Letter to the Editor

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Reply to: "B vitamins for NASH: Use methylcobalamin, not cyanocobalamin"

To the Editor:

We appreciate the letter by Dr. Spence advocating the use of methylcobalamin or hydroxycobalamin rather than the cyanocobalamin form of vitamin B12 (B12) in future clinical trials investigating the efficacy of B vitamins to prevent or treat NASH.[1] This is similar to the concern that he raised previously regarding studies that employed B12 for the prevention of stroke.[3,4] Although several large trials previously showed no benefit of folate and/or B vitamins (B6 and B12) in reducing cardiovascular events,[4] reanalysis of data from one of them (the VISP trial) showed there was a 34% reduction in stroke/myocardial infarction events over 2 years when patients with impaired renal function were excluded.[5] Subsequent studies using folate supplementation of enalapril in the China Stroke Primary Prevention trial and folate, B6, and low dose B12 in the Su.Fol.M3 trial also showed beneficial stroke prevention effects.[6,7]Almost all clinical studies for stroke prevention by B12 to date were conducted with cyanocobalamin. Dr. Spence has argued that the use of cyanocobalamin in individuals with renal impairment may have obscured the benefit of B vitamins in stroke prevention in earlier studies,[2,3,5] since it possible that increased cyanocobalamin leads to harmful accumulation of cyanide and thiocyanate in patients with impaired renal function.[8]

While Dr. Spence's recommendation of methylcobalamin or hydroxycobalamin makes sense based upon current available clinical data, it is noteworthy that no clinical studies have directly compared these two compounds vs. cyanocobalamin for stroke prevention in individuals with normal and/or impaired renal function. Moreover, the relative efficacy of these B12 compounds and the generation of toxic metabolites in the context of liver disease has not been examined. Interestingly, Talari et al. recently treated individuals with NASH with 1,000 ug cyanocobalamin for 12 weeks in a randomized control trial and observed statistically significant decreases in serum homocysteine and alanine aminotransferase, and hepatic steatosis after treatment in the treatment group, but found no significant changes when compared to the placebo group.[9] Although this study suggested there might be beneficial results with cyanocobalamin, it is not clear whether the findings would have been more robust if patients were treated with either methylcobalamin or hydroxycobalamin. Thus, while it appears that cyanocobalamin may confound the assessment of stroke prevention in patients with renal failure, it is not known whether this is the case for NASH without direct comparisons or further study of the B12 compounds. However, Dr. Spence's caution on the use of particular B12 compounds in individuals with NASH is reasonable and needs to be considered, particularly if patients have concomitant renal impairment. Thus, in the absence of definitive data in individuals with NASH and renal failure, it still may be prudent to use methylcobalamin or hydroxycobalamin rather than cyanocobalamin for the treatment or prevention of NASH in clinical studies.

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Supplementary data

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