## Editorial

## **Does vitamin E play a role in the primary prevention** of stroke?

## Adi Hidayat

Department of Community Medicine, Medical Faculty, Trisakti University

A few decades ago it was generally accepted from experimental studies, animal experiments, and epidemiological cohort studies that atherogenesis is linked to oxidative stress and that antioxidant supplementation, notably vitamin E supplementation, is associated with a low incidence of cardiovascular disease (CVD). This view led to the widespread use of vitamin E and other antioxidants for reducing CVD morbidity and mortality. In vitro and animal studies on antioxidant and anti-inflammatory properties of alpha- and gamma-tocopherols also found that these antioxidants had anti-inflammatory properties.<sup>(1-3)</sup>

However, many large-scale prospective randomized trials failed to find beneficial effects of high dose vitamin E supplementation either to healthy persons or to CVD patients.<sup>(4,5)</sup> Recent meta-analytical studies concluded that vitamin E supplementation results in increased mortality.<sup>(5)</sup> Although this conclusion has been much criticized, a decision analysis using Markov modeling on the same data also found that indiscriminate supplementation of high doses of vitamin E is not beneficial in preventing CVD.<sup>(6)</sup>

In contrast, available evidence indicates that vitamin E may have beneficial effects on stroke. One study reported a significant inverse association between stroke mortality and dietary vitamin E intake (RR from lowest to highest fifth of intake, 1.0, 0.80, 0.93, 0.67, and 0.40; P for trend < 0.008) in women with a mean age of 61 years.<sup>(7)</sup> A meta-analysis of 9 randomized controlled trials on the effect of vitamin E on incident stroke found a differential effect on stroke subtypes, as vitamin E supplementation resulted in a 10% decrease in risk of ischemic stroke, but increased the risk of hemorrhagic stroke by 22%. This differential effect may be due the different mechanisms underlying ischemic and hemorrhagic events.<sup>(8)</sup> These opposing effects of vitamin E on stroke subtypes should be clarified previous to issuing public health recommendations on the use of vitamin E in potential stroke patients.<sup>(7)</sup>

In absolute terms, the reduction in ischemic stroke events by vitamin E is relatively small. Actually, considerably lower ischemic stroke risks may be produced by other preventive measures, such as healthy lifestyle, low body mass index, moderate alcohol consumption, abstinence from smoking, regular physical activity, and healthy diet. In this setting, vitamin E supplements may not lead to further risk reduction. The use of vitamin E for primary prevention of hemorrhagic stroke should ideally be under regular medical supervision, since this subtype of stroke carries a higher morbidity and mortality, while vitamin E in high doses may increase all cause mortality.<sup>(8)</sup> The best alternative to vitamin E as a primary preventive measure against stroke, especially ischemic stroke, seems to be the adoption a low-risk lifestyle by healthy individuals, who at the same time will be achieving a state of long-term well-being.

## REFERENCES

- 1. Jiang Q, Ames BN. Gamma-tocopherol, but not alpha-tocopherol, decreases proinflammatory eicosanoids and inflammation damage in rats. FASEB J 2003;17:816–22.
- 2. Singh U, Jialal I. Anti-inflammatory effects of alpha-tocopherol. Ann N Y Acad Sci 2004;1031:195-203.
- 3. Young IS, Woodside JV. Antioxidants in health and disease. J Clin Pathol 2001;54:176–86.
- 4. Cook NR, Albert CM, Gaziano JM, Zaharris E, MacFadyen J, Danielson E, et al. A randomized factorial trial of vitamins C and E and beta carotene in the secondary prevention of cardiovascular events in women: results from the Women's Antioxidant Cardiovascular Study. Arch Intern Med 2007;167:1610-8.
- 5. Miller ER, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. Ann Intern Med 2005;142:37-46.
- 6. Dotan Y, Pinchuk I, Lichtenberg D, Leshno M. Decision analysis supports the paradigm that indiscriminate supplementation of vitamin E does more harm than good. Arterioscler Thromb Vasc Biol 2009;29:1304-9.
- 7. Donnan GA, Fisher M, Macleod M, Davis SM. Stroke. Lancet 2008;371:1612-23.
- 8. Schürks M, Glynn RJ, Rist PM, Tzourio C, Kurth T.Effects of vitamin E on stroke subtypes: metaanalysis of randomised controlled trials. BMJ 2010;341:c5702 doi:10.1136/bmj.c5702.