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Review Article

Exploration of the Putative Role of Vitamin B12 and Vitamin D in Cardiovascular, Immunological and Auto-immune Disorders: An Appraisal

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Abstract

The present review throws light on the association existing between both these set of vitamin with their defined implications such as cardio-metabolic disorders, in the progression and staging of auto-immune disorders and overall health outcomes and hospital stay duration for patients. The polar vitamin B complex and the lipophilic vitamin D areubiquitously expressed in different tissues of the haemopoietic and osseous system. They serve putative roles in as a reversible cause of the red bone marrow failure and in demyelination nervous system disease. Vitamin B12also known ascyanocobalamin is synthesized by microorganisms. The most frequent cause of severe vitamin B12 deficiency is a loss of intrinsic factor due to autoimmune atrophic gastritis episodes that is historically attributed as pernicious anemia even though many patients present with mainly neurologic manifestations. On the other hand, deficiency of vitamin D produces bone deformities like rickets.

Keywords: cyanocobalamin, cholecalciferol, auto-immunity, immunomodulation.

Introduction

Vitamin B12 and Vitamin D both plays a significant role in the regulation of various metabolic processes pertaining to the proper functioning and other systemic activities. The importance of the Vitamin B12 specially in case of the elderly patients requires more attention since deficiency of this may lead to clinical manifestation of many unrecognized conditions for instance neuropsychiatrical and haematological issues develop. Although cobalamine deficiencies attributes to the serum levels of homocystein, cobalamin and methyl malonic acid. High serum values of homocysteine may be because of folate and vitamin B6 deficiency. Now Vitamin D has some major role, being a seco steroid hormone and are formed photochemically in the epidermis. The ultraviolet radiation acts upon 7dehydrocholesterol results in the formation of pre vitamin D and after few hydroxylations finally 1,25 dihydroxyvitamin ids formed.Although this review article entails the underlying benefits and effects of vitamin B12 and Vitamin D in brain diseases, immune mediated disorders, systemic lupus erythromatosus , multiple sclerosis and rheumatoid arthritis.

Vitamin B12and its Endogenous functions [1-14]

Vitamin B12 also known as cyanocobalamin, comprises a number of forms including cyano-, methyl-,deoxyadenosyl- and hydroxy-cobalamin. The cyano form, which is used in supplements, is found in trace amounts in food [1]. The other forms of cobalamin can be converted to the methyl- or 5-deoxyadenosyl forms that are required as co factors for methionine synthetase and L-methyl-malonyl-CoA mutase.Methionine synthase is essential for the synthesis of purines and pyrimidines. The methyl cobalamin reaction which is entirely dependenton a co-factor and also found dependent on folate, where amethyl group of methyltetrahydrofolate is transferred to homocysteine to form tetrahydrofolate and methionine . The megaloblastic anaemia is caused due to the deficiency of vitamin B12.Folate deficiency may also cause megaloblastic anaemia [2].Methylmalonyl CoAto succinyl CoA by methylmalonyl CoA, having 5-deoxyadenosyl cobalamin that acts as cofactor. The subsequent accumulation of methylmalonyl CoA may be responsible for certain neurological effects in vitamin B12 deficiency [2]. Vitamin B12 in serum is bound to proteins known as transcobalamins (TC). Approximately 80% of the major vitamins, is transported on the inactive TCI (also called haptocorrin). The active transport protein for vitamin B12 is transcobalamin II (TCII), which carries about 20% of the vitamin in the circulation [3]. Holo-transcobalamin (holo-TC) is TCII with attached cobalamin, which helps in delivering vitamin B12 to cells. A low serum vitamin B12 concentration can be associated with a deficiency of TCI, while TCII levels and so vitamin B12 status remain adequate [4].

Vitamin B12 and Cardiovascular and immunological Disease (CVD)[5-18]

Nutritional risk factors for CVD include hypercholesterolemia, hypertension and obesity. When tHcy concentrations gets elevated they are also considered a risk factor, although, it is unclear if tHcy whether it an independent marker of the disease process or a modifiable risk factor. Mostly the researchinto CVD and tHcy is associated to the effects of folate supplementation with or without the addition of vitamins B12. The investigation on the interrelationship between CVD and vitamin B12 are limited. Meta-analyses pertaining to the prospective studies have consistently shown correlation between tHcy and increased risk of CVD. Supplementation with vitamin B12 of doses ranging from 0.02–1 mg/d produces approximately 7% decrease in tHcy, while folate produces 10–30% decrease in risk.

Table 1: Meta-analyses of studies assessing vitamin B12 and CVD[21-33.]

Trial Type	Study Details	Main Outcomes
Meta-analysis	9 case-control studies. Assessed associations between tHcy and CVD risk.	5μM tHcy increment associated with increased risk of CAD, OR = 1.6 (95% CI:1.4 to 1.7) for males and 1.8(95% CI:1.3 to 1.9) for females

Trial Type	Study Details	Main Outcomes
Meta-analysis	30 prospective or retrospective studies assessed tHcy and CVD risk.	25% lower tHcy associated with lower risk of IHD & stroke
Meta-analysis 7 RCTs	B vitamin supplementation and tHcy lowering, assessed effect of vitamin B12 (range 0.02–1.0mg/day)	Vitamin B12 (median dose 0.4 mg/d) - further decrease (-7%) in tHcy
Meta-analysis 12 RCTs	Preexisting CVD or renal disease-included 3 studies of vitamin B12supplementation, with doses0.4–1.0 mg B12/day.	Reduction in stroke risk in vitamin B12 (1 mg/d) intervention OR = 0.76 (95% CI:0.59, 0.96)
Meta-analysis 8 RCTs	4 studies assessed vitamin B12 supplementation (0.018–1 mg) and stroke risk	Reduction in stroke greater in longer trials with more tHcy lowering and no stroke history. No specific effect of vitamin B12
Meta-analysis of 24 RCTs	Assessed CIMT: 3 with vitamin B12: 0.4–0.5 mg/d; endothelial function: 5 with B12: 6 µg–1 mg/day	↓ CIMT, ↑ FMD found in short-term not long term trials

WhereµM = micromolar, tHcy = total homocysteine, CAD = coronary artery disease, OR = odds ratio,CI=confidence intervals, CVD = coronary vascular disease, IHD=ischemic heart disease, CIMT = carotidintima media thickness, FMD = flow mediated dilation

The recent B vitamin supplementation trials investigating the effect of tHcy reduction and CVD did not show the expected reductions in risk of CVD. All of these randomized controlled trials (RCTs) included vitamin B12 supplementation (ranging from 6 µg-1 mg) in tandem with folate, and it is not possible to determine the individual impact of vitamin B12. A number of reviews have discussed the limitations of these trials and identified inadequate treatment with vitamin B12 as one of the limitations.

Subgroup analysis of the VISP Trial found that patients with higher baseline vitamin B12concentrations, taking high dose vitamins, had the best outcomes and those with lower baseline vitamin B12 taking low-dose vitamins had the poorest outcomes for stroke, death, and coronary events, suggesting higher vitamin B12 doses may be needed in some patients. Vitamin B12 has been shown to be a major determinant of tHcy concentrations in subjects with adequate folate status and the existence of vitamin B12 deficiency could be one reason for the lack of effect of intervention with folate

Basic vitamin D metabolism[34-52]

Sunlight-induced vitamin D synthesis in the skin accounts for about 80% of obtained vitamin D.5 Specifically, ultraviolet-B(UV-B) radiation induces the conversion of 7-dehydrocholesterol to previtamin D, which spontaneously isomerises to vitamin D.6 This vitamin D production by sunlight exposure is particularly efficient in individuals with low levels of skin melanin. Therefore, an intriguing hypothesis suggests that in human evolution, those individuals migrating to northern regions developed a fair skin to efficiently synthesize vitamin D under conditions of less UV-B exposure, whereas those individuals residing in sunny regions have a high melanin content of the skin, which protects against sunlight induceddamage.7,8 Diet makes a relatively small contribution tovitamin D status.1,5 Vitamin D can be obtained from natural foods(e.g. oily fish, eggs or UV-irradiated and sun-dried mushrooms), vitamin D-fortified food (e.g. vitamin D-fortified milk and orange juice in the United States) or vitamin D supplements.1 Two major forms of vitamin D exist: vitamin D3 (cholecalciferol), the main vitamin D form derived mainly from synthesis in the skin and from animal sources and vitamin D2 (ergocalciferol), the plant- and yeast-derived form. Unless otherwise stated, we do not differentiate between these two isoforms in this review and usually refer to vitamin D (meaning both vitamin D2 and D3) in general.

Conclusion

The systematic review study throws light on the causal association of Vitamin B12 to cardiovascular, immunological and auto-immune disorders that is already established. This review highlights studies that have suggested that vitamin D (particularly Vitamin D3) and its involvement in the etiopathogenesis of immunological disorders as well as their well-defined role in the pathogenesis of a variety of cardiovascular diseases.

Conflicts of interest

The authors report no conflict of interest.

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