Review Articles

Effect of vitamin B_{12} supplementation on neurologic and cognitive functions in older people- A review

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ABSTRACT

Ageing is associated with decline in vitamin B_{12} and cognitive function. Many clinical trial studies provided the evidence of improvement in biomarker and cognitive functions after supplementation of B_{12} vitamin. This systematic review is an effort to use of these data to know the effect of vitamin supplementation in improving cognitive functions. The present study reviewed the evidences that investigated vitamin B_{12} supplementation and biomarkers of vitamin B_{12} status and cognitive function. This review included all RCTs, prospective cohort studies, nested case-control studies, and cross-sectional studies in healthy elderly populations published during the period from 2010 to 2019 that included vitamin B_{12} supplementation and measured serum or plasma. Vitamin B_{12} or methylmalonic acid (MMA), homocysteine or holo-transcobalamin and cognitive function. We followed prisma guidelines for selecting the evidence. Selected final evidence were discussed and summarized. Six articles were selected for full length after applying prisma guidelines, evidences of which showed improvement of biomarkers and there is limited improvement in cognitive functions. Some of the neurological impairments are irreversible hence need to screen for B_{12} level and initiate proper therapy at the earliest.

Keywords: Vitamin B_{12}; cobalamin; supplementation; older people.

INTRODUCTION

The world's older age population is gradually increasing and was around 7.9 million according to World Population Prospects 2019 (1). Vitamin B_{12}/Cobalamin an essential water-soluble vitamin, since mammals/humans unable to synthesis. However, an efficient ability of absorption and transport mechanisms renders delay in the possibility of deficiency manifestations to several years of deficient diet. Deficiency manifestations can result in devastating and irreversible complications / consequences. A common cause of deficiency is malnutrition or malabsorption (2).

The geriatric population is vulnerable/ at high risk to have Vitamin B_{12} / cobalamin deficiency mainly due to gastric atrophy and other causes related to GIT as well as due to their exposure to medication those interfere with B_{12} metabolism (3). Along with the cognitive impairment, study reports propose the significance of B_{12} in the development of mood and psychiatric disorder. This may be the early sign of deficiency even before the hematological manifestations- a common deficiency, and often missed problem in geriatric patients (4).

Ageing is associated with a decrease in the status of vitamin B_{12} and rise in the incidence of vitamin B_{12} deficiency. B_{12} is an indispensable micronutrient, adequate level is necessary for RBC maturation, single carbon metabolism, synthesis of neurotransmitter, choline, nucleotides and phospholipids, central and peripheral neurologic function. Deficiency of vitamin B_{12} in aged population attributes to gastric atrophy (5-8). Severe deficiency of vitamin B_{12} causes sensory disturbances in the extremities, loss of sensation, motor problems, abnormal gait, impaired cognition and depression. Symmetric paresthesia, numbness or altered gait, impaired posture and cutaneous feeling, diminished sense of vibration and weakness are signs of vitamin B_{12} deficiency associated with peripheral neuropathy (9-11). Most of these symptoms will disappear if treated early (12, 13), but recovery can take some time (14). That is, the state at which the neurologic abnormalities are recognized will decide the duration and extent of recovery. Oral supplementation of crystalline vitamin B_{12} is commonly used to correct moderate-deficiency and hematologic variables. (11). Neurological, psychological and cognitive impairments also exist in people with moderate levels of vitamin B_{12} (serum vitamin B_{12} concentrations: 107–210 pmol / L; 15), though the evidence of a direct correlation between the status of vitamin B_{12} wrenched evidence on the efficacy of vitamin B_{12}supplementation on restoring of neurologic or cognitive functions in geriatric people. In this literature survey, we have tried to gather the effect of B_{12} supplementation in the older / geriatric population.

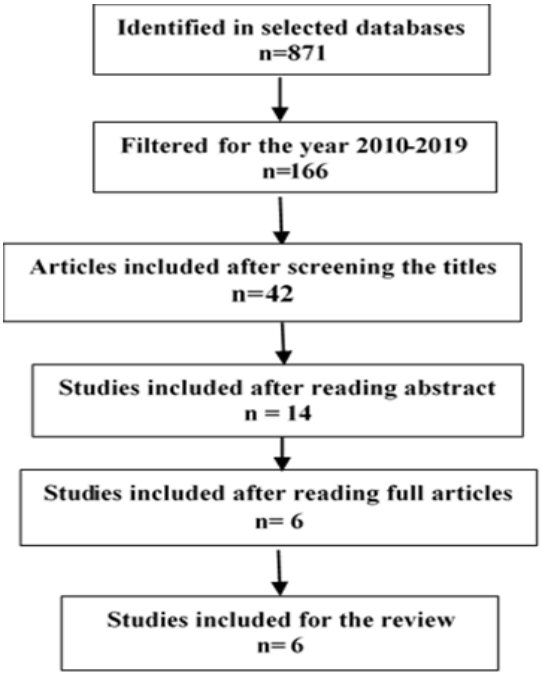
Data source and search strategy

The articles searched in single window of health science library- Scopus, web of science, Cinhal plus, PubMed/Medline, Cochrane, Google scholar, Proquest, Embase databases available in Health Science Library of Manipal Academy of Higher Education during the study period May to July 2019. Articles published during the period from 2010 to 2019 were included for the review. Key words used for the search strategy included, Vitamin B_{12}, Supplementation, older people. Articles published in English and full text articles published during the year 2010 to 2019 were included. Articles published in newspaper, only abstract without full text articles and articles in other language were excluded. Articles on clinical trial, randomized control trial, observational studies with vitamin B_{12} supplementation were included for the study.

Study selection

The titles of the articles were collected from the databases using selected key words and were checked for duplicates and de-duplicated. Selected titles were in accordance with the set criteria with the help of second investigator. Again, all the selected titles with abstracts were verified for inclusion criteria. Finally, selected only articles fulfilled all criteria with full text. These selected articles were reviewed and analyzed as per the format and studied extensively under the title study setting, study population, details of the intervention and control conditions, outcomes and times of measurement.

Enrollment and analysis



Following are the selected studies for the review:

A double-blind placebo randomized controlled trial conducted by Dangour *et al.,* (22) in asymptomatic older age group with moderate deficiency, where one group received 1 mg of crystalline vitamin B_{12} supplementation and other with placebo as daily oral tablets for a period of one year. Study report shows that daily supplementation of B_{12} did not result in any improvement and also suggests having more focused delineations in above conditions to justify the impact of deficiency, supplementation and its outcome.

Elevated Homocysteine concentrations, which is one of the consequences of vitamin B_{12} and or B_9 deficiency. de Koning *et al.,* conducted a randomized controlled trial in geriatric population were exposed to a combination of 500 µg of Vitamin B_{12} with 400 µg of B_9 daily or placebo for a period of 2 years along with vitamin D (23). They concluded that long-term supplementation may have some benefit against hyperhomocystenemia, however observation states a small positive influence on health-related general quality of life without any benefit towards depressive symptoms. The observations also had a question mark weather the improvement perceived or is due to the combined Vit. D in the supplementation or only because of Vit B_{12} and B_9.

Walker *et al.,* performed a randomized controlled trial (RCT) in 900 adults aged 60-74 years with elevated psychological distress, with an oral intervention of 400µg folic acid and100 µg vitamin B_{12} on daily basis for a period of 2 years (24). The study reports apprise the long-term vitamin supplementation since there was a convalescing status in the cognitive function especially in memory, particularly in immediate and delayed memory performance.

In a study conducted by Swart *et al.,* which is double blinded randomized placebo-controlled trial (25) where a group of elderly people had supplementation of 500µg of vitamin B_{12} and 400µg of folic acid and 600IU vitamin D_3 for with problem with risk of falling, hand grip strength and physical performance. It has been found that two-year supplementation of vitamin B_{12} and B_9 was not successful either in reducing the age-related decline in physical ability and handgrip strength, or in preventing elderly people from falling.

A randomized, double blind, placebo-controlled trial conducted by Harris (26) in a group of elderly people aged 55-65 years by supplementing multivitamin daily for 16 weeks, found that supplementation has improved a variety of cognitive-relevant blood biomarkers but changes in these biomarkers have not been followed by improvements in cognitive functions.

Brito *et al.,* conducted a pre-and-post-treatment study in elderly Chileans with a combination of 10 mg Vit B_{12}, 100 mg pyridoxine, and 100 mg thiamin (27). The subjects, who were asymptomatic and with low B_{12} levels exposed to intramuscular injection of above combination. The study reports confirmed that

vitamin B_{12} injection elevated the serum vitamin B_{12} as reflected by the estimated metabolic biomarkers of vitamin B_{12} status. It also has been reported a progressive positive impact on the functioning of peripheral myelinated nerve as well. In continuation, result says that the study subjects showed a better status with reference to sensory nerve conduction in the lower extremities and the improvement observed is mainly because of vitamin B_{12}, since there was no much effect on the blood levels of thiamin and pyridoxine after supplementation.

CONCLUSION

The review rules out that vitamin B_{12} supplementation is not an exclusive supplementation and independently did not show any improvement in cognitive function in elderly people however; a mild improvement in memory after supplementation was reported. Moreover, review also suggests having more focused delineations in the above conditions to justify the impact of deficiency, supplementation and its outcome.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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