

Selenium intake may worsen prostate cancer in some, study reports

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BOSTON--Higher selenium levels in the blood may worsen prostate cancer in some men who already have the disease, according to a study by researchers at Dana-Farber Cancer Institute the University of California, San Francisco.

A higher risk of more-aggressive [prostate cancer](#) was seen in men with a certain genetic variant found in about 75 percent of the prostate cancer patients in the study. In those subjects, having a high level of selenium in the blood was associated with a two-fold greater risk of poorer outcomes than men with the lowest amounts of selenium. By contrast, the 25 percent of men with a different variant of the same gene and who had high selenium levels were at 40 percent lower risk of aggressive disease. The variants are slightly different forms of a gene that instructs cells to make manganese superoxide dismutase (SOD2), an enzyme that protects the body against harmful oxygen compounds.

The research findings suggest that "if you already have prostate cancer, it may be a bad thing to take selenium," says Philip Kantoff, MD, director of Dana-Farber's Lank Center for Genitourinary Oncology and senior author of the study that is published by the [Journal of Clinical Oncology](#) on its website now and later will be in a print journal. The lead author is June Chan, ScD, of the University of California, San Francisco.

The unexpected results are the first to raise concern about this potentially harmful consequence of taking supplemental selenium. Kantoff says, "These findings are interesting particularly in light of the

recent negative results from the SELECT prevention study, which asked if selenium could protect against prostate cancer."

The new study reveals the strong interaction between selenium and SOD2 to influence the biology of prostate cancer, a finding that these investigators had shown in a previous study. The authors say the current research demonstrated that variations in the make up of the SOD2 gene dramatically alter the effects of selenium on the risk of aggressive prostate cancer.

Selenium is a mineral found widely in rocks and dirt. Small amounts of selenium are essential for health: 40 to 70 micrograms is the recommended daily intake. In recent years, supplemental selenium has been sold and promoted as a means of preventing prostate cancer, largely based on observational studies that found higher risk of prostate cancer incidence and mortality in areas of the country that are naturally low in selenium.

However, research aimed at confirming the benefits of selenium supplementation have been mixed. Recently, the SELECT study, which involved 35,000 men, was halted early when, after more than five years, it showed that the supplements didn't affect the incidence of prostate cancer.

Previous studies had found that the risk of developing prostate cancer was modified by a strong interaction between SOD2 and selenium. The new research was designed to look at the effect of this interaction on men already diagnosed with prostate cancer.

Scientists examined banked blood samples, DNA, and medical records of 489 male Dana-Farber patients diagnosed between 1994 and 2001 with localized or locally advanced prostate cancer. Their mean age was 62, and their mean PSA (prostate-specific antigen) measurement was 6.0

ng/mL. About half the men were assessed as having a good disease risk, one-third had an intermediate risk, and the remaining one-sixth were at poor risk. The researchers measured the level of selenium in the blood and, using the stored DNA, they determined the SOD2 genotype -- the specific form of the SOD2 gene carried by each patient.

Simply having a high level of selenium was associated with a slightly elevated risk of aggressive prostate cancer. But the risk was much more strongly affected by the interaction of selenium levels and whether the patient had a certain variant of the SOD2 gene. Men with the highest selenium levels and the "AA" form of the SOD2 gene were 40 percent less likely to have been diagnosed with aggressive prostate cancer than the men with same gene form but low levels of selenium.

But for men carrying the "V" form of the gene, selenium had the opposite effect. In these men, those with the highest levels of selenium in their blood were about twice as likely to have an aggressive type of prostate cancer as their counterparts with low selenium levels, says Kantoff, who is also a professor of medicine at Harvard Medical School.

The study couldn't determine whether any of the men had been taking selenium supplements or not. But the researchers noted that men in the large SELECT prevention trial had a much higher average selenium level than those in the current study.

"Among the 25 percent of men with the AA genotype, having greater selenium levels may protect against aggressive disease," the authors concluded. "However, for the 75 percent of men who carry a V allele, higher selenium levels might increase the likelihood of having worse characteristics."

Therefore, they add, it is important to know which type of SOD2 gene a man has when considering the risks and potential benefits of taking

selenium supplements. Additionally, the authors say the effects of the interaction between the SOD2 genotype and [selenium](#) may help explain apparently conflicting results of previous studies.

The results may seem counterintuitive to the public, who have been told for years that antioxidants can help people live longer, healthier lives with a lowered risk of cancer. However, Kantoff says, "There is some precedent to this - research has suggested that antioxidants could be protective if you don't have cancer, but once you do, then antioxidants may be a bad thing."

Source: Dana-Farber Cancer Institute

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