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PROSTATE CANCER

Vitamin E and prostate cancer—what is the real risk?

Follow-up results of the Selenium and Vitamin E Cancer Prevention Trial (SELECT) have been published, sparking widespread controversy. Previous studies in long-term smokers hinted at protective roles for selenium and vitamin E against prostate cancer, and experts hypothesized that these micronutrients might act synergistically to inhibit carcinogenesis.

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At the turn of this century, researchers were eagerly anticipating a large RCT to test this theory. From 2001 to 2004, 34,887 healthy men (aged >50 years) were randomized to receive either vitamin E (α-tocopherol), selenium, both supplements or placebo. After 3 years, treatment was discontinued due to a lack of clear benefit, but follow-up continued.

At final analysis in July 2011, prostate cancer detection rates were higher in all active treatment groups than in placebo, although this increase was only statistically significant in patients receiving vitamin E alone (7% versus 6% incidence). The addition of selenium to vitamin E reduced prostate cancer risk, suggesting that selenium sequesters vitamin E away from its sites of action.

One criticism of SELECT is that it only assessed the effects of one vitamin isoform. Although α-tocopherol is the major form found in supplements, γ-tocopherol is more common in the US diet. The γ form is a more potent antioxidant and might thereby provide greater protection against the oxidative stress that accompanies prostate carcinogenesis.

Another study—the CLUE II trial—found a significant (5-fold) protective effect of vitamin E against prostate cancer, but only for the γ isoform. As α-tocopherol supplementation reduces plasma and tissue γ-tocopherol levels, it is possible that α-tocopherol increases cancer risk via this mechanism—explaining the SELECT data.

Another issue under debate is the dose administered. Although the SELECT results have raised concerns regarding the risks associated with taking multivitamins, the high dose of vitamin E used in the study means that these worries are largely unjustified. “The dose of vitamin E used in SELECT (400 IU) far exceeds that contained in most multivitamins (usually 15–25 IU),” says lead researcher Eric Klein.

However, it is becoming clear that very high doses of micronutrients are probably not good for us. According to Klein, “There is no compelling evidence that high-dose supplements make people live longer or prevent any important diseases and there is evidence that these can be harmful—I would not advise their use.”

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Original article Klein, E. A. *et al*. Vitamin E and the risk of prostate cancer. *JAMA* doi:10.1001/jama.2011.1437