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Renal function determines response to B vitamin therapy for homocysteine

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Background: B vitamin therapy to lower homocysteine has been thought to be ineffective in reducing cardiovascular risk. However, interpretation of clinical trial results has not adequately taken account of the role of renal function.

Aim: To interpret clinical trial results in the light of new evidence that B vitamin therapy is harmful in patients with impaired renal function.

Methods: Contrasting beneficial effect of B vitamin therapy in the VISP efficacy analysis, from which patients with renal impairment were excluded, with those of the DIVINE study, in patients with diabetic nephropathy.

Results: In the VISP efficacy analysis, from which patients with GFR in the lowest 10% (<47) were excluded, along with those with B12 deficiency, B vitamins significantly reduced cardiovascular risk. In the DIVINE study in patients with diabetic nephropathy, B vitamins doubled the risk of cardiovascular events, among those with GFR<50.

Discussion and Conclusion: Increased production of asymmetric dimethylarginine, an antagonist of NO, and accumulation of cyanide from cyanocobalamin (leading to consumption of hydrogen sulfide (an endothelium-derived relaxing factor) may explain the harmful effects of B vitamins in renal failure. To lower tHcy in patients with renal failure it will be better to use methylcobalamin and more intensive dialysis; thiols such as mesna are also being studied in this group.

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