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RESEARCH NEWS

Folic acid significantly reduces risk of first stroke, large Chinese study finds

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The use of folic acid for the primary prevention of stroke, particularly among populations with low folate levels, is supported by a large randomised controlled trial reported in *JAMA*.

The China Stroke Primary Prevention Trial included 20 702 adults with high blood pressure but without a history of stroke or heart attack.[1] They were randomly assigned to receive daily treatment with 10 mg of the angiotensin converting enzyme (ACE) inhibitor enalapril and 0.8 mg folic acid or to enalapril alone.

The trial was terminated early, after 4.5 years, because of the emergence of a significant reduction in the incidence of first stroke among the group that received the combination of folic acid and enalapril. The study recorded 282 stroke events (2.7%) in the folic acid/enalapril group and 355 events (3.4%) in the enalapril only group. This represents an absolute risk reduction of 0.7% and a relative risk reduction of 21% (hazard ratio 0.79 (95% confidence interval 0.68 to 0.93)).

The study was the first large randomised trial to measure individual baseline folate levels. The benefit was most pronounced in the subgroup that had the lowest baseline levels of plasma folate (below 5.6 ng/mL): the rate of first stroke was 2.8% (73 events among 2600 participants) in the enalapril/folic acid group, compared with 4.6% (116 events among 2548 participants) in the enalapril only group (0.61 (0.45 to 0.82)).

The researchers also found that the participants taking folic acid and enalapril had a significantly reduced risk of ischaemic stroke (2.2 % *v* 2.8%) and of composite cardiovascular events (3.1% *v* 3.9%). No significant difference was found between groups in the risk of haemorrhagic stroke, heart attack, or all cause death or in the frequency of adverse events.

Stroke is the leading cause of death in China and the second leading cause of death in the world. Ideally, adequate folate levels would be achieved from food sources such as dark green leafy vegetables, fruits, nuts, beans, and peas, but many populations find it hard to achieve this from diet alone because of expense or availability. Some countries, such as the United States, fortify foods with folic acid to reduce the incidence of neural tube defects, but these countries still have subgroups with inadequate folate levels.

In an accompanying editorial Meir Stampfer and Walter Willett, of the Harvard T H Chan School of Public Health in Boston, USA, wrote that the trial had important implications for stroke prevention worldwide. “Large segments of the world’s population, potentially billions of people, including those living in northern China, Bangladesh, and Scandinavia, have low levels of folate,” they noted, adding, “This study seems to support fortification programs where feasible, and supplementation should be considered where fortification will take more time to implement.”

1 Huo Y, Li J, Qin X, et al; CSPPT Investigators. Efficacy of folic acid therapy in primary prevention of stroke among adults with hypertension in China: the CSPPT randomized clinical trial. *JAMA* March 2015; doi:10.1001/jama.2015.2274.

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