British Heart Foundation

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HOMOCYSTEINE

Homocysteine is a sulphur-containing amino acid produced by demethylation of dietary methionine, an essential amino acid. Rare genetic disorders of homocysteine metabolism are characterised by homocysteinuria and markedly elevated concentrations of homocysteine in plasma. These are associated with a high risk of thromboembolic events, including myocardial infarction and stroke in early adolescence or even in childhood.

In recent years it has become clear that moderately elevated plasma homocysteine concentrations are common in the general population. Moderate hyperhomocysteinaemia reflects less critical genetic defects and a deficiency of nutritional factors, specifically folic acid, vitamin B12 and possibly vitamin B6. There is now considerable evidence that moderate hyperhomocysteinaemia is associated with increased risk of vascular events, including coronary heart disease (CHD), stroke and venous thrombosis[1]. There are also preliminary data suggesting a link between hyperhomocysteinemia with cognitive decline in the elderly and with vascular and non-vascular dementia[2].

However, it must be emphasised that as yet most of the data on homocysteine and vascular disease are derived from cross-sectional and case control studies, both of which are susceptible to various biases and/or confounding. For example, elevated homocysteine levels are associated with declining renal function, male gender, increasing age and, to a variable degree, with other risk factors including cigarette smoking, hypertension, elevated cholesterol levels and lack of exercise. Data from prospective studies of homocysteine and CHD risk are inconsistent. Moreover, homozygosity for a defective thermolabile variant of MTHFR (a common genetic polymorphism that results in hyperohomocysteinemia) is not clearly linked with cardiovascular disease. It is possible therefore that elevated homocysteine levels are simply a marker for established risk and of an atherogenic diet, deficient in fruit and vegetables, B vitamins and other potentially cardio-protective nutrients.

Clinical and public health implications

Folate supplementation effectively lowers homocysteine levels, regardless of their origin[3]. Ultimately, the case for a causal role for elevated homocysteine concentrations will depend upon the outcome of randomised controlled trials of folate supplementation in the primary and secondary prevention of vascular disease. However, given the high prevalence of hyperhomocysteinemia in apparently well nourished populations and the tendency for concentrations to increase with age, quite modest effects on cardiovascular disease risk could have profound implications for both clinical practice and public health. Nevertheless until the results of randomised, controlled trials are available, folate supplementation is not recommended as a cardiac preventative measure in primary care. However, a diet containing folate rich foods e.g. green vegetables should be encouraged.

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Factfile *is produced by the British Heart Foundation in association with the British Cardiac Society and is compiled with the advice of a wide spectrum of doctors, including general practitioners. It reflects a consensus of opinion.*

References:

1) Hankley GJ, Eikelboom JW (1999) Homocysteine and vascular disease. The Lancet. 354:407-413.

2) Lehman M, Gottfries CG, Regland B (1999) Identification of cognitive impairment in the elderly. Dementia and geriatric cognitive disorders 10, 12-20.

3) Brattstrom L, Landgren F, Israelsson B et al (1998) Lowering blood homocysteine with folic acid-based supplements: meta-analysis of randomized trials. British Medical Journal 316, 894-895.