News and Views From the Literature

Prostate Cancer

Randomized Trials of Selenium, Vitamin E, or Vitamin C for Prostate Cancer Prevention

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The use of vitamins and supplements is extremely common among the US population. In the 1999-2000 National Health and Nutrition Examination Survey (NHANES), 52% of adults reported use of a dietary supplement within the past month.[1] Numerous lifestyle and demographic factors have been associated with the likelihood of supplement use, including gender, age, dietary habits, education level, physical activity, and body mass index.[2] Among participants from the Prostate Cancer Prevention Trial, 85% reported using at least 1 dietary supplement.[3] Other studies have similarly reported that men with prostate cancer represent a specific subpopulation with a greater than average history of supplement use.[4] In this study, the most common supplements used were multivitamins, vitamin E, and vitamin C.[4]

Interestingly, several prior studies suggested that both selenium and vitamin E were associated with a reduction in prostate cancer risk. For example, the α-Tocopherol, β-Carotene Cancer Prevention (ATBC) study randomized 29,133 Finnish male smokers to α-tocopherol, β-carotene, both, or placebo.[5] The incidence rate of prostate cancer was significantly lower in participants who received α-tocopherol, compared with those who did not. In the Nutritional Prevention of Cancer (NPC) randomized trial, selenized yeast supplementation was associated with a substantial reduction in prostate cancer risk (relative risk [RR] 0.51; 95% confidence interval [CI], 0.29-0.87).[6] The encouraging results of these and other studies formed the basis for a large-scale prostate cancer chemoprevention trial using selenium and vitamin E. The findings from this study were recently published along with another large trial of vitamins E and C, both of which will be reviewed herein.

Effect of Selenium and Vitamin E on Risk of Prostate Cancer and Other Cancers

Lippman SM, Klein EA, Goodman PJ, et al.
JAMA. 2009;301:39-51.

This study reports the findings from the Selenium and Vitamin E Cancer Prevention Trial (SELECT), designed

to determine whether these supplements (alone or in combination) lead to a reduction in prostate cancer risk. Beginning in 2001, a total of 35,533 men aged 50 to 55 years and older were enrolled in this double-blind, randomized, controlled trial. There were 4 arms to the study: selenium only (200 μg/day L-selenomethionine), vitamin E (400 IU/day all-rac-α-tocopherol), both selenium and vitamin E, or placebo.

Results from SELECT were not anticipated until 2013[7]; however, the data and safety monitoring committee met in September 2008 and decided to discontinue the study prematurely due to a lack of benefit from either agent in reducing prostate cancer risk. Specifically, prostate cancer was detected in 4.56%, 4.93%, 4.56%, and 4.43% of the selenium, vitamin E, combination, and placebo groups, respectively, at a median follow-up of 5.46 years. The corresponding hazard ratios (HR) for prostate cancer were 1.04 (95% CI, 0.87-1.24) for selenium, 1.13 (95% CI, 0.95-1.35) for vitamin E, and 1.05 (95% CI, 0.88-1.25) for selenium plus vitamin E. Interestingly, pairwise comparisons revealed a nonsignificant trend toward higher prostate cancer risk with vitamin E compared with placebo ($P = .06$).

An examination of secondary endpoints further revealed a slight increase in diabetes risk in the selenium-only group versus placebo (RR 1.07; 95% CI, 0.94-1.22; $P = .16$). Selenium supplementation was also significantly associated with alopecia and grade 1/2 dermatitis.

Overall, the results of this study indicate that these formulations of selenium and vitamin E were not useful for prostate cancer prevention, and may have potential associated risk. These findings are important for patient counseling, particularly given the high prevalence of supplement use in the aging male population.

Vitamins E and C in the Prevention of Prostate and Total Cancer in Men

Gaziano JM, Glynn RJ, Christen WG, et al.

JAMA. 2009;301:52-62.

In this study, Gaziano and colleagues report on the findings from the Physicians' Health Study II, which, beginning in 1997, enrolled 14,641 male physicians aged 50 years and older. In this double-blind, factorial trial, participants were randomized to active vitamin E (400 IU synthetic α-tocopherol) and vitamin C (500 mg), active vitamin E with placebo vitamin C, active vitamin C with placebo vitamin E, or placebo for both. The study population included 1307 men with a history of malignancy at baseline.

During a mean follow-up of 8.0 years, there were 1943 cancer diagnoses. Unfortunately, neither vitamin E (HR 1.04; 95% CI, 0.95-1.13; $P = .41$) nor vitamin C (HR 1.01; 95% CI, 0.92-1.10; $P = .86$) reduced the risk of total cancer. Furthermore, overall survival was similar between users and nonusers of both vitamins.

Prostate cancer risk was also examined in the subset of 13,983 men without prostate cancer at baseline. As in the prior study, vitamin E did not lead to a significant reduction in prostate cancer compared with placebo (HR 0.97; 95% CI, 0.85-1.09; $P = .58$). Similarly, vitamin C supplementation had no effect on prostate cancer risk (HR 1.02; 95% CI, 0.90-1.15; $P = .80$).

In contrast to earlier studies, both the SELECT and Physicians' Health Study II showed no effect of selenium, vitamin E, or vitamin C supplementation on prostate cancer risk. Because the patient populations and supplement formulations differed between the various studies, it is therefore possible that the results may have been different within specific subpopulations or using an alternate supplement preparation. Nevertheless, these trials provide strong evidence that these particular supplements are not useful for prostate cancer chemoprevention in the general population. ■

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