Abstract


Oral N-acetylcysteine reduces plasma homocysteine concentrations regardless of lipid or smoking status.

Hildebrandt W, Sauer R, Bonaterra G, Dugi KA, Edler L, Kinscherf R.

Departments of Immunochemistry and Department of Neurology, University Hospital Erlangen, Erlangen, Germany; Departments of Anatomy and Cell Biology III and Internal Medicine I, University of Heidelberg, Heidelberg, Germany; Biostatistics, Deutsches Krebsforschungszentrum, Heidelberg, Germany.

BACKGROUND: Elevated total plasma homocysteine (tHcy) is considered to be an independent cardiovascular disease risk factor, although tHcy lowering by B-vitamins improves only certain clinical endpoints. N-acetylcysteine (NAC), a thiol-containing antioxidant, acutely lowers tHcy and possibly also blood pressure. However, to our knowledge, at present no conclusive long-term evaluation exists that controls for factors such as hyperlipidemia, smoking, medication, and disease stage, all of which affect the thiol redox state, including tHcy.

OBJECTIVE: We reanalyzed 2 double-blind, placebo-controlled trials in unmedicated middle-aged men, one in a hyperlipidemic group (HYL group; n = 40) and one in a normolipidemic group (NOL group; n = 42), each stratified for smokers and nonsmokers.

DESIGN: We evaluated the effect of 4 wk of oral NAC (1.8 g/d) on tHcy (primary endpoint), plasma thiol (cysteine), and intracellular glutathione concentrations as well as on blood pressure. The HYL group had total cholesterol >220 mg/dL or triglycerides >150 mg/dL.

RESULTS: NAC treatment significantly (P = 0.001, multivariate analysis of variance for repeated measures) lowered post absorptive plasma concentrations of tHcy by -11.7% ± 3.0% (placebo: 4.1% ± 3.6%) while increasing those of cysteine by 28.1% ± 5.7% (placebo: 4.0% ± 3.4%) with no significant impact of hyperlipidemia or smoking. Moreover, NAC significantly decreased systolic (P = 0.003) and diastolic (P = 0.017) blood pressure within all subjects with a significant reduction in diastolic pressure in the HYL group (P = 0.006) but not in the NOL group. An explorative stepwise multiple regression analysis identified 1) post-treatment cysteine as well as 2) pretreatment tHcy and 3) albumin plasma concentrations as being significant contributors to tHcy reduction.

CONCLUSIONS: Four weeks of oral NAC treatment significantly decreased plasma tHcy concentrations, irrespective of lipid or smoking status, and lowered systolic blood pressure in both normolipidemic and hyperlipidemic men, with significant diastolic blood pressure reductions in the HYL group only. Increased oral intake of cysteine may therefore be considered for primary or secondary prevention of vascular events with regard to the 2 independent risk factors of hyperhomocysteinemia and arterial hypertension.

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