

## **Oral folate reduces plasma homocyst(e)ine levels in hemodialysis patients with cardiovascular disease.**

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**INTRODUCTION:** Hyperhomocyst(e)inemia (plasma homocyst(e)ine concentration  $>16.0$  micromol/l) is an independent risk factor for atherosclerosis, and is ubiquitous in patients with end-stage renal disease (ESRD). Oral folate supplementation in the non-ESRD population has been demonstrated to reduce plasma homocyst(e)ine (Hcy) concentration, and may reduce atherosclerotic morbidity. This study was undertaken to evaluate the efficacy of folate supplementation in reducing Hcy in patients with ESRD and cardiovascular disease.

**METHODS:** Twenty-eight chronic hemodialysis patients with demonstrated hyperhomocyst(e)inemia (mean Hcy  $35.2 \pm 13.3$  micromol/l) were enrolled in the study. The presence of atherosclerosis was documented by history, physical examination, or ultrasonographic criteria. Hcy was determined initially and following six weeks' supplementation with 5.0mg folate and multivitamins.

**RESULTS:** Hcy fell a mean of  $15.0 \pm 10.4$  micromol/l ( $38.9 \pm 19.9\%$ ) following supplementation ( $p < 0.0005$ , paired  $t$ test). In patients whose Hcy 'normalized' ( $n=10$ ) Hcy fell a mean of  $51 \pm 14\%$  compared to a reduction of  $32 \pm 20\%$  in 18 patients whose Hcy remained  $>16.0$  micromol/l ( $p=0.02$ ). A significant positive correlation was observed between initial Hcy and both absolute and percent reduction after folate supplementation ( $r=0.87$ ,  $p < 0.005$  and  $0.53$ ,  $p < 0.005$ , respectively). Seven patients with documented atherosclerosis were older ( $68 \pm 8$  yr vs  $51 \pm 5$  yr,  $p=0.007$ ) and tended to have lower initial and final Hcy than the 21 patients without atherosclerosis ( $26.8 \pm 9.9$  vs.  $38.0 \pm 13.3$  micromol/l,  $p=0.051$  and  $16.5 \pm 5.0$  vs.  $21.3 \pm 6.7$ ,  $p=0.06$ , respectively). The presence of atherosclerosis was not associated with significant alteration in the response to folate.

**CONCLUSIONS:** Supplementation with high-dose folate significantly reduces plasma Hcy in patients with and without atherosclerosis, and the presence of atherosclerosis does not impact on patients' response to folate and multivitamin supplementation. Hcy remained  $>16.0$  micromol/l in the majority of patients, however, despite large absolute reductions in Hcy. Doses of folate greater than

5mg, or additional therapy may be required to further reduce Hcy in the majority of ESRD patients