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Homocysteine-lowering therapy does not affect inflammatory markers of atherosclerosis in patients with stable coronary artery disease

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Abstract

Objectives: A high level of total homocysteine (tHcy) is a risk marker for cardiovascular disease (CVD), and is related to inflammation. We wanted to test the effect of homocysteine-lowering B-vitamin therapy, as used in the Western Norway B-vitamin Intervention Trial (WENBIT), on inflammatory markers associated with atherosclerosis.

Design: Single centre, prospective double-blind clinical interventional study, randomised in a 2 · 2 factorial design. **Subjects and methods.** Ninety patients (21 female) with suspected coronary artery disease (CAD), aged 38– 80 years, were blindly randomised into one of four groups of daily oral treatment with (A) folic acid (0.8 mg)/vitamin B12 (0.4 mg)/vitamin B6 (40 mg), (B) folic acid/vitamin B12, (C) vitamin B6 alone or (D) placebo. Blood samples were collected before and after 6 months of treatment.

Results: Before intervention, median levels of the analytes were: tHcy 11.0 lmol L⁻¹, neopterin 8.1 nmol L⁻¹, soluble CD40 ligand (sCD40L) 3.9 ng mL⁻¹, interleukin (IL)-6 1.9 pg mL⁻¹, C-reactive protein (CRP) 1.9 mg L⁻¹ and low-density lipoprotein (LDL) cholesterol 3.3 mmol L⁻¹. tHcy was significantly associated with neopterin ($r \frac{1}{4} 0.49$, $P < 0.001$) and with IL-6 ($r \frac{1}{4} 0.29$, $P \frac{1}{4} 0.01$), but not with CRP or sCD40L. Neither treatment with folic acid/B12 nor with B6 induced significant changes in any of these inflammatory biomarkers ($P \frac{1}{4} 0.14$). In patients receiving folic acid/B12 (groups A and B), tHcy was reduced with 33% ($P < 0.001$).

Conclusions: In patients with stable CAD, homocysteine- lowering therapy with B-vitamins does not affect levels of inflammatory markers associated with atherogenesis. Failure to reverse inflammatory processes, may partly explain the negative results in clinical secondary B-vitamin intervention trials.

Keywords: atherosclerosis, B-vitamins, homocysteine, inflammation, neopterin, soluble CD40 ligand.