

Methylcobalamin in Vitamin B₁₂ Deficiency: To Give or not to Give?

Sir,
Vitamin B₁₂ deficiency is a common nutritional disorder characterized by hematological and neurological manifestations. Cyanocobalamin (CNCbl) or hydroxocobalamin (OHCbl) have been the traditional B₁₂ formulations recommended for deficiency states. Methylcobalamin (MeCbl), an active form of Vitamin B₁₂, has been increasingly dominating the nutritional formulation market. In India, it is available as parenteral, oral, and sublingual formulations, either alone or in combination with other B-group vitamins (multivitamin formulations). Internationally, MeCbl formulations are widely available as health supplements in the unregulated market. It is likely that a large number of people are prescribed or self-medicate these supplements either for deficiency states or for prophylaxis. MeCbl is also commonly prescribed for neuropathies. However, the clinical evidence for the use of MeCbl in deficiency states in the form of controlled trials is scanty. It has also been argued that use of MeCbl in Vitamin B₁₂ deficiency will not reverse the neurological deficit.^[1] MeCbl and 5'-deoxyadenosylcobalamin (AdoCbl) are the active coenzyme forms of Vitamin B₁₂ formed intracellularly. It has been suggested that these coenzymes are necessary for normalization of the hematological and neurological manifestations of B₁₂ deficiency, respectively. AdoCbl-dependent methylmalonyl CoA mutase reaction, a step in propionate metabolism, is proposed to be responsible for myelin synthesis.^[1] Hence, it is suggested that AdoCbl cannot be substituted by MeCbl and thereby patients receiving MeCbl would not experience the full therapeutic benefits unless AdoCbl was also added or CNCbl/OHCbl were administered which subsequently get converted intracellularly to both the active forms. However, the assertion that AdoCbl deficiency is responsible for the neurological impairment has been challenged. It has been suggested that deficiency of methionine synthase (requires MeCbl) and the block of the conversion of methionine to S-adenosylmethionine is responsible for the neuropathy in B₁₂ deficiency states.^[2] In this context, it is also important to consider the role of methylmalonic aciduria and homocystinuria type C protein, a cytosolic chaperon.^[2] This protein removes the ligands attached to the cobalamin molecule (cyano, hydroxyl, methyl, or adenosyl groups by decyanation or dealkylation) for further synthesis of the necessary coenzyme forms. This

suggests that there is interchangeability of cobalamin forms within the body.^[3] In terms of clinical evidence, a systematic review of controlled trials did not demonstrate any inferiority of MeCbl in comparison to Vitamin B complex containing CNCbl in patients with diabetic neuropathy.^[4] MeCbl and its combination with prostaglandin E1/lipoic acid have been found to be beneficial in diabetic neuropathy.^[5] Thus, MeCbl may be a suitable alternative to CNCbl/OHCbl in the treatment of Vitamin B₁₂ deficiency. In India, oral MeCbl formulations are more easily available than oral CNCbl. There is clinical evidence that oral B₁₂ supplementation is as effective as parenteral supplementation. The effectiveness of MeCbl would be of concern to those taking it for treatment or prophylaxis. Notwithstanding the above observations or the cost concerns, there is a need for a well-designed controlled clinical trial comparing the various forms of Vitamin B₁₂ since the absence of evidence is not to be considered as evidence of absence in either case.

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Conflicts of interest

There are no conflicts of interest.

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