

Direction of the Evidence

What popular mineral supplement is likely to be harmful to your patients' health?

By Ron Feise, DC

Lippman SM, Klein EA, Goodman PJ, Lucia MS, et al. Effect of selenium and vitamin E on risk of prostate cancer and other cancers: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). *JAMA* 2009; 301:39-51.

Synopsis. This was a randomized, placebo-controlled trial to determine whether selenium, vitamin E, or both could prevent prostate cancer and other diseases with little or no toxicity in relatively healthy men. Over 35,000 men from 427 participating sites in the United States, Canada, and Puerto Rico were randomly assigned to 4 groups (selenium, vitamin E, selenium + vitamin E, and placebo) in a double-blind fashion. Tested interventions were oral selenium (200 microg/d from L-selenomethionine) and vitamin E (400 IU/d of all rac-alpha-tocopheryl acetate).

The overall follow-up was 5 years. There were no statistically significant differences in the rates of prostate cancer among the 4 groups: placebo, 416 cases; selenium, 432 cases; vitamin E, 473 cases; selenium + vitamin E, 437 cases. Hazard ratios for prostate cancer were 1.13 for vitamin E, 1.04 for selenium, and 1.05 for selenium + vitamin E vs. 1.00 for placebo. There were statisti-

cally non-significant increased risks of prostate cancer in the vitamin E group and type 2 diabetes mellitus in the selenium group.

Research Quality. Overall, this study had reasonable methodological rigor.

Quality Details. This study used the following: 1) appropriate design; 2) clearly stated inclusion and exclusion criteria; 3) randomization assignment; 4) treatment methods described; 5) valid, reliable, and relevant outcome measures; 6) suitable measurement period; 7) acceptable sample size; 8) groups clinically similar at the start of the trial; 9) acceptable loss to follow-up; and 10) intention-to-treat analysis.

Conclusion. Neither selenium nor vitamin E, alone or in combination at the doses and formulations used, prevented prostate cancer in this population of relatively healthy men.

Comment. Previous research supports the findings of this most recent study. Lawson et al. examined the relationship between the use of multivitamins containing selenium and the risk of prostate cancer.¹ The study investigated 295,344 men with a mean age of 62 years who were cancer free at enrollment. The researchers discovered that persons taking

high levels of multivitamins containing selenium have increased risks of advanced and fatal prostate cancers. In another study, an international medical research team reported in *Annals of Internal Medicine* that selenium supplements are likely to increase the risk for diabetes.² In this randomized, double-blind, placebo-controlled trial, 1,202 participants were given either oral selenium or placebo. During a follow-up of over 7 years, type 2 diabetes developed in 58 selenium recipients but in only 39 placebo recipients. Another study investigated selenium for the prevention of cardiovascular disease. In this randomized, double-blind, placebo-controlled trial, over 1,000 subjects were given either oral selenium or placebo.³ This research team found no overall effect of selenium with any of the cardiovascular disease endpoints.

Selenium supplementation might be beneficial in certain populations, like those with HIV or those with severe gastrointestinal problems, such as Crohn's disease. Additionally, selenium supplementation may be beneficial in regions of the world where diets are low in selenium, such as China. But there is no evidence of selenium deficiency in the United

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States. Thus, selenium supplementation is a real public health concern. More than 1% of the U.S. population takes selenium supplements, and more than 35% takes multivitamin and multi-mineral supplements that often contain selenium.

In light of information that selenium may be associated with increased health risks, caution is recommended. Selenium supplementation should be viewed as having uncertain and possibly toxic effects.^{4,5} Overt symptoms of acute and chronic selenium toxicity include brittleness and loss of hair and nails, fatigue, neurologic damage, hepatic de-

generation, gastrointestinal disturbances, enlarged spleen, and chronic dermatitis.⁵

Warning. Practitioners should not automatically use information from research studies (especially abstracts) to make decisions about patient care. Health care literature suffers from inconsistent quality and frequently distorts research findings. Before relying on the findings of a research study, a practitioner should perform a critical appraisal to determine whether the conclusion is supported by the study's data. He or she should also locate and examine previous relevant research to integrate the current findings and form a conclusion

based upon the preponderance of quality evidence. Even conclusions from multiple studies do not provide a definitive answer. Rather, they indicate the *direction* of the evidence. ■

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