

Review Article

Potential Benefits of Methylcobalamin: A Review

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Abstract

Methylcobalamin is an active form of vitamin B₁₂ that helps in synthesis of methionine and S-adenosylmethionine. It is required for integrity of myelin, neuronal function, proper red blood cell formation and DNA synthesis. The largest group of vitamin B₁₂ deficiency is found in typical vegetarians all over the world, which can be alleviated with its analogue Methylcobalamin. It is a beneficial drug to most of the common disorders like cardiovascular disorders, diabetes, anemia, hyperhomocysteinemia and degenerative disorders. Methylcobalamin helps in the synthesis of neuronal lipids, regeneration of axonal nerves and has neuroprotective activity, which promote neurons to function in proper way and thus improves Alzheimer disease, Parkinsonism, Dementia and neuropathic syndromes. It is an approved treatment for peripheral neuropathy.

Keywords: Methylcobalamin; Neuropathy; Anemia; Nootropic; Dietary supplement

Abbreviations

SAMe: S-Adenosyl Methionine; ERK: Extracellular Signal-Regulated Kinases; PKB: Protein Kinase B; B-globulin: Beta Globulin; ENFD: Epidermal Nerve Fiber Density; DPN: Diabetic Peripheral Neuropathy; NSAIDs: Non Steroidal Anti Inflammatory Drugs; THF: Tetrahydrofolate; BHMT: Betaine Homocysteine Methyltransferase.

Introduction

Methylcobalamin is a potent and active form of vitamin cyanocobalamin. It plays a key role in maintaining good health. Dietary cobalamin deficiency causes many serious health problems. The commonest are blood deficiency, depression, irritability and psychosis. The long term deficiency of vitamin B₁₂ substance can lead to hyperhomocysteinemia and finally cardiovascular disorder. In today's world, healthcare plays an important role in our personal lives. This merges a huge responsibility for improving and saving thousand lives on earth. Despite having incredible improvements in health since 1950, there are number of challenges which have to be solved. Each year 36 million deaths are caused by non communicable diseases such as hyperhomocysteinemia, cancer, chronic lung disease, anemia, diabetes and almost 17.5 millions died from cardiovascular disease in 2005 [1].

Folate and vitamin B₁₂ are essential nutrients which are not synthesized in humans and whose deficiency is considered as health problem worldwide such as anemia and neuronal dysfunction. Vitamin B₁₂ deficiency is observed more in elderly and pregnant women. Methylcobalamin (commonly known as methylcobalamin or methyl B₁₂) is an analog of vitamin B₁₂ which treats or prevents the pathology arising from the deficiency of vitamin B₁₂. It contains methyl alkyl bonds and is different from cyanocobalamin because it contains cyanide [2]. It has an octahedral cobalt (III) center and is produced in laboratory by reducing cyanocobalamin with sodium borohydride in alkaline solution which is followed by the addition of methyl iodide. Methylcobalamin (5 mg, 60 mg vegetarian lozenges) is active in the central nervous system outside the mitochondrion and is

essential for cell growth and replication. Sometimes the liver cannot convert cyanocobalamin into adequate amount of methylcobalamin needed for proper neuronal functioning. Through enhanced methylation, it exerts its nerve cell protective effect and accelerates its growth. A lot of energy is required for cyanocobalamin to remove its cyanide and replaces it with methyl group [3]. Methylcobalamin is the only form of vitamin B₁₂ that can cross the blood brain barrier without biotransformation. Its methyl group stimulates serotonin creation, a neurotransmitter which is responsible for mood enhancement and protects the brain from damage against excitotoxins. High homocysteine level is the main culprit for brain, vascular diseases, strokes risk and causes sclerosis in the arteries. Methylcobalamin converts homocysteine to methionine and reduces the potential to damage. It also forms adenosylcobalamin, the other form of vitamin B₁₂ for mitochondrial energy production. Along with methylcobalamin, 5-methyltetrahydrofolate is also an important element to eliminate homocysteine. Vitamin supplements reduce the chances of building homocysteine associated with stress. Sublingual absorption of methylcobalamin has become very popular because it can be easily absorbed with better bioavailability. It also increases the available amount of SAMe (S-adenosylmethionine), which acts as a mood enhancer and works as an effective alternative to tricyclic antidepressant [4].

Therapeutic use of Methylcobalamin

Methylcobalamin is used in the treatment of diabetic neuropathy, degenerative disorders and in the preliminary treatment of amyotrophic lateral sclerosis. It has been used to treat some nutrition based disease such as dementia, rheumatoid arthritis and exerts neuronal protection by promoting regeneration to injured nerves. It antagonizes the glutamate induced neurotoxicity and also manifests analgesic effects. It alleviates pain behavior in diabetic neuropathy, low back pain, neuralgia and promotes nerve conduction. It helps the body to use fats and carbohydrates for energy.

Oral administration of 500 mcg three times daily for four weeks results in improvement of peripheral neuropathy and it produces very

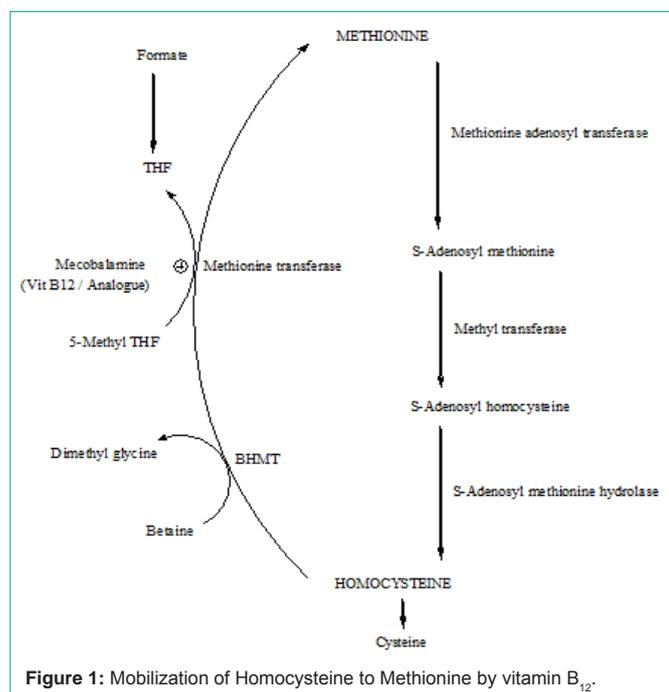


Figure 1: Mobilization of Homocysteine to Methionine by vitamin B₁₂.

significant effect after 12 weeks of treatment [5]. An improvement in vibration sense, lower motor neuron weakness and sensitivity to pain is also observed. It also improves visual function in Bell's palsy, sleep wake rhythm disorder [6].

Human urinary excretion of methylcobalamin is about one third that of a similar dose of cyanocobalamin that indicate greater tissue retention. It improves sperm count by 37.5% at a dose of 6mg per day for 16 weeks. When given at a dose of 1,500 microgram per day for 4-28 weeks results in 38% sperm concentration, sperm motility increases in 50% of cases [7-11]. Glutamate neurotoxicity was prevented by chronic exposure to methylcobalamin and SAME. Its chronic exposure with SAME also inhibits the neurotoxicity induced by sodium nitroprusside which is mediated by nitrous oxide. Its chronic dose also up regulate gene transcription and therefore protein synthesis. Methylcobalamin at concentration above 100nm promote neuronal survival and neurite growth, increases ERK ½ and AKT activities through methylation cycle. Continuous administration of high dose of methylcobalamin results in nerve regeneration and functional recovery in rat sciatic nerve injury. Methylcobalamin (1 mg/kg intramuscular) inhibits ototoxic action of gentamycin and promote visual field defects in normal tension glaucoma. Combination of methylcobalamin, alpha lipoic acid and pregabalin improves sleep interference, nerve function and pain relief [12].

Mechanism of Action

It works by functioning in the production of a compound called myelin, which covers and protect nerve fibers [13]. Methylcobalamin rejuvenates the damaged neuron. Without enough methylcobalamin, myelin sheath does not form properly due to which nerve fibers suffers and people experience irreversible nerve damage. An intrinsic factor made in the stomach, must be present in the intestinal tract to allow its proper absorption. People lacking this factor show vitamin B₁₂ deficiencies such as pernicious anemia (a slow and

insidious process that can end in death. Pernicious anemia in fact means 'leading to death'). Methylcobalamin is used as a cofactor in methionine transferase enzyme, an enzyme which converts aminoacid homocysteine to methionine via folate cycle [14-16].

Pharmacokinetics

Methylcobalamin can be administered orally, parenterally and intranasal. Methylcobalamin binds with an intrinsic factor and form a complex which is absorbed in distal ileum. Its half life is 6 days. The absorption is mediated by very specific receptor mediated transport system. It is distributed to every cell of the body upon binding to Transcobalamin II, a B-globulin carrier protein and is stored in the liver in an amount of 300- 500 microgram. It is eliminated through bile. Methylcobalamin nasal sprays bioavailability is 9% [17-19].

Dose

For daily stress relief, methylcobalamin should be taken in the dose of 500 mcg per day. In the acute cases of neuropathy, dose of 1500 mcg per day can be safely taken. Dose of 1 mg per day is required to be taken for age related brain decay. Methylcobalamin can be combined with similar dose of folic acid and pyridoxine [20]. Deficiency of vitamin B₁₂ is strictly seen in pure vegetarian, dose of 100 mg day can rebalance its requirement in the intestine. All human being need at least 3 mg per day of this drug for the basic nerve support. The medicine is stored in the refrigerator below 41°F (5°C) to avoid moisture. Methylcobalamin is also injected deep in to the muscles [21].

Combinations / Interactions

Fixed dose combination of sustained release pregabalin and methylcobalamin reduces neuropathic pain. Treatment with lipoic acid – methylcobalamin for 2-4 weeks is associated with better outcome in nerve conduction velocity and neuropathic symptoms. Oral combinations of methylcobalamin, L-methylfolate and Pyridoxal-5 phosphate improves Epidermal Nerve Fiber Density (ENFD) with Diabetic Peripheral Neuropathy (DPN). Medicines such as Antibiotics (penicillin, cefalexin, ciprofloxacin), metformin, nitrous oxide, colchicines, NSAIDs (Ibuprofen, Para aminosalicyclic acid, sulphasalazine) decrease the absorption and induce reversible mal-absorption of methylcobalamin by altering the function of ilea mucosa. Some drugs like nitrates (nitroglycerin), fluorouracil interacts with methylcobalamin and their side effects are increased [22]. Chloramphenicol antagonizes the hematopoietic action of this drug. Administration of methylcobalamin during pregnancy and breast feeding is dangerous because it can cross maternal-fetal barriers and also gets excreted in milk. Barbiturates (phenobarbitol), primidone, pyrimethamine, valproic acid, hydantoin should not be taken along with methylcobalamin because their effectiveness is inhibited. Aminoglycosides, proton pump inhibitors, anti hyperglycemic medications (metformin), anticonvulsants interfere with methylcobalamin absorption and function. Consumption of ethanol along with methylcobalamin therapy counteracts its action [13,23-25].

Adverse Effects

At a very high dose, methylcobalamin causes blood clots, diarrhea, paresthesia, rhinitis, ataxia, pruritis and allergic reactions.

People with polycythemia should consult with a physician before taking this therapy [26-29]. This drug can be applied as a topical paste on the skin without any adverse reaction. Sometimes intravenous injection of this drug leads to hypersensitivity reactions and end up to anaphylactic shock. In some cases, hypokalemia and thrombocytosis has occurred in the patient while treating megaloblastic anemia with methylcobalamin [30-37].

Conclusion

Methylcobalamin aids in growth of healthy blood cells, nerve cells in the body. It is a best treatment as well as dietary supplement for the people who cannot absorb vitamin B₁₂ and / or suffers from its deficiencies. Monotherapy of methylcobalamin improves plasma / serum homocysteine level and improve the neuropathic symptoms also [28-37]. Combination therapy with other vitamin B complexes seems to be more effective. Hence methylcobalamin may be considered as one of the promising dietary supplement and medicine having a number of potential benefits [5,38-41].

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