Homocysteine plasma levels correlate with intimal carotid artery thickness in haemodialysis patients

Sir,

Contradictory findings have recently been published, showing either a relation [1,2] or no relation [3] between plasma levels of homocysteine (Hcy) and vascular changes in dialysis patients. However, since Hcy accumulates in uraemic patients [4] and increased plasma Hcy levels are already present in the early stage of renal failure, a possible role for uraemia-associated hyperhomocysteinaemia (HHcy) should be considered. Recent data from a murine model of atherosclerosis showed that atherosclerotic lesions increased when mice were fed with a diet enriched in methionine but depleted in folate and vitamins B6 and B12 [5]. These changes were suppressed when diet was supplemented with folate and vitamins B6 and B12, implicating Hcy directly in atherosclerotic plaque progression.

In the present investigation, we evaluated whether plasma Hcy levels correlate with an index of generalized atherosclerosis (i.e. intimal wall thickness (IWT)) of the extracranial carotid artery (CA). We studied 85 patients (age 62.5 ± 14 years, range 22–78; dialysis duration 66.7 ± 53.4 months, range 12–238) who were on regular dialysis treatment (RDT) for at least 1 year. Patients with CA plaques were excluded. Standard bicarbonate dialysis was performed three times a week (180–270 min/session to achieve a Kt/V > 1.2). Plasma levels of total Hcy (including both homocysteine–homocysteine disulfide and mixed homocysteine–cysteine disulfide) were measured by automated high performance liquid chromatography with reversed-phase and fluorescence detection in venous blood collected from fasting patients just before the start of a dialysis session. Serum total cholesterol and triglycerides were measured by a Technicon Chem 1 assay. All patients underwent ultrasound examination (Acuson instrument, 7.5 MHz, Milan, Italy) to evaluate IWT-CA (measured 10 mm distal from common carotid artery). Data are presented as mean ± SD. Linear regression analysis was used to examine a possible relation between Hcy and other variables.

Plasma Hcy levels were increased in 71 out of 85 RDT patients (83.5%) RDT patients in comparison with the normal range 5–15 μmol/l. In RTD patients, IWT-CA (mm) averaged 0.68 ± 0.23 on the right and 0.65 ± 0.27 on the left side, overall 0.67 ± 0.25. Patients with plasma Hcy levels greater than 15 μmol/l also showed a thicker IWT echostucture than patients with plasma Hcy levels within the normal range (0.71 ± 0.09, n = 71 vs 0.57 ± 0.07, n = 14; P < 0.001). Linear regression analysis showed a significant positive relation between Hcy levels and mean IWT-CA (r = 0.74; P < 0.01) (Figure 1). IWT-CA was also correlated with age (r = 0.57; P < 0.03), dialysis duration (r = 0.48; P < 0.05), and systolic blood pressure (r = 0.63; P < 0.01). No significant correlation was found between IWT-CA thickness and plasma levels of cholesterol (r = 0.14) or triglycerides (r = 0.19).
Our results confirm that haemodialysis patients are prone to develop high Hcy plasma levels, probably due to the combination of reduced renal clearance and impaired Hcy catabolism [6]. The strong correlation between plasma Hcy, but not plasma lipids, and IWT-CA emphasizes the role of HHcy as a major risk factor for atherosclerosis in chronic haemodialysis patients. This might represent an incentive to administer to such patients a Hcy-lowering therapy.

Units of Nephrology and Vascular Surgery, University and IRCCS Policlinico San Matteo, Pavia and Division of Nephrology S. Maugeri, Pavia, Italy

Carmelo Libetta
Giuseppe Villa
Stefano Pirrelli
Vincenzo Sepe
Elena Gori
Manuela Zucchi
Antonio Dal Canton