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Short Communication

Effect of Folic Acid for Lowering Plasma Homocysteine Levels on Cardiovascular Disease Prevention in Renal Transplant Recipients

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Abstract

Chronic kidney disease (CKD) patients have a high prevalence of obstructive cardiovascular disease (CVD), which may contribute to their high cardiovascular mortality. Plasma levels of homocysteine (Hcy) increased frequently in patients with CKD, even before they begin dialysis. Effects of immunosuppression and hyperhomocysteinemia associated with renal transplant (RTR) should be taken into account. Our findings indicate effect of folic acid for lowering plasma Hcy levels did not reduce CVD prevention in RTRs, however, could have a beneficial effect of the treatment on carotid intima-media thickness (CIMT). CIMT is a sensitive indicator of the atherosclerotic process Additional large, randomized studies should be performed and further resolve the uncertainty regarding the effect of folic acid supplementation on CVD outcomes.

Keywords: Folic acid; Homocysteine; Renal transplant recipient

Introduction

Chronic kidney disease (CKD) is associated with increased risk of coronary heart disease [1]. CKD patients have a high prevalence of obstructive cardiovascular disease(CVD), which may contribute to their high cardiovascular mortality [2]. Glomerular filtration rate (GFR) declines worsen the incidence and severity of obstructive CVD. Some studies suggest that this incidence exceeds 50% in unselected dialysis-dependent CKD stage 5 patients, including hemodialysis and peritoneal dialysis; equivalent to end-stage renal disease [3].

Atherosclerosis is a manifestation of the pathophysiology underlying CVD and positively associated with a number of factors. Insulin resistance, inflammation and oxidative stress have been warranted to establish to the pathogenesis of plaque formation and plaque rupture; they are associated with worse cardiovascular events and mortality [4-5]. Circulating endothelial cell biology may play a major role in the pathogenesis of vascular disease by an effect on both endothelial injury and the capacity for endothelial repair. The dysfunction is a strict association between the clinical phase of atherosclerosis and early disease [6].

Plasma levels of homocysteine (Hcy) increased frequently in patients with CKD, even before they begin dialysis [7]. Effects of immunosuppression and hyperhomocysteinemia associated with renal transplant recipient (RTR) should be taken into account. The possible reason may be a state of relative vitamin B complex deficiency where folic acid supplementation as cofactors in the process of remethylation and transsulfuration of homocysteine [8].

Study Collection

We searched the MEDLINE database (via Pub Med) from January, 1966 to May, 2015, with the MeSH terms “folic acid” or “folate” and “kidney transplant recipient” or “renal transplant recipient”. The searches were restricted to human studies and clinical trials. We restricted our review to randomized clinical trials. There were no language restrictions.

Results and Discussion

Upon screening the title, reading the abstract and the entire article, only four RCTs, involving 7399 patients, were included.

In a double-blind controlled trial, 7273 patients were screened, of whom 2056 and 2054 were randomized to high-dose and low-dose multivitamins of folic acid, vitamin B6, and vitamin B12over about a 4-year period. Primary arteriosclerotic cardiovascular disease outcome included myocardial infarction, stroke, cardiovascular disease death, resuscitated sudden death, coronary artery or renal artery revascularization, lower-extremity arterial disease, carotid end arterectomy or angioplasty, or abdominal aortic aneurysm repair. Treatment with a high-dose multivitamin in RTRs significantly reduced Hcy level, but did not reduce CVD outcomes or total mortality [9].

There were three effect of folic acid for lowering plasma Hcy levels about carotid intima-media thickness (CIMT) trials in RTRs. Sixty patients who had undergone a RTR were studied in this double-blind, randomized, placebo-controlled clinical trial. Those participants were randomized to receive of folic acid (5 mg/d) alone. Folic acid supplementation reduced both the plasma total Hcy level and CIMT [10]. CIMT is an intermediate phenotype for the progression of atherosclerosis. Vascular disease begins with endothelial injury, a sensitive indicator of the atherosclerotic process, occurring before the clinical outcomes of CVD.

In addition, another study demonstrated daily administration of folic acid, vitamin B6, and vitamin B12 to patient’s with 56 stable hyperhomocysteinemic RTRs or placebo treatment for 6 months. They also demonstrated a beneficial effect of the treatment of

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hyperhomocysteinemia by multivitamin supplementation on CIMT in a group of RTRs [11].

A double-blind, placebo-controlled crossover study was conducted in 10 CsA-treated RTRs. Three months of folate supplementation decreases plasma Hcy but has no effect on endothelial function or CIMT in RTRs [12].

Consistent with these studies, folic acid supplementation was associated with a significant decrease in CIMT compared with the control group in three small trials. It is an argument that folic acid for lowering plasma Hcy levels in this population may have affected the CVD lowering effect.

Conclusion

Our findings indicate effect of folic acid for lowering plasma Hcy levels did not reduce CVD prevention in RTRs, however, could have a beneficial effect of the treatment on CIMT.CIMT is a sensitive indicator of the atherosclerotic process. Additional large, randomized studies should be performed and further resolve the uncertainty regarding the effect of folic acid supplementation on CVD outcomes.

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