

EDITORIAL

Thiamine deficiency in elderly people

Thiamine (vitamin B1), as thiamine pyrophosphate (TPP), is an essential coenzyme in several important energy yielding reactions, including the transketolase reaction in the pentose phosphate pathway. Whole-grain cereals, beans and nuts are rich sources of thiamine. White bread and cereals are fortified with thiamine in many countries. Body storage is minimal. The daily requirement of thiamine is commonly linked to energy intake and expenditure; the current UK recommended nutrient intake for elderly people is 0.4 mg of thiamine per 1000 kcal [1]. Minimum needs may be markedly increased when there is raised metabolic demand (as in acute illness) or when absorption is reduced [2].

In the Western world, overt thiamine deficiency is usually associated with alcoholism. However, biochemical thiamine deficiency has often been found in elderly populations. The reported prevalence in the UK ranges from 8 to 31% for elderly people living at home, and from 23 to 40% for those in nursing homes [3–5]. Biochemical thiamine deficiency has also been reported in 48% of patients admitted to an acute geriatric unit [6].

Two questions arise from this high frequency of biochemical deficiency. First, can we rely on the methods used to measure thiamine levels? Secondly, what, if any, are the clinical implications of these findings?

Measurement of thiamine status

The traditional method of assessing thiamine deficiency was to measure the percentage increase in the erythrocytic activity of transketolase, a thiamine-dependent enzyme, after addition of TPP—the ‘TPP effect’. TPP effects of 15–24% and of $\geq 25\%$ usually indicate marginal and definite deficiency respectively. However, the TPP effect can be misleading in people with gross thiamine deficiency [7]. Since it is derived from two measurements of transketolase activity, the precision of the TPP effect is much lower than either measurement alone. Induced or inherited variants of transketolase are common [8]. This variation may contribute to differences in clinical susceptibility to the effects of thiamine deficiency, but it also complicates interpretation of transketolase levels and the TPP effect.

Direct measurement of erythrocyte TPP using high-performance liquid chromatographic techniques is now possible. The method is simple and precise,

and erythrocyte TPP levels are more sensitive to the development of dietary thiamine deficiency than transketolase levels or the TPP effect [9]. The study by Wilkinson *et al.* in the current issue of *Age and Ageing* is the first direct comparison of TPP levels in young and elderly subjects [10]. It confirms that thiamine levels are lower in older people, including those without major medical illness. Using the fifth percentile of the range in young (39–44 years) blood donors as a cut-off, the prevalence of biochemical thiamine deficiency was 45% in elderly people who were not taking vitamin supplements. Longitudinal data in a subset of the study population showed a 20% decline in TPP levels over 3 years. As the authors note, reduced dietary intake of thiamine in older people seems the most likely explanation. In New Zealand, where this study was carried out, as in the Republic of Ireland, where strikingly high levels of biochemical thiamine deficiency have also been reported [11], there is no policy of enriching foodstuffs with thiamine.

Clinical significance of biochemical thiamine deficiency

The major clinical manifestations of thiamine deficiency are heart failure and peripheral oedema (wet beriberi), peripheral neuropathy (dry beriberi) and acute (Korsakoff's syndrome) or chronic (Wernicke's syndrome) encephalopathy. Heart failure, peripheral neuropathy and cognitive impairment are common in elderly people. Although the classical thiamine-related syndromes are presumed to be rare in Western countries, they may be underdiagnosed, partly because the clinical features are not always clear cut and, in elderly people particularly, because thiamine deficiency may be a contributor rather than the sole cause of cardiac or neurological impairment. Also, there is evidence that subclinical thiamine deficiency may contribute to non-specific symptoms common in elderly patients, such as lassitude, impaired mobility and anorexia [11].

Thiamine deficiency and the heart

Although the original descriptions of cardiac beriberi emphasized the hyperdynamic circulation with marked peripheral vasodilatation and peripheral oedema, studies in Western populations indicate that these findings are often absent, and that the diagnosis

may be easily missed [12, 13]. A study from Wales reported five patients with severe thiamine-responsive heart failure presenting to a single team in a district general hospital over 11 months [13].

Overt thiamine-responsive heart failure is most common in alcoholic patients. However, animal studies have found that prolonged diuretic therapy can cause thiamine deficiency [14]. Seligmann *et al.* found thiamine deficiency (measured using the TPP effect) in 21 of 23 heart failure patients (mean age 70 years) receiving between 80 and 240 mg frusemide daily [15]. In a subsequent trial, left ventricular ejection fraction, one of the main predictors of mortality in heart failure patients, rose by 22% in patients randomized to intravenous followed by oral thiamine supplements [16]. However, subsequent studies have failed to confirm these findings, and, for the present, use of thiamine in general heart failure patients remains experimental [17, 18].

Thiamine deficiency and the central nervous system

Autopsy studies have consistently shown a higher incidence of Wernicke-Korsakoff syndrome than was recognized in life. In an Australian study, 131 cases (3%) were identified from 4700 brains examined over 9 years [19]. Although most occurred in known alcoholics, only 16% of cases had the clinical triad of mental signs, eye signs and ataxia. Isolated delirium was the most common feature in cases which were not diagnosed clinically before death.

Thiamine deficiency is associated with a diffuse decrease in cerebral glucose metabolism and in cholinergic neurotransmission, both important pathogenic mechanisms in the production of delirium. In a study of 36 patients admitted to an acute geriatric unit, delirium was present in 13 (76%) of 17 patients with thiamine deficiency (one of whom had a full Wernicke's syndrome) and six (31%) of 19 patients without thiamine deficiency [6]. However, although thiamine deficiency is common after surgery for hip fractures in elderly patients and was associated with post-operative confusion in one study [20], a double-blind controlled trial failed to show any beneficial effect for thiamine supplements given pre-operatively [21].

Difficulties with recent memory can be found after 8 weeks in young healthy subjects on a thiamine-deficient diet. It is likely that elderly people, even those without pre-existing dementia, would be more susceptible to cognitive effects of deprivation. There is a relationship in elderly subjects between thiamine status and electroencephalographic indices and neuropsychological performance [22, 23]; however, patient numbers in these studies were relatively small and many were deficient in several vitamins.

Several studies have reported an association

between thiamine deficiency in elderly subjects and loss of deep tendon reflexes in the legs and absent vibration sense below the knees [6, 10, 23].

Conclusion

Biochemical thiamine deficiency is common in elderly people. However, the clinical significance of this finding remains uncertain. Recent development of more reliable assays for measuring thiamine status may facilitate studies to resolve this important issue.

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References

1. Department of Health and Social Security. Dietary reference values for food energy and nutrients for the United Kingdom. Report on Health and Social Subjects, no. 41. London: HMSO, 1991.
2. Anderson SH, Vickery CA, Nicol AD. Adult thiamine requirements and the continuing need to fortify processed cereals. *Lancet* 1986; 2: 85-9.
3. O'Rourke NP, Bunker VW, Thomas AJ *et al.* Thiamine status of healthy and institutionalized elderly subjects. *Age Ageing* 1990; 19: 325-9.
4. Vir SC, Love AHG. Thiamine status of institutionalized and non-institutionalized aged. *Int J Vitam Nutr Res* 1977; 47: 325-35.
5. Griffiths LL, Brocklehurst JC, Scott DL *et al.* Thiamine and ascorbic acid levels in the elderly. *Gerontol Clin* 1967; 9: 1-10.
6. O'Keeffe S, Tormey WP, Glasgow R *et al.* Thiamine deficiency in elderly hospital patients. *Gerontology* 1994; 40: 18-24.
7. Nixon PF, Price J, Norman-Hicks M *et al.* The relationship between erythrocyte transketolase activity and the 'TPP effect' in Wernicke's encephalopathy and other thiamine deficiency states. *Clin Chim Acta* 1990; 192: 89-98.
8. Martin PR, McCool BA, Singleton CK. Genetic sensitivity to thiamine deficiency and development of alcoholic organic brain disease. *Alcohol Clin Exp Res* 1993; 17: 31-7.
9. Baines M, Davies G. The evaluation of erythrocyte thiamin diphosphate as an indicator of thiamin status in man, and its comparison with erythrocyte transketolase activity measurements. *Ann Clin Biochem* 1988; 25: 698-705.
10. Wilkinson TJ, Hanger HC, George PM *et al.* Is subclinical thiamine deficiency in the elderly related to age or comorbidity? *Age Ageing* 2000; 29: 111-6.
11. Smidt LJ, Cremin FM, Grivetti LE *et al.* Influence of thiamine supplementation on the health and general well-being of an elderly Irish population with marginal thiamine deficiency. *J Gerontol* 1991; 46: M16-22.
12. Ikram H, Maslowski AH, Smith BL *et al.* The haemodynamic, histopathological and hormonal features of alcoholic cardiac beriberi. *Quart J Med* 1981; 200: 359-75.
13. Anderson SH, Charles TJ, Nicol AD. Thiamine deficiency at a

district general hospital: report of five cases. *Quart J Med* 1985; 216: 15-32.

14. Yui Y, Itokawa Y, Kawai C. Furosemide-induced thiamine deficiency. *Cardiovasc Res* 1980; 14: 537-40.

15. Seligmann H, Halkin H, Rauchfleisch S *et al.* Thiamine deficiency in patients with congestive heart failure receiving long-term furosemide therapy. *Am J Med* 1991; 91: 151-5.

16. Shimon I, Almog S, Verad Z *et al.* Improved left ventricular function after thiamine supplementation in patients with congestive heart failure receiving long-term furosemide therapy. *Am J Med* 1995; 98: 485-90.

17. Kwok T, Falconer-Smith JF, Potter JF *et al.* Thiamine status of elderly patients with cardiac failure. *Age Ageing* 1992; 21: 67-71.

18. Leslie D, Gheorghiade M. Is there a role for thiamine

supplementation in the management of heart failure? *Am Heart J* 1996; 131: 1248-50.

19. Harper CG, Giles M, Finlay-Jones R. Clinical signs in the Wernicke-Korsatoff complex. *J Neurol Neurosurg Psychiatry* 1986; 49: 341-5.

20. Older MWJ, Dickerson JWT. Thiamine and the elderly orthopaedic patient. *Age Ageing* 1982; 11: 101-7.

21. Day JJ, Bayer AJ, McMahon M *et al.* Thiamine status, vitamin supplements and postoperative confusion. *Age Ageing* 1988; 17: 29-34.

22. La Rue A, Koehler KM, Wayne SJ *et al.* Nutritional status and cognitive functioning in a normally aging sample: a 6-year reassessment. *Am J Clin Nutr* 1997; 65: 20-9.

23. Tucker DM, Penland JG, Sandstead HH *et al.* Nutrition status and brain function in aging. *Am J Clin Nutr* 1990; 52: 93-102.