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Potential Consequences of Vitamin B_{12} Methylcobalamin Deficiency

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Abstract

Vitamin B_{12} (Methylcobalamin) deficiency can lead to a variety of health problems, including anaemia, fatigue, weakness and memory loss. If left untreated, it can also lead to more serious problems such as nerve damage and problems with vision, hearing and balance. Methylcobalamin, an active form of vitamin B_{12}, aids in producing S-adenosylmethionine and methionine. It is necessary for the synthesis of DNA, the appropriate creation of red blood cells, the integrity of myelin and brain function. worldwide, the most common form of vitamin B_{12} insufficiency is observed among vegetarians and its equivalent, methylcobalamin, may help. The majority of common illnesses, including cardiovascular disorders, diabetes, anaemia, hyperhomocysteinemia and degenerative conditions, may benefit from this medication. Methylcobalamin enhances correct neuron function, which lessens the symptoms of Alzheimer's disease, Parkinsonism, dementia and neuropathic syndromes. It also aids in the production of neuronal lipids and the regeneration of axonal nerves. Peripheral neuropathy may be treated using it. Also, taking methylcobalamin supplements has been shown to ease the symptoms of Parkinson's disease, speed up remyelination in diseases that damage the nerves (which is why this compound is used in experiments) and help the body make more red blood cells.

Keywords: Methylcobalamin; Neuropathy; Methionine; Deficiency; Homocysteine

Introduction

Methylcobalamin is a strong and functional version of the nutrient cyanocobalamin. It is essential for maintaining one's health. A lack of dietary cobalamin may result in a variety of grave health issues [1]. Insufficiency of blood, sadness, irritability and psychosis are the most prevalent. A chronic lack of vitamin B_{12} may cause hyperhomocysteinemia and ultimately a cardiovascular problem [2]. In the modern world, healthcare is crucial to our daily lives. This combines a significant obligation to better and save thousands of lives worldwide. Even though health has advanced dramatically since 1950, a lot of problems still need to be addressed [3]. Noncommunicable illnesses such as cancer, chronic lung disease, anaemia, diabetes, hyperhomocysteinemia and over 17.5 million fatalities from cardiovascular disease in 2005 account for 36 million deaths annually [4]. If this is not a serious and sensitive enough issue, obesity is also a major concern in some parts of the world, with a quarter of the world's population being overweight and another quarter undernourished [5]. And if this is not enough, we should consider the massive number of people living on less than $1 a day and the number of individuals who die prematurely due to health-related factors such as poverty, malnutrition and preventable illnesses [6]. For example, the economic costs imposed by illness are estimated at over $4.6 trillion per year in high-income nations alone. Obviously, medicine and its applications play a key role in life and our existence on this planet [7]. However, these numbers could even be considered insignificant when we take into consideration the number of people who die every year as a consequence of preventable diseases that could be eliminated with improved nutrition and public health interventions [8].

The absence of important nutrients like folate and vitamin B_{12}, which humans cannot produce, is thought to be a global health issue since it may lead to anaemia and brain malfunction [9]. Those who are elderly or pregnant are more likely to have a vitamin B_{12} deficiency. Methylcobalamin, often known as mecobalamin or methyl B_{12}, is an analogue of vitamin B_{12} that may be used to treat or prevent pathologies brought on by vitamin B_{12} deficiency [10]. It differs from cyanocobalamin because it includes cyanide and has methyl alkyl linkages. It is created in a lab by reducing cyanocobalamin with sodium borohydride in an alkaline solution, followed by the addition of methyl iodide [11]. It possesses an octahedral cobalt (III) core. In the central nervous system, methylcobalamin (5 mg, 60 mg vegetarian lozenges) is active [12].

Literature Review

Deficiency of vitamin B_{12}

Cobalamin, often known as vitamin B_{12}, is a water-soluble vitamin that is found in foods including dairy, eggs and red meat. A glycoprotein called intrinsic factor, which is produced by parietal cells in the stomach, is required for B_{12} absorption in the terminal ileum [13]. After being absorbed, B_{12} is employed as a cofactor for enzymes that are involved in the production of DNA, fatty acids and myelin. Hematologic and neurologic problems might therefore result from B_{12} insufficiency [14]. B_{12} is stored in excess in the liver, but when it cannot be absorbed for an extended length of time (due to nutritional insufficiency, malabsorption or a lack of intrinsic factor, for example), hepatic reserves are depleted and a shortage results [15]. The deficiency manifests initially as megaloblastic anaemia, in which red blood cells are larger than normal because they are immature. B_{12} is involved in the formation of DNA, fatty acids and myelin [16]. The neurologic manifestations of B_{12} deficiency include paraesthesia (sensations of tingling and numbness in the hands and feet), tremors, progressive weakness and reflex changes [17].

Pathophysiology

A protein known as R-factor, which dietary vitamin B_{12} interacts with, is secreted by the salivary glands in healthy people [18]. Once the mixture enters the small intestine, pancreatic enzymes remove the B_{12} from the R-factor so that it may connect to an intrinsic factor, a glycoprotein produced by the gastric parietal cells [19]. The newly created compound of vitamin B_{12} and intrinsic factor may then attach to receptors on the ileum, allowing for B_{12} absorption. After ingestion, B_{12} takes part in metabolic activities that are essential for hematologic and neurologic functions. No matter the reason, if B12 cannot be absorbed, a number of deficiencies may manifest.

The enzyme methionine synthase, which is utilized to convert homocysteine into methionine, requires vitamin B_{12} as a cofactor. By products of this reaction include the conversion of methyl-THF to THF and intermediates required for the production of the pyrimidine nucleotides found in DNA. Homocysteine cannot be converted to methionine with B_{12} insufficiency and as a result, methyl-THF cannot be converted to THF. Homocysteine levels rise as a consequence and the inability to synthesize pyrimidine bases slows down DNA synthesis, resulting in megaloblastic anaemia. Symptoms of weariness and pallor, which are often seen in people with B_{12} deficiency, are then brought on by the anaemia. Polymorphonuclear leukocytes and other rapidly proliferating cell lines are negatively affected by decreased DNA synthesis (PMNs). Consequently, B_{12} insufficiency often causes a condition known as pernicious anaemia, which causes symptoms of hypersensitivity to touch and sound, psychosis, peripheral neuropathy (tingling or numbness in the hands and feet), tinnitus (ringing in the ears), megaloblastic anaemia.

The enzyme methylmalonyl-CoA mutase, which changes methylmalonyl-CoA into succinyl-CoA, also uses vitamin B_{12} as a cofactor. Methylmalonic Acid (MMA) levels will rise in people with a B_{12} deficiency because it cannot be converted to succinyl-CoA. The neurologic impairments, such as neuropathy and ataxia, reported in these individuals are thought to be caused by myelin degradation, which is thought to be exacerbated by increased levels of MMA and homocysteine. Subacute Combined Degeneration of the Spinal Cord (SCDSC) is a disorder brought on by myelin degradation. The dorsal columns, lateral corticospinal tracts and spinocerebellar tracts are among the areas of the spinal cord affected by this illness, which also causes dementia, ataxia, peripheral neuropathy and loss of proprioception.

Beneficial use of methylcobalamin

Methylcobalamin's urine excretion in humans is around one-third that of cyanocobalamin at the same dosage, which suggests increased tissue retention. When taken for 16 weeks at a dosage of 6 mg per day, it increases sperm count by 37.5%. Sperm concentration rises by 38% when administered at a dosage of 1,500 micrograms per day for four to twenty-eight weeks and sperm motility improves in 50% of instances. Chronic exposure to methylcobalamin and SAMe protected against glutamate neurotoxicity. Chronic SAMe administration also prevents sodium nitroprusside-induced neurotoxicity, which is mediated by nitrous oxide. Additionally, a continuous dosage of it stimulates protein synthesis by up-regulating gene transcription. Through the methylation cycle, methylcobalamin improves neuronal survival and neurite development and raises ERK 12 and AKT activity at concentrations of over 100 nm. SAMe increases the levels of neurotransmitters, phospholipids, biogenic amines and their metabolites. Because SAMe has so many uses, it is being looked at as a treatment for a wide range of health problems, such as depression, schizophrenia and stroke.

Mechanisms of action

It functions in the synthesis of myelin, a substance that coats and protects nerve fibers. The injured neuron is rejuvenated by methylcobalamin. Lack of methylcobalamin causes improper myelin sheath formation, which damages nerve fibers and causes irreparable nerve damage. For optimal absorption, an intestinal tract intrinsic factor created in the stomach must exist. People who lack this component exhibit vitamin B_{12} deficits, such as pernicious anaemia (a gradual, sneaky condition that may be fatal). In reality, pernicious anaemia implies "leading to death." The methionine transferase enzyme, which uses the folate cycle to change the amino acid homocysteine into methionine, uses methylcobalamin as a cofactor. When two metabolites are altered, the amino acid is converted into the metabolite homocysteine, a precursor to creatine synthesis. This uses the folate cycle to change homocysteine into methionine, a precursor to creatine synthesis. When methylcobalamin is present, the enzyme might change the homocysteine into methionine (the reason why we should supply our bodies with an adequate level of B_{12}), which is one of the starting points for creatine synthesis. It is made out of the amino acid methionine, which is an essential metabolite in the urea cycle to determine

whether the methionine-transferase enzyme requires vitamin B_{12} to convert homocysteine into methionine or if the change can be made another way. The folate cycle is necessary because it allows the body to convert homocysteine into methionine, which is one of the starting points for creatine synthesis.

Pharmacokinetics and dosage

Methylcobalamin may be given parenterally, intravenously or orally. Methylcobalamin forms a compound with an intrinsic factor absorbed in the distal ileum. It has a six-day half-life. A highly specialized receptor-mediated transport mechanism mediates the absorption. When it binds to Transcobalamin II, a B-globulin carrier protein, it is disseminated to all of the body's cells. It is then stored in the liver for 300-500 micrograms. Bile is used to expel it. The bioavailability of methylcobalamin in nasal spray is 9%. Methylcobalamin should be taken daily at a level of 500 mcg to relieve stress. A daily dosage of 1500 mcg may be given safely in situations of acute neuropathy. For age related brain deterioration, a dose of 1 mg daily is necessary. Methylcobalamin may be taken with a comparable amount of pyridoxine and folic acid. A daily intake of 100 mg may balance the intestinal demand for vitamin B_{12}, which is only a problem for severe vegetarians. Every human being needs at least 3 mg of this medication each day to provide basic nerve support. To keep the medication dry, it is kept in the refrigerator at or below 41°F (5°C). Additionally, methylcobalamin is administered deeply into the muscles.

Discussion

Transport mechanisms for vitamin B_{12} in individuals

The metabolism benefits from vitamin B_{12}. Energy is made and used by the body's metabolic functions, which include digestion, absorption, excretion, breathing, circulation and controlling body temperature. The digestive system of humans has a sophisticated system for absorbing dietary vitamin B_{12}. In the stomach, haptocorrin, a protein that binds vitamin B_{12}, initially releases vitamin B_{12} from dietary protein. The liberated vitamin B_{12} binds to intrinsic factor (IF, gastric vitamin B_{12}-binding protein) in the proximal ileum after the proteolysis of the haptocorrin-vitamin B_{12} complex by pancreatic proteases in the duodenum. By means of receptor-mediated endocytosis, the IF-vitamin B_{12} combination may get into mucosal cells in the distal ileum. This gastrointestinal absorption has a considerable impact on the bioavailability of dietary vitamin B_{12}. Recent research suggests that vitamin B_{12} may lower the risk of a number of long-term illnesses and birth defects.

The way PA is handled differs from nation to nation and from region to region. Although there is no known permanent treatment for PA, it is anticipated that replenishing B_{12} will stop anaemia-related symptoms, stop the neurological decline and in cases where neurological issues are not advanced, restore neurological function and cause complete and long lasting remission of all symptoms. There are several methods for replenishing B_{12}. Natural healthcare professionals seem to be split on whether vitamin B_{12} therapy for individuals with pernicious anaemia should be administered orally, intramuscularly, *via* a buccal patch or in any other way. It's difficult to investigate supplements since the majority of scientific studies appear to be inconclusive and cannot determine whether treatment is effective. Despite having the best interest of their patients in mind, naturopathic physicians in Oregon will be forced to choose between offering treatment they believe is scientifically proven and can completely alleviate symptoms or practicing medicine with their limited scope of practice as dictated by a regulatory organization, presumably using out-of-date reference materials.

Conclusion

Methylcobalamin is an active form of vitamin B_{12} and aids in producing S-adenosylmethionine and methionine. It also enhances correct neuron function, which lessens the symptoms of Alzheimer's disease, Parkinsonism, dementia and neuropathic syndromes. Worldwide, the most common form of vitamin B_{12} insufficiency is observed among vegetarians. Methylcobalamin supports the body's ability to produce healthy blood cells and nerve cells. For those who cannot absorb vitamin B_{12} and/or suffer from its shortages, it is the finest therapy as well as a dietary supplement. Methylcobalamin monotherapy decreases neuropathic symptoms as well as plasma/serum homocysteine levels. It seems that combination treatment with additional vitamin B complexes is more successful. So, it is possible to see methylcobalamin as one of the promising dietary supplements and medicines with a range of potential advantages.

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