

Issue 89 In a nutshell

Marginal status of the B group vitamins B₁₂, folate and B₆ is common in the elderly and can result in elevated homocysteine levels.

It seems increasingly likely that these deficiencies can cause cognitive impairment. What remains to be shown is whether improving the vitamin and homocysteine levels reverses or prevents cognitive deficit.

Homocysteine & the elderly: cognition

Arbor Clinical Nutrition Updates 2001 (April);89:1-2
ISSN 1446-5450

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NUTRITION RESEARCH REVIEW

Study one: Homocysteine correlates with cognitive function

Serum homocysteine levels correlate with cognitive and psychosocial function in elderly patients according to the results of a recent Swedish study.

Subjects: Eighty psychogeriatric patients (average age 77 years) were compared with 50 controls (average age 76 years).

Method: Plasma homocysteine, blood folate, serum methylmalonic acid, and serum cobalamin (B₁₂) were measured, as well as several tests for cognitive and behavior performance. Regression analysis was performed on the results.

Results: Plasma homocysteine was elevated in 45% of the demented patients and the mean value was significantly higher in demented patients than in the controls (20.5 µmol/L vs 15.3 ± 4.7 µmol/L p <0.01).

In the demented patients, there was a significant correlation between plasma homocysteine levels and the severity of dementia (r = 0.36; p <0.01). There was also a significant correlation between the homocysteine levels and several measures of psychosocial performance (Katz ADL index r = 0.29 p <0.05, Berger scale r = 0.29 p <0.05, score of symptoms r = 0.39 p <0.001).

There were also significant correlations between these measures and blood folate levels, but not with serum cobalamin and methylmalonic acid. Stepwise multiple regression analysis involving all four biochemical values showed that plasma homocysteine was the only significant predictor of the severity of dementia (r² = 0.11 p <0.01) and of the score of symptoms (r² = 0.16 p <0.001).

Ref.: Nilsson K et al. The plasma homocysteine concentration is better than that of serum methylmalonic acid as a marker for sociopsychological performance in a psychogeriatric population. *Clinical Chemistry*. 2000;46:691-696

Study two: Homocysteine does not correlate with cognitive function

There is no independent relationship between measures of B₁₂ and folate status and cognitive functioning in the elderly, according to Italian researchers.

Subjects: 54 healthy subjects with normal mental function, aged 65 years and over.

Method: Blood tests were taken for serum B₁₂, folate and plasma homocysteine. A battery of neuropsychological tests were performed.

Results: 24% of the patients had elevated plasma homocysteine levels. Although vitamin B₁₂ levels were associated with both verbal memory and visuo-spatial skills, this relationship was no longer present once adjustment was made for confounding variables such as age, education etc.

Ref.: Ravaglia G et al. Blood homocysteine and vitamin B levels are not associated with cognitive skills in healthy normally ageing subjects. *J Nutr Health Aging*. 2000;4(4):218-22.

Study three: B12 supplements help cognition

Treatment with vitamin B₁₂ can help improve higher brain function in patients with cognitive impairment, according to English researchers.

Subjects: 125 patients seen at a memory disorders clinic who were found to have low serum B12. Of these, 66 had dementia and 22 cognitive impairment, based on neuropsychological testing.

Method: The patients with low B₁₂ were treated with B₁₂ supplementation. Their test scores were compared before and after treatment, and with age-matched control patients from the clinic.

Results: The majority of patients with low serum B₁₂ had normal blood pictures (MCV, Hb). The patients with cognitive impairment improved significantly in

test scores for the verbal fluency test ($p < 0.01$) after treatment, compared to matched control patients. There was no significant improvement in dementia patients after treatment.

Ref.: Eastley R et al. Vitamin B12 deficiency in dementia and cognitive impairment: the effects of treatment on neuropsychological function. *Int J Geriatr Psychiatry*. 2000;15: 226-33

Comments

Clinicians and nutritionists have been interested for some time in the tendency of elderly people to have a deficiency (or marginal status) of several B group vitamins - vitamin B₆, B₁₂ and folate - which are involved in common biochemical pathway which affects the blood homocysteine level.

The clinical consequences of deficiencies of these three vitamins have attracted a lot of attention over recent years. There is a known association of elevated homocysteine levels with ischaemic heart disease, but there is also great interest is whether these deficiencies are associated with other dysfunction, for example in relation to endothelial cells and in relation to the brain. One area where there has been a lot of research is in relation to dementia disorders, such as Alzheimer's disease.

It is a reasonable idea to speculate that there could be a relationship between these deficiencies and brain function, because brain metabolism involves the one-carbon pathway that these three vitamins are involved in. However, it has been hard to prove the clinical connection in practice. The kind of contradictory results that these three studies reveal are typical of the current status of research on this topic.

There is no doubt that elderly patients are inclined to be deficient in these B vitamins and that this is seen more often in cognitive-impaired patients. The prevalence depends to some degree on how carefully you measure them and in what setting (e.g. whether the patients are living at home, are hospitalised etc.) But it is certainly common enough to make it well worth routinely thinking about in our elderly patients. This is particularly true of those patients with impaired brain function.

Using ordinary serum B₁₂ levels, prevalence of deficiency of vitamin B₁₂ or folate is typically 15-20% in ambulatory elderly patients. Serum homocysteine and methylmalonic acid (MMA) are more sensitive measures of the biochemical pathway, and when these tests are used the

prevalence of deficiency rises - in the case of our first study to nearly 50%.

There are three main questions that need to be answered in this area of research:

1. What is the cause of the deficiencies - is it dietary, malabsorption or some other combination, and can it be easily corrected?
2. Do the deficiencies cause cognitive impairment, or is it the other way around (or neither) ?
3. Is it worth treating, and if so do you need to prescribe supplements, or can simple dietary change work just as well?

The cause of the deficiencies is almost certainly partly malabsorption (particularly in the case of vitamin B₁₂). But this does not mean that the clinician should ignore dietary factors and the effects of medication, particularly for folic acid. Studies have shown that folate status worsens shortly after institutionalisation (e.g. ¹) and many drugs affect it. Many intervention studies have also shown that it is not hard to correct the deficiencies with simple supplementation.

In relation to the second question, it seems increasingly likely that the deficiencies do cause some of the cognitive deficit. Where opinions differ is the third question - can treatment correct the brain function once deterioration has occurred?

Although the third study summarised here reports positive results, it was not a randomised, placebo controlled trial, and there other similar studies have not found a positive effect. Given the impact on the community of dementia in the elderly, it is perhaps surprising that no such large scale studies have been done. We hope they will be.

Next week, we will continue our discussion of these B vitamins in the elderly and look at some research on the role of dietary factors.

Ref.: 1. Essama-Tjani JC et al. Folate status worsens in recently institutionalized elderly people without evidence of functional deterioration. *J Am Coll Nutr* 2000 ;19(3):392-404

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