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Why homocysteine-lowering therapy does not have beneficial effects on patients with cardiovascular disease?

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Abstract

Homocysteine is a sulfur-containing amino acid produced during the metabolism of methionine and elevated plasma levels of homocysteine have been linked to an increased risk of atherosclerosis and cardiovascular ischemic events by numerous authors. Several mechanisms by which elevated homocysteine impairs vascular function have been proposed including impairment of endothelial function and at least some of those mechanisms are induced via homocysteine-associated DNA hypomethylation. Oral administration of folic acid and B vitamins, required for remethylation of homocysteine to methionine, decreased plasma total homocysteine levels but clinical trials using folic acid and B vitamins did not confirm that the decreased plasma levels of homocysteine through diet or drugs may be paralleled by a reduction in cardiovascular risk. In our view a plausible explanation for the discordance between the epidemiologic studies and the results of the clinical trials may be related to the homocysteine-associated global DNA hypomethylation which cannot easily be reversed by homocysteine-lowering therapy.

Author keywords

DNA hypomethylation; Homocysteine

Indexed Keywords

EMTREE drug terms: DNA methyltransferase ۱; DNA methyltransferase ۳A; DNA methyltransferase ۳B; folic acid; genomic DNA; homocysteine; methionine; vitamin B group

EMTREE medical terms: amino acid blood level; amino acid metabolism; article; atherosclerosis; cardiovascular disease; cardiovascular risk; clinical trial; diet therapy; DNA methylation; endothelium cell; enzyme activity; gene expression regulation; heart protection; high risk population; human; hyperhomocysteinemia; hypothesis; primary prevention; risk factor; risk reduction; upregulation

Chemicals and CAS Registry Numbers: folic acid, ۵۹-۳۰-۳, ۶۴۸۴-۸۹-۵; homocysteine, ۴۵۴-۲۸-۴, ۶۰۲۷-۱۳-۰; methionine, ۵۹-۵۱-۸, ۶۳-۶۸-۳, ۷۰۰۵-۱۸-۷; vitamin B group, ۱۲۰۰۱-۷۶-۲

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