

# Abstract

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## High-dose folic acid supplementation effects on endothelial function and blood pressure in hypertensive patients: a meta-analysis of randomized controlled clinical trials

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**OBJECTIVE:** Folic acid supplementation has been shown to be an effective agent for improving endothelial function, a prognostic factor for cardiovascular disease; but its effects on systolic and diastolic blood pressure in hypertensive individuals has been met with mixed results. Therefore, the purpose of this study was to provide a comprehensive meta-analysis of randomized controlled trials to investigate the effect of high-dose folic acid supplementation on blood pressure and endothelial function in hypertensive patients.

**METHODS:** Twelve randomized controlled trials published between 1970 and December 2007 were identified using Medline and a manual search. All 12 studies used hypertensive subjects who were supplemented with at least 5000  $\mu\text{g}/\text{d}$  of folic acid for between 2 and 16 weeks. Three separate meta-analyses were carried out using a random-effects model, and the overall effect sizes were calculated for changes in systolic and diastolic blood pressures and for changes in endothelial function as measured through the percentage of change in flow-mediated dilation.

**RESULTS:** The pooled estimate of effect of folic acid supplementation on systolic and diastolic blood pressure was  $-2.03$  mm Hg (95% confidence interval [CI],  $-3.63$  to  $-0.43$ ;  $P = .04$ ) and  $0.01$  mm Hg (95% CI,  $-1.12$  to  $1.13$ ; not significant), respectively. The pooled estimate of effect of folic acid supplementation on change in flow-mediated dilation was  $1.61\%$  (95% CI,  $1.27$  to  $1.96$ ;  $P = .000$ ).

**CONCLUSION:** Based upon the studies used in this meta-analysis, supplementation with at least 5000  $\mu\text{g}/\text{d}$  of folic acid, for a minimum of 6 weeks, can lower systolic blood pressure slightly; but the real clinical benefit is achieved through improved endothelial function.

