarce amount.

Therefore, the better way is to use the sublingual tablet of methycobalamine 1000mg, which easily dissolves in the mouth, but some physicians can suggest injection per month in order to overcome the deficiencies especially in the elderly or in patients already diagnosed with lower levels of B12. Yet, the preference of injections over sublingual tablets has to be evaluated with proper scientific reasoning.¹⁷

Results suggest that serum Vitamin B12 is low almost > 205pg/ml when in comparison with clinical insufficiency. To conclude our report supplements of B12 aids in the treatment of trigeminal neuralgia.

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- Muhammd Sheraz Alam- Data collection
- Gulmeena Massood- Data collection
- Muhammad Irsad- Critical and final review