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REVIEW ARTICLE

# Neuropathy in Vitamin Deficiency

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## Abstract

Neuropathy is a disorder of the motor nerves, sensory disorders and also autonomic and tendon reflexes. The Neuropathy that occurs can be caused by systemic diseases (diabetes, hypothyroidism), drugs, infections and also vitamin deficiencies. Vitamins are organic components with a high level of potential. Vitamins themselves are classified into 2 which are air soluble and fat-soluble, for fat-soluble vitamins, there are vitamins A, D, E, K and for vitamin B complex including vitamins that are soluble in air. Vitamin B plays an important role as a co-factor or co-enzyme in various metabolic processes in the body. A continuous lack of vitamins will cause damage to the peripheral nervous system so that symptoms of neuropathy appear. Deficiency of vitamin E and vitamin B can cause damage to the nervous system and neuropathy occurs. Vitamin B which has several kinds, such as B1 (thiamine), B2 (riboflavin), B3 (niacin), B5 (pantonetate), B6 (pyridoxine), B7 (biotin), B9 (folate) and B12 (cobalamin) where this B vitamin has a neurotrophic function. Vitamin B cannot be produced by mammals, so we can get this vitamin through food and supplementation. Vitamins themselves function to maintain the body's physiological functions and also maintain optimal health.

**Keyword:** *Neuropathy, Vitamin, Thiamine, Cobalamin, Pyridoxine.*

## Introduction

In countries such as the United States and the United States, the vitamin B deficiency rate reaches 6% in patients younger than 60 years and reaches 20% in people over 60 years. While the prevalence of neuropathy increases by about 2.4% in the world which is increasingly increasing by about 8% as age increases. In the United States, surveys based on data collection show 89.8% of men and 96.3% of women who receive 19 years or more have low or insufficient alpha-tocopherol intakes [1, 2].

### Pathogenesis

All B vitamins play an important role as coenzymes for enzymatic reactions in various biological systems. Vitamin B has an important role in the central nervous system and peripheral nervous system. The combination of vitamins B1, B6 and B12 interacts synergistically to improve neuropathy, motor control, nociceptive, and neuropathic pain. Vitamin B deficiency can cause a variety of disorders such as Wernicke encephalopathy, depression, beriberi, seizures, spinal cord degeneration, and peripheral neuropathy [3].

### Vitamin B1 Deficiency (Thiamine)

Thiamine is a water-soluble vitamin that we get from animal and plant tissue. Thiamine is absorbed in the small intestine by passive diffusion and also active transport, which is then converted to thiamine diphosphate (TDP) which will be useful in cellular respiration, ATP production, glutamic synthesis and gamma-aminobutyric acid and also maintain myelin sheath. Thiamine deficiency conditions can be found in people with chronic alcohol abuse, repeated vomiting, AIDS, long-term use of TPN, eating disorders [2-4].

## Vitamin B6 Deficiency (Pyridoxine)

Pyridoxine is a vitamin that cannot be produced by humans, so we can go through a diet. Pyridoxine will be absorbed and then converted to pyridoxal phosphate, which acts as a co-factor in several metabolic reactions. Pyridoxine has the function of maintaining the regulation of the glutamatergic system and thus GABA and glutamate levels. Pyridoxine is useful in falsifying the neurotransmitter and myelin synthesis and controlling glutamate excitability and neuronal metabolism.

Pyridoxine deficiency can be found in patients undergoing treatment with isoniazid, phenelzine, hydralazine and also in patients who undergo long-term hemodialysis, heavy drinkers, and in patients with high metabolic needs (breastfeeding, pregnant) [2-4].

## Vitamin B12 Deficiency (Cobalamin)

Cobalamin is widely found in food products and also animals. Cobalamin itself is synthesized by specific microorganisms. Cobalamin is released by stomach acid and also pepsin which will bind to the R protein secreted in saliva and stomach. Cobalamin that has been released from protein R in the small intestine will bind to intrinsic factors and be absorbed in the terminal ileum.

Cobalamin has biochemical reactions in humans; the first is the formation of methionine due to the methylation process of homocysteine so that it will produce tetrahydrofolate which plays an important role in the synthesis of purines and pyrimidines. The second important reaction is the conversion of L-methylmalonyl coenzyme A to succinyl coenzyme A which is important in the formation of the myelin sheath.

The most common cause of vitamin B12 deficiency is malabsorption, pernicious anemia and vegetarian [2-5].

**Table 1: Mechanism of Vitamin B for Nerve Function** [2]

| Vitamin | Processes | Coenzym for | Implication in nervous system |
|---|---|---|---|
| **B1 (Thiamine)** | Citric acid cycle | 1. Pyruvate dehyrdogenase<br>2. Tranketolase<br>3. Alpha-ketoglutarate dehydrogenase | Provide energy for synthesis nucelic acid, myelin and neurotransmitters |
| **B6 (Pyridoxine)** | HCY metabolism dopamine and serotonin synthesis | 1. Serine-hydroxymethyltranferase<br>2. Cystathionine-beta-synthase<br>3. Aromatic L-amino acid decarboxylase | Metabolisme neurotransmiter |
| **B12 (Cobalamin)** | Hcy metabolism methymalonyl CoA pathway | 1. Methionine synthase<br>2. Methylmalonyl CoA mutase | Metabolisme neurotransmitter, myelin |

## Vitamin E Deficiency (Alpha-Tocopherol)

Vitamin E is the most powerful antioxidant component and also as a free radical scavenger. This vitamin is a fat-soluble vitamin that can prevent the oxidation of fatty acids in cell membranes. This vitamin E can be obtained from animal fats, nuts, vegetable oil and wheat. The pathogenesis of vitamin E still cannot be discussed in detail. Vitamin E will be added to the tissue through chylomicrons and passively absorbed from the chylomicrons will be transferred to VLDL through alpha-tocopherol transfer protein (TTP). This process requires bile acids, fatty acids, and monoglycerides for absorption. If there is interference with the antioxidant function, there will be a pathological change. Vitamin E deficiency often occurs because of impaired fat absorption, the presence of abetalipoproteinemia [2,4].

## Diagnosis

In vitamin B1 deficiency or thiamine symptoms that are often caused are distal sensory loss, burning pain, paresthesias and muscle weakness (paralysis) in the legs can occur cramps. If it is not continued it will further increase weakness. In beriberi, facial weakness can occur and facial manifestations will also appear. This deficiency will also affect physiological reflexes (decreased tendon reflexes) and also increase in the presence of muscle atrophy. To find out if this patient has vitamin B 1 deficiency, thiamine pyrophosphate examination can be performed with high-performance liquid

 

chromatography or erythrocyte transketolase, and sensorimotor examination [1-2,4].As a result of a deficiency in vitamin B6 or pyridoxine, namely the presence of seizures, numbness, paresthesias and burning sensation in the legs or also on the hands. On neurological examination, there was a decrease in tendon reflexes and also a mild distal weakness. To establish the diagnosis, blood and urine checks can be done to see pyridoxal phosphate in the blood and nerve biopsy can be done to see axonal degeneration [1-2,4].

In vitamin B12 deficiency or cobalamin there will be disruption in the hematological, neurological and psychiatric systems. Usually, the symptoms that appear are sensory in the feet or hands. Symptoms can appear on the hands before they are often called dead hand syndromes, but there is also an increase in tone, weakness in the distribution of corticospinal tracts and tetraparesis and also in the arms and pathologies reflexes such as Hoffman and Babinski.

This deficiency will disrupt daily activities. To make a diagnosis, serum methylmalonic acid (MMA) and homocysteine (Hcy) metabolites can be examined. It is hoped that increasing MMA and also Hcy can be considered a vitamin B12 deficiency [1-2,4,5]. Because vitamin E is stored in fat tissue, it will take about 5-10 years for symptoms to occur.

Usually, the onset of symptoms will begin to slowly appear and progress. Disorders that occur due to vitamin E deficiency are a decrease in proprioceptive and vibration sensation. If the deficiency is very severe, it can cause pseudoathetosis. Also, it can occur decreased or loss of tendon reflexes, tremors, dysarthria, nystagmus, proximal muscle weakness. Pathological features that can be found are swelling and the presence of degeneration of large myelinated axons in the posterior column, peripheral nerves and sensory roots. An examination that can be done is electrodiagnostic test to see a decrease in the conduction velocity of the axon sensory reflex. Serum alpha-tocopherol examination can be performed (normal range 5.5-17 mg / L) [2,4].

**Management**

Management needed in the treatment of neuropathy is to control the disease and provide therapy for symptoms. Also, treatment can be provided which consists of supplementation or can be changed by eating patterns to prevent further deficiency [1-3]. Management that can be done in vitamin B deficiency is the provision of oral, intravenous, or intramuscular supplementation.

For supplementation of vitamin B1 can be given intravenously or intramuscularly with an initial dose of 100g and consumed a dose of 100mg per day. This therapy will show results after several months of treatment, but this improvement is needed on the severity or condition of the patient. The weekly contribution to vitamin B1 is 1-1.5 mg per day for young patients. Vitamin B12 can be given at a dose of 1000mg per day or can be given intramuscularly 1000mcg per day for 5-7 days and then given 1000mcg intramuscularly every month.

Vitamin B6 supplementation can also be given to patients on isoniazid or hydralazine treatment at a dose of 50 mg. Provision of 10 mg of vitamin E per day for men and 8 mg per day for women is highly recommended because there are no reports of side effects from the administration of vitamin E. Whereas therapy for deficiency can be given at a dose of 200 mg to 2 g per day or vitamin E 400 international units 2 times a day, whereas in patients with impaired absorption can be given at a dose of 1-4 g per day or may require soluble vitamin E with water. This therapy is useful to prevent the progression of neuropathy [1-3,6].

**Table 2: Treatment of Vitamin B and E Deficiency [1-3,6]**

| Vitamin | Treatment of deficiency |
|---|---|
| **Vitamin B1 (Thiamine)** | 1. Mild polyneuropathy : 10-20mg orally per day for 2 weeks<br>2. Moderate or advanced: 20-30mg orally per day until symptoms disappear |
| | 50-100mg orally per day for specific causes |

 

| | |
|---|---|
| **Vitamin B6 (Pyridoxine)** | |
| **Vitamin B12 (Cobalamin)** | 1. Mild to moderate neurological sign and symptoms : 1000-2000mcg each day<br>2. For severe deficiency: 1 mg intramuscularly, 1-4 times per weeks |
| **Vitamin E** | 1. Deficiency : 200mg-2 g per day or vitamin E 400 international units<br>2. For daily need : 10 mg of vitamin E per day for men and 8 mg per day for women |

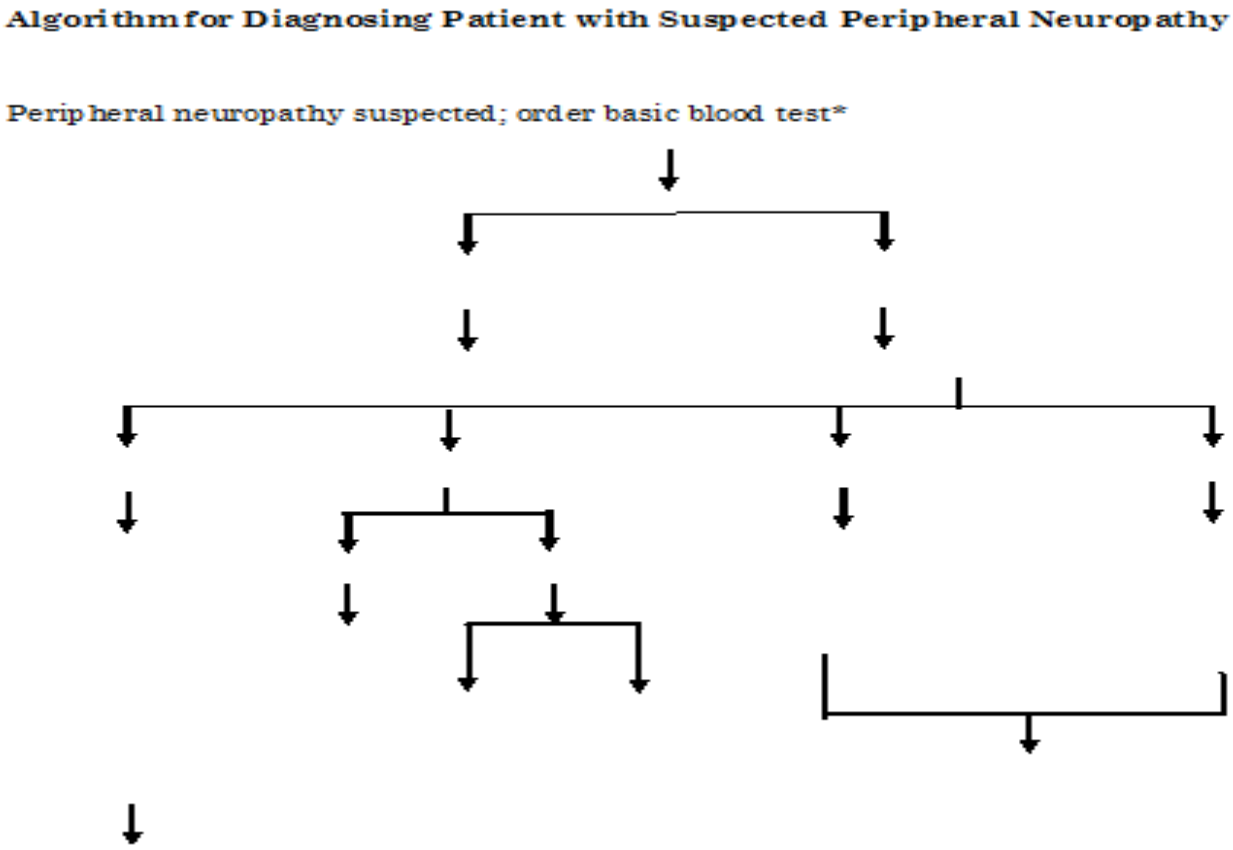


**Figure 1: Algorithm diagnosis peripheral neuropathy [7]**

## Conclusion

A continuous lack of vitamins will cause damage to the peripheral nervous system so that symptoms of neuropathy appear. Deficiency of vitamin E and vitamin B can cause damage to the nervous system and neuropathy occurs. Vitamin B which has several kinds, such as B1 (thiamine), B2 (riboflavin), B3 (niacin), B5 (pantonetate), B6 (pyridoxine), B7 (biotin), B9 (folate) and B12 (cobalamin) where this B vitamin has a neurotrophic function.

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