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[Intervention Review]

Homocysteine-lowering interventions for preventing cardiovascular events

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ABSTRACT

Background

Cardiovascular disease (including coronary artery disease, stroke and congestive heart failure), is a leading cause of death worldwide. Homocysteine is an amino acid with biological functions in methionine metabolism. A postulated risk factor is elevated circulating total homocysteine levels, which are associated with cardiovascular events. This is an update of a review previously published in 2009.

Objectives

To assess the clinical effectiveness of homocysteine-lowering interventions in people with or without pre-existing cardiovascular disease.

Search methods

We searched The Cochrane Central Register of Controlled Trials (CENTRAL) on *The Cochrane Library* (2012, Issue 2), MEDLINE (1950 to Feb week 2 2012), EMBASE (1980 to 2012 week 07), and LILACS (1986 to February 2012). We also searched ISI Web of Science (1970 to February 2012). We handsearched the reference lists of included papers. We also contacted researchers in the field. There was no language restriction in the search.

Selection criteria

We included randomised controlled trials assessing the effects of homocysteine-lowering interventions for preventing cardiovascular events with a follow-up period of one year or longer. We considered myocardial infarction and stroke as the primary outcomes. We excluded studies in patients with end-stage renal disease.

Data collection and analysis

We performed study selection, 'Risk of bias' assessment and data extraction in duplicate. We estimated risk ratios (RR) for dichotomous outcomes. We measured statistical heterogeneity using I^2. We used a random-effects model.

Main results

In this updated systematic review, we identified four new randomised trials, resulting in a total of 12 randomised controlled trials involving 47,429 participants. In general terms, the trials had a low risk of bias. Homocysteine-lowering interventions compared with placebo did not significantly affect non-fatal or fatal myocardial infarction (pooled RR 1.02, 95% CI 0.95 to 1.10, I^2 = 0%), stroke (pooled RR 0.91, 95% CI

0.82 to 1.0, I^2 = 11%) or death by any cause (pooled RR 1.01 (95% CI 0.96 to 1.07, I^2: 6%)). Homocysteine-lowering interventions compared with placebo did not significantly affect serious adverse events (cancer) (1 RR 1.06, 95% CI 0.98 to 1.13; I^2 = 0%).

Authors' conclusions

This updated Cochrane review found no evidence to suggest that homocysteine-lowering interventions in the form of supplements of vitamins B6, B9 or B12 given alone or in combination should be used for preventing cardiovascular events. Furthermore, there is no evidence suggesting that homocysteine-lowering interventions are associated with an increased risk of cancer.

PLAIN LANGUAGE SUMMARY

B-complex vitamin therapy for preventing cardiovascular events

Cardiovascular disease is the number one cause of death worldwide. The most common causes of cardiovascular disease leading to both morbidity and mortality are ischaemic heart disease, stroke, and congestive heart failure. Many people with cardiovascular diseases may be asymptomatic, and may have a high risk for developing myocardial infarction, angina pectoris, stroke (ischaemic, haemorrhagic or both). 'Emergent or new risk factors' for cardiovascular disease have been recently added to the established risk factors (diabetes mellitus, high blood pressure, active smoker, adverse blood lipid profile). One of these risk factors is elevated circulating total homocysteine levels. Homocysteine is an amino acid, and its levels in blood are influenced by blood levels of B-complex vitamins: cyanocobalamin (B12), folic acid (B9) and pyridoxine (B6). High plasma total homocysteine levels are associated with an increased risk of atherosclerotic diseases. Hence, it has been suggested that B vitamin supplementation might reduce the risk of myocardial infarction, stroke, and angina pectoris. Preventive strategies might include healthy people with low or high risk for developing cardiovascular disease (primary prevention) and people with an established cardiovascular disease (secondary prevention). In this updated review, we included 12 randomised clinical trials involving 47,429 participants living in countries with or without mandatory fortification. We found no evidence that homocysteine-lowering interventions, in the form of supplements of vitamins B6, B9 or B12 given alone or in combination, at any dosage compared with placebo or standard care, prevent myocardial infarction, stroke, or reduce total mortality in participants at risk or with established cardiovascular disease. Homocysteine-lowering interventions compared with placebo did not significantly affect serious adverse events (cancer).