Vitamin B 12 and its Health Impacts

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Introduction

The source of vitamin B12 ranges from naturally occurring foods to dietary supplements. Ingredients that contain the action of vitamin B12 are called "cobalamins" as vitamin B12 contains the substance cobalt. The most effective metabolic forms of vitamin B12 are methylcobalamin and 5-deoxyadenosylcobalamin. However, after conversion to methylcobalamin or 5-deoxyadenosylcobalamin, two additional types, hydroxycobalamin and cyanocobalamin, are physically active. Vitamin B12 deficiency is very common in vegetarians and vitamin B12 deficiency affects about 20% of the elderly, with food-cobalamin malabsorption syndrome causing more than 60% of these deficiencies [1-4]. Due to severe cerebral palsy and life-threatening anemia caused by a deficiency of the internal factor, such people need treatment, which includes giving them vitamin B12. Due to severe cerebral palsy and life-threatening anemia caused by a deficiency of the internal factor, such people need treatment, which includes giving them vitamin B12. Anorexia nervosa, which is the only good source of vitamin B12, is a major cause of vitamin B12 deficiency in dedicated vegans. Vitamin B12 should be consumed at a rate of 2.4 g per day. Because between 10% and 30% of adults are unable to absorb vitamin B12 from the diet, the Institute of Medicine of the National Academies in the United States recommends that people over the age of 50 eat B12-rich foods or supplements. This is because, despite stomach problems, high doses of vitamin B12 may cause improved absorption. Vitamin B12 deficiency was first recorded in 1849, and it was thought to be fatal until 1926, when a diet high in vitamin B12 was found to slow down the progression of the disease. Much is now being understood about the biochemistry of vitamin B12 and metabolism. Vitamin B12 deficiency was previously thought to be chronic and especially in devout vegetarians or people with severe anemia [5, 6]. Vitamin B12 has a diverse array of functions. It is a nutrient that helps to produce healthy red blood cells, aids in DNA formation and nourishes the brain and nervous system [5, 7]. Vitamin B12 also helps prevent megaloblastic anemia, a blood disorder that causes fatigue and weakness. Nutrients can be synthesized in the laboratory and are found naturally in meat, fish, and dairy products. Some people do not have the protein that helps absorb vitamin B12 in foods and supplements. Vitamin B-12 is needed

to combine DNA, methionine resynthesis and methylation, as well as to prevent the formation of homocysteine. Vitamin B-12, in the form of 5'-deoxyadenosylcobalamin, is also required for the mitochondrial enzyme methylmalonyl CoA mutase, which converts Methylmalonyl CoA into Succinyl CoA, a step in the synthesis of odd-chain fatty acids and and ketogenic amino catabolism. acids. Despite the fact that vitamins can be found in a variety of foods, B12 deficiency and insufficiency are common. Limited diet, malabsorption, certain medical conditions, or the use of B12-reducing drugs are common causes. Deficiency is very common in the elderly because their ability to absorb B12 from the diet decreases with age. However, this does not mean that there is a possibility of B12 deficiency in children and adults, including those who are pregnant or breastfeeding. Unfortunately, B12 deficiency is often misdiagnosed and overlooked. This review discusses the different health effects of Vitamin B 12 based on the various available reports and findings.

Vitamin B 12 and cardiovascular disease (CVD)

Increased plasma homocysteine levels have been identified as a significant risk factor for cardiovascular disease (CVD). Supplementing with folic acid and other B vitamins, which is a reasonably inexpensive approach of lowering plasma homocysteine levels, could reduce CVD risk. Several studies have demonstrated that folic acid in combination with B12 lowers homocysteine levels, although the impact of vitamin B12 alone to homocysteine reduction has yet to be defined [8]. After 12 weeks, a supplement containing 5 mg folic acid and 250 mg vitamin B12 reduced fasting plasma homocysteine levels by 32% in patients with coronary artery disease, according to one study [9, 10]. In another trial, daily supplementation with 500 mg of vitamin B12, 0.8 mg of folic acid, and 3 mg of vitamin B6 for four months significantly lowered plasma homocysteine levels (P.001). The participants were from both genders (70-93 years). According to the study's authors, low vitamin levels are a major cause of high homocysteine levels in the elderly, even in those who are otherwise healthy. Several studies have looked at possible links between vitamin B12 and homocysteine levels in patient populations such as those with type 2 diabetes and dialysis patients (who are at risk for cardiovascular problems) [11, 12]. Metformin, a drug often used to treat type 2 diabetes, may lower vitamin B12 levels. Wulffele and colleagues found that metformin reduced both folic acid (7 percent reduction) and vitamin B12 (14 percent reduction) levels in the study. The change in folic acid and vitamin B12 status is likely to blame for the minor increase in homocysteine levels (4%). Neither intramuscular [11] nor intravenous dosages of vitamin B12 had an effect on homocysteine levels that was independent of folic acid in hemodialysis patients with increased

homocysteine levels. However, a rise in homocysteine levels was documented in pregnant women with vitamin B12 insufficiency during the fourth and ninth months of pregnancy [13]. Neither intramuscular nor intravenous dosages of vitamin B12 had an effect on homocysteine levels that was independent of folic acid in hemodialysis patients with increased homocysteine levels. However, a rise in homocysteine levels was seen in a small study of pregnant women with vitamin B12 insufficiency during the fourth and ninth months of pregnancy.

B12 and Cerebrovascular disease

Studies on the influence of vitamin B12 intake in the diet on the risk of stroke have generated mixed results. In one study, folate and vitamin B6 intakes, but not vitamin B12 intakes, were found to be substantially linked with lower cerebrovascular mortality, whereas folate and vitamin B12 intakes, but not vitamin B6, were found to be inversely associated with the risk of ischemic stroke [14]. Quinlivan and colleagues revealed that after supplementing with increasing dosages of folic acid, plasma homocysteine levels became less dependent on folate, and vitamin B12 became the key predictor of plasma homocysteine levels [15]. These researchers hypothesised that fortifying foods with both folic acid and vitamin B12 would help to lower homocysteine levels more efficiently, perhaps lowering the risk of vascular disease. According to one study, the kind of stroke has a role in determining the effect of blood vitamin levels on risk. Only with major artery strokes did Asian men younger than 50 years of age have higher homocysteine levels; vitamin B12 levels were considerably lower in cases compared to controls (P.001), but there were no significant variations in serum folate levels [16, 17]. Hyperhomocysteinemia's proatherogenic impact, according to the authors, may raise the risk of stroke. The use of folic acid, vitamin B12, and vitamin B6 to treat hyperhomocysteinemia has been found to minimise thrombin generation. Overall, high homocysteine levels lead to atherosclerosis, and optimal folic acid, vitamin B12, and vitamin B6 levels may lower homocysteine and the risk of clotting. In the case of heart disease and stroke, a better understanding of homocysteine metabolism is required, especially when homocysteine levels are increased considerably above normal. Furthermore, reducing homocysteine levels with vitamin supplementation has not been found to improve secondary prevention, as evaluated by recurrent myocardial infarction, stroke, or death from cardiovascular causes. Multivitamin therapy does not reduce blood levels of inflammatory biomarkers, endothelial dysfunction, or hypercoagulability, according to Dusitanond and colleagues' findings from the VITATOPS trial. They speculate that this is because the biomarkers are not

sensitive to decreases in homocysteine, homocysteine may have different mechanisms of action, or elevated homocysteine may be a marker for, but not a cause of, increased vascular risk [18-20].

What is also unknown is the point at which the inflammatory process of atherosclerosis outweighs any supplement's capacity to counteract unfavourable outcomes. In fact, determining nutritional benefits in secondary prevention trials is one of the most difficult tasks for researchers. Recent research has found that combining vitamin B12 with other B vitamins reduces insulin resistance and oxidative stress and inflammation markers in patients with metabolic syndrome; however, two randomised clinical trials found no effect of B vitamins on venous thrombosis, and a meta-analysis found no benefit in the progression of atherosclerosis.

Vitamin B12 and Cancer

Folic acid is well-known for its role in DNA synthesis and repair. According to Ames, folate insufficiency, as well as vitamin B12 and B6 deficiency are linked to cancer because uracil, rather than the proper base, is incorporated into human DNA, resulting in chromosomal breakage [21]. A tiny study found some indication of a slight link between vitamin B12 intake and cervical cancer [22]. There is some evidence of connections between micronutrient consumption, genotype, and cancer. The methylenetetrahydrofolate reductase (MTHFR) gene has several variants that increase the risk of colon cancer. The CC genotype has the highest risk of colon cancer due to inadequate vitamin intake [23]. High folate, vitamin B6, and vitamin B12 intakes were linked to a 30% to 40% lower risk of colon cancer in those with the TT genotype compared to those with the CC genotype and low intakes, according to Slattery et al. An earlier study that used data from the Nurses' Health Study found no link between the TT variant of the MTHFR gene and diet and colorectal adenoma, which is the immediate precursor to colorectal cancer [23]. Other data from the Physicians' Health Study and the Health Professionals Follow-up Study suggested that there was an interaction between the variant MTHFR genotype and the risk of colorectal cancer, but merely a insignificant decrease for the methionine synthase variation [24, 25]. There was no correlation between vitamin B12 and either variant genotype. Overall, there aren't many distinctions between genotype, micronutrient consumption, and colorectal cancer. Relationships between dietary intakes, genotypes, and some malignancies seem probable; nevertheless, nutritional genomics is still in its early stages, and additional study is required to evaluate whether any detected interactions are true.

Association with Mental Health

Biochemical variables like homocysteine, according to researchers, may be involved not just in heart disease but also in brain function. As a result, the association between B vitamins and homocysteine and cognitive function is being researched. In a normal ageing population, homocysteine levels, but not vitamin B12 levels, were linked to deterioration in cognitive ability [26]. Another study found that supplementing with B vitamins (2 mg folic acid and 1 mg vitamin B12) reduced plasma homocysteine levels by 30% in people with dementia or mild cognitive impairment, but had no effect on cognitive function. Although some studies suggest that folic acid is more crucial for cognitive function than vitamin B12, B12 supplementation has been proven to alleviate symptoms of delirium or enhance some skills in patients with cognitive impairment, even when the underlying dementia diagnosis stays the same. According to a systematic evaluation of vitamin B12 and cognition, there is currently inadequate data to suggest that B12 improves the cognitive performance of dementia patients [27, 28]. Those with Alzheimer's disease who had lower-than-normal vitamin B12 levels exhibited more frequent psychological symptoms of dementia than patients with normal levels, according to Meins and colleagues [29]. Although Engelborghs et al found no link between serum vitamin B12 levels and behavioural and psychological symptoms of dementia in Alzheimer's disease patients, they did detect a link between frontotemporal dementia and serum vitamin B12. Although vitamin B12 deficiency becomes more common as people get older, only approximately 10% of those with low vitamin B12 also have low folate levels [30]. Given the high prevalence of both vitamin B12 deficiency and mental disability among the elderly, vitamin B12 supplementation may reduce the risk of age-related mental disability or improve the quality of life for those living with dementia, but more research should be promoted in determining the biological importance of vitamin B12.

Depression has also been linked to hyperhomocysteinemia, vitamin B12 insufficiency, and poor 1-carbon metabolism due to genetic polymorphism. Higher vitamin B12 levels were related with a better treatment outcome for major depression, according to Hintikka and colleagues, suggesting that vitamin B12 supplementation could be utilised to support antidepressant therapy. Vitamin B12, on its own, is unlikely to have a significant impact on cognitive function or depression, though it has been proven to reduce homocysteine levels [31]. In fact, recent studies spanning 6 months to 2 years have found no benefit from vitamin B12. Future

research should focus on the nutritional benefits of vitamin supplementation in conjunction with pharmacotherapy rather than the pharmacologic ones.

Vitamin B12 and Birth Outcome

Folate deficiency has been linked to a higher risk of neural tube defects (NTDs), and fortification has been found to enhance outcomes in Canada [32]. However, some experts believe that optimal vitamin B12 levels are also required. In India, where a large portion of the population is vegetarian and vitamin B12 deficiency is common, folate alone may be ineffective. It's possible that increasing vitamin B12 intake will improve the function of the enzyme methionine synthase, which converts homocysteine to methionine [33]. A comprehensive review of the literature revealed that there may be a moderate link between maternal B12 status and the risk of NTDs, but that additional research into this relationship would require a large observational study [34].

Families at risk for NTDs may have genetic abnormalities that impair folate and vitamin B12 metabolism. A variation in methionine synthase reductase (the enzyme that activates B12-dependent methionine synthase) in combination with a mutation in the MTHFR gene has recently been demonstrated to increase the risk of NTDs by up to 5 times. According to other research, the interactions between genes and enzyme activity may raise the incidence of Spina bifida [35]. Others have speculated that genetics may influence the delivery of vitamin B12 to tissues via transcobalamin II (TC II) [36]. Genetic mutation in the TC II gene, according to Afman and colleagues, is likely to induce a lower affinity for vitamin B12. B12 supplementation may improve TC II levels while also raising cellular vitamin B12 and lowering homocysteine levels, which are greater in mothers of children with NTDs.

Conclusion

Although a small number of studies has demonstrated that vitamin B12 improves folic acid's role in the homocysteine–cardiovascular disease pathway, its biological importance has been difficult to determine. Although a fortification programme for vitamin B12 similar to that for folic acid in flour may be more efficient in lowering homocysteine levels, physicians should make sure that their patients over 50 are getting enough vitamin B12 from fortified foods or supplements. Because of genetic variations, vitamin B12 levels may have a minor impact on cancer development. Nutritional genomics, a novel area, is expected to yield useful

information about nutrient-gene interactions and chronic disease. B12 supplementation may help some behavioural or psychological indices linked to dementia and depression, and it should be used in conjunction with medicine.

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References

1. Andres E, Loukili NH, Noel E, Kaltenbach G, Abdelgheni MB, Perrin AE, et al. Vitamin B12 (cobalamin) deficiency in elderly patients. CMAJ 2004;171(3):251-9.
2. Food and Nutrition Board, Institute of Medicine. Dietary reference intakes for thiamine, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline. Washington, DC: National Academy Press; 1998.
3. Allen LH. Folate and vitamin B12 status in the Americas. Nutr Rev 2004; 62 (6 Pt 2):S29-33.
4. Gupta AK, Damji A, Uppaluri A. Vitamin B12 deficiency. Prevalence among South Asians at a Toronto clinic. Can Fam Physician 2004; 50:743-7
5. Shipton MJ, Thachil J. Vitamin B12 deficiency - A 21st century perspective. Clin Med (Lond). 2015 Apr;15(2):145-50. doi: 10.7861/clinmedicine.15-2-145.
6. Oo TH, Rojas-Hernandez CM. Challenging clinical presentations of pernicious anemia. Discov Med. 2017 Sep;24(131):107-115.
7. O'Leary F, Samman S. Vitamin B12 in health and disease. Nutrients. 2010 Mar;2(3):299-316. doi: 10.3390/nu2030299. Epub 2010 Mar 5.
8. Schwammenthal Y, Tanne D. Homocysteine, B-vitamin supplementation, and stroke prevention: from observational to interventional trials. Lancet Neurol 2004;3:493-5
9. Lee BJ, Huang MC, Chung LJ, Cheng CH, Lin KL, Su KH, et al. Folic acid and vitamin B12 are more effective than vitamin B6 in lowering fasting plasma homocysteine concentration in patients with coronary artery disease. Eur J Clin Nutr 2004;58:481-7.
10. Lewerin C, Nilsson-Ehle H, Matousek M, Lindstedt G, Steen B. Reduction of plasma homocysteine and serum methymalonate concentrations in apparently healthy elderly subjects after treatment with folic acid, vitamin B12 and vitamin B6: a randomized trial. Eur J Clin Nutr 2003; 57:1426-36.

11. Polkinghorne KR, Zoungas S, Branley P, Villanueva E, McNeil JJ, Atkins RC, et al. Randomized, placebo-controlled trial of intramuscular vitamin B12 for the treatment of hyperhomocysteinemia in dialysis patients. Intern Med J 2003;33:489-94.
12. Sombolos K, Fragia T, Natse T, Bartholomatos G, Karagianni A, Katsaris G, et al The effect of long-term intravenous high dose B-complex vitamins with or without folic acid on serum homocysteine in hemodialysis patients. J Nephrol 2002;15:671-5.
13. Chery C, Barbe F, Lequere C, Abdelmouttaleb I, Gerard P, Barbarino P, et al. Hyperhomocysteinemia is related to a decreased blood level of vitamin B12 in the second and third trimester of normal pregnancy. Clin Chem Lab Med 2002; 40:1105-8.
14. He K, Merchant A, Rimm EB, Rosner BA, Stampfer MJ, Willett WC, et al. Folate, vitamin B6, and B12 intakes in relation to risk of stroke among men. Stroke 2004;35:169-74.
15. Quinlivan EP, McPartlin J, McNulty H, Ward M, Strain JJ, Weir DG, et al. Importance of both folic acid and vitamin B12 in reduction of risk of vascular disease. Lancet 2002;359:227-8.
16. Tan NC, Venketasubramanian N, Saw SM, Tjia HT. Hyperhomocyst(e)inemia and risk of ischemic stroke among young Asian adults. Stroke 2002; 33:1956-62.
17. Undas A, Domagala TB, Jankowski M, Szezeklik A. Treatment of hyperhomocysteinemia with folic acid and vitamins B12 and B6 attenuates thrombin generation. Thromb Res 1999; 95:281-8
18. Lonn E, Yusuf S, Arnold MJ, Sheridan P, Pogue J, Micks M, et al. Homocysteine lowering with folic acid and B vitamins in vascular disease. N Engl J Med 2006;354(15):1567-77.
19. Bonaa KH, Njolstad I, Ueland PM, Schirmer H, Tverdal A, Steigen T, et al. Homocysteine lowering and cardiovascular events after acute myocardial infarction. N Engl J Med 2006; 354(15):1578-88.
20. Dusitanond P, Eikelboom JW, Hankey GJ, Thom J, Gilmre G, Loh K, et al. Homocysteine-lowering treatment with folic acid, cobalamin, and pyridoxine does not reduce blood markers of inflammation, endothelial dysfunction, or hypercoagulability in patients with previous transient ischemic attack or stroke: a randomized substudy of the VITATOPS trial. Stroke 2005; 36:144-6.
21. Ames BN. DNA damage from micronutrient deficiencies is likely to be a major cause of cancer. Mutat Res 2001; 475:7-20.
22. Alberg AJ, Selhub J, Shah KV, Viscidi RP, Comstock GW, Helzlsouer KJ. The risk of cervical cancer in relation to serum concentrations of folate, vitamin B12, and homocysteine. Cancer Epidemiol Biomarkers Prev 2000; 9:761-4
23. Slattery ML, Potter JD, Samowitz W, Schaffer D, Leppert M. Methylenete trahydrofolate reductase, diet, and risk of colon cancer. Cancer Epidemiol Biomarkers Prev 1999; 8:513-8.
24. Chen J, Giovannucci E, Hankinson SE, Ma J, Willett WC, Spiegelman D, et al. A prospective study of methylenetetrahydrofolate reductase and methionine synthase gene polymorphisms, and risk of colorectal adenoma. Carcinogenesis 1998; 19:2129-32.
25. Ma J, Stampfer MJ, Christensen B, Giovannucci E, Hunter DJ, Chen J, et al. A polymorphism of the methionine synthase gene: association with plasma folate, vitamin B12, homocyst(e)ine, and colorectal cancer risk. Cancer Epidemiol Biomarkers Prev 1999;8:825-9.

26. Teunissen CE, Blom AH, Van Boxtel MP, Bosma H, de Bruijn C, Jolles J, et al. Homocysteine: a marker for cognitive performance? A longitudinal follow-up study. J Nutr Health Aging 2003; 7:153-9.
27. Clarke R, Harrison G, Richards S; Vital Trial Collaborative Group. Effect of vitamins and aspirin on markers of platelet activation, oxidative stress and homocysteine in people at high risk of dementia. J Intern Med 2003; 254:67-75.
28. Hassing L, Wahlin A, Winblad B, Backman L. Further evidence on the effects of vitamin B12 and folate levels on episodic memory functioning: a population-based study of healthy very old adults. Biol Psychiatry 1999; 45:1472-80.
29. Meins W, Muller-Thomsen T, Meier-Baumgartner HP. Subnormal serum vitamin B12 and behavioural and psychological symptoms in Alzheimer's disease. Int J Geriatr Psychiatry 2000; 15:415-8.
30. Engelborghs S, Vloeberghs E, Maertens K, Mariën P, Somers N, Symons A, et al. Correlations between cognitive, behavioural and psychological findings and levels of vitamin B12 and folate in patients with dementia. Int J Geriatr Psychiatry 2004; 19:365-70.
31. Tiemeier H, van Tuiji HR, Hofman A, Meijer J, Kiliaan AJ, Breteler MM. Vitamin B12, folate, and homocysteine in depression: the Rotterdam Study. Am J Psychiatry 2002;159:2099-101
32. Ray JG, Meier C, Vermeulen MJ, Boss S, Wyatt PR, Cole DE. Association of neural tube defects and folic acid food fortification in Canada. Lancet 2002; 360:2047-8.
33. Refsum H. Folate, vitamin B12 and homocysteine in relation to birth defects and pregnancy outcome. Br J Nutr 2001;85(Suppl 2):S109-13.
34. Ray JG, Blom HJ. Vitamin B12 insufficiency and the risk of neural tube defects. QJM 2003; 96:289-95.
35. Wilson A, Platt R, Wu Q, Leclerc D, Christensen B, Yang H, et al. A common variant in methionine synthase reductase combined with low cobalamin (vitamin B12) increases risk for spina bifida. Mol Genet Metab 1999; 67:317-23.
36. Afman LA, Van Der Put NMJ, Thomas CMG, Trijbels JMF, Blom HJ. Reduced vitamin B12 binding by transcobalamin II increases the risk of neural tube defects. QJM 2001; 94:159-66.