

## Issue 83

### In a nutshell

Results from the different arms of the large ATBC study give different perspectives on whether vitamin E supplementation increases or decreases the risk of stroke.

More data is needed before we can be sure whether some patients, (e.g. hypertensives) are at greater risk of subarachnoid bleeding from taking vitamin E, although it may also protect against some strokes.

## Vitamin E and stroke

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## NUTRITION RESEARCH REVIEW

Should vitamin E be given to prevent stroke in high risk patients, or will it only increase the likelihood of bleeding in the brain?

### Studies: Vitamin E supplements and stroke

Prior dietary intake of Vitamin E does not lower the incidence of ischaemic stroke in high risk men, but vitamin E supplementation does. This is especially true if the person also has high blood pressure.

These conclusions come from a series of recently published results which are all from the Alpha-Tocopherol, Beta-Carotene (ATBC) Cancer Prevention Study conducted in Finland in the 1990's. In this issue we deal with the results as published in three separate articles

**Subjects:** Male smokers, none of whom had had a previous stroke:

- a) Observational study: 28,519 subjects.
- b) Intervention trial: 28,519 subjects.

### Method:

- a) Observational study: At baseline the subjects completed a dietary questionnaire and were observed for 6.1 years.
- b) Intervention trial: Subjects were randomised in a double-blind, placebo-controlled 2x2 factorial design trial to be given supplements of either alpha-tocopherol (50 mg), beta-carotene (20 mg), both vitamins, or placebo. They were then monitored for a median follow-up of 6 years.

### Results:

- a) Observational study: There was no association between vitamin E intake and the risk of having a stroke.
- b) Intervention trial: Vitamin E supplementation increased the risk of subarachnoid hemorrhage by 50% (95% CI: -3% to 132%, P=0.07) but decreased the risk of cerebral infarction by 14% ((95% CI -25% to -1%, P=0.03).

When the results were analysed in just the hypertensive men, there was a similar pattern but of greater degree. See Table. There was no effect in normotensive men.

If these hypertensive men also had diabetes, there was an greater reduction in the risk of cerebral infarction associated with taking vitamin-E supplements (RR=0.33; 95% CI:0.14-0.78).

**Table: Relative risk of stroke in hypertensives after vitamin E supplementation**

	Rel.risk
Subarachnoid hemorrhage (95% CI)	2.45 (1.08-5.55)
Cerebral infarction (95% CI)	0.70 (0.55-0.89)

(References for these studies shown on the next page)

References:

a) Hirvonen T et al. Intake of flavonoids, carotenoids, vitamins C and E, and risk of stroke in male smokers. *Stroke* 2000;31: 2301-6

b) Leppala JM et al. Vitamin E and beta carotene supplementation in high risk for stroke: a subgroup analysis of the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Arch Neurol* 2000; 57:1503-1509  
*and*

Leppala JM et al. Controlled trial of alpha-tocopherol and beta-carotene supplements on stroke incidence and mortality in male smokers. *Arterioscler Thromb Vasc Biol* 2000;20:230-5

## Comments

These results add to an already interesting but still unclear picture.

Previous epidemiological studies have not come up with any consistent answer on whether there is a relationship between intake of antioxidant vitamins - including vitamin E - and stroke.

Although the data summarised above are based on a large number of subjects, we still have to be cautious about what to recommend to patients. There was certainly clear evidence of a negative impact of vitamin E supplementation on subarachnoid bleeding, but also of a positive impact on cerebral infarction. These impacts were seen in hypertensive but not in normotensive patients.

So this is clearly not an area where the physician can as yet give their high risk patients clear-cut advice with complete confidence. The higher incidence of bleeding observed in the ATBC intervention is sobering, particularly considering that many of these high risk patients may already have been prescribed aspirin. A previous research paper has described a higher level of

gum bleeding in those patients taking both aspirin and vitamin E <sup>1</sup>.

On the other hand, laboratory studies suggest that antioxidant vitamins, including vitamin E, may protect brain cells against the damage that ischaemic or infarction can cause (e.g. <sup>2</sup>).

So we have no choice but to await further clinical trials. Those patients who opt to take vitamin E in the meanwhile are doing so at their own risk.

References:

1. Liede KE et al. Increased tendency towards gingival bleeding caused by joint effect of alpha-tocopherol supplementation and acetylsalicylic acid. *Ann Med* 1998;30:542-6

2. Tagami M et al. Vitamin E prevents apoptosis in hippocampal neurons caused by cerebral ischemia and reperfusion in stroke-prone spontaneously hypertensive rats. *Lab Invest* 1999;79: 609-15

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