

# **Folic Acid Supplementation and Target Organs Protection in Hypertensive Population**

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High plasma homocysteine is a risk factor for mortality and vascular disease in observational studies. Folic acid and B vitamins decrease the homocysteine levels. However, uncertainty remains about the efficacy of folic acid supplementation for the primary prevention of stroke due to limited and inconsistent data.

In the China Stroke Primary Prevention Trial (CSPPT), a double-blind, randomized, controlled trial conducted in China, a total of 20,702 hypertensive adults without history of stroke or myocardial infarction (MI) were randomly assigned to daily treatment with enalapril 10mg and folic acid 0.8mg (in a single pill, n=10,348) or enalapril 10mg alone (n=10,354) for median of 4.5 years. Compared to the enalapril group, enalapril and folic acid treatment significantly reduced the risk of first stroke [absolute risk reduction=0.7%; hazard ratio (HR)=0.79, 95%CI:

0.68-0.93]; the first ischemic stroke (absolute risk reduction=0.6%; HR=0.76; 95%CI: 0.64-0.91), and the composite cardiovascular events consisting of cardiovascular death, MI and stroke (absolute risk reduction=0.8%; HR=0.80; 95% CI: 0.69-0.92). There were no significant differences between the two treatment groups in terms of the frequencies of adverse events.

To test whether folic acid supplementation slow down renal function decline in patients with hypertensive chronic kidney disease, CSPPT Renal Sub-Study, a randomized controlled trial, was conducted in 1474 hypertensive patients who had chronic kidney disease at baseline. Treatment with enalapril and folic acid reduce the risk of primary endpoint (serum creatinine increase  $\geq 50\%$  or need for dialysis) by 64% (OR=0.36; 95% CI: 0.20-0.62, P=0.002) as compared with enalapril alone (OR=0.94; 95% CI: 0.73-1.20). Enalapril and folic acid treatment also reduced the risk of composite outcomes of primary endpoint and death.

These results suggest that folic acid supplementation may reduce the risk of first stroke and loss of renal function in regions without folic acid fortification.