

Issue 72

In a nutshell

Epidemiological evidence linking low selenium levels with prostate cancer has now been followed by results from a large randomised clinical trial showing a strong protective effect of selenium supplementation.

Although further trials are warranted, and selenium is toxic in overdose, this is an important finding.

Selenium and prostate cancer

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NUTRITION RESEARCH REVIEW

Study one: Toenail selenium and prostate cancer

Subjects: 33,737 male health professionals aged 40-75 years.

Method: Case-control study where subjects initially provided toenail clippings, and the incidence of advanced prostate cancer was monitored over the next 7 years.

Results: There was a positive association between higher selenium levels and lower risk of advanced prostate cancer. The subjects in the highest quintile of toenail selenium level had half the incidence of prostate cancer compared with the lowest quintile (odds ratio= 0.49; 95% CI 0.25-0.96). Once data were controlled for family history of prostate cancer, body mass index, calcium, lycopene and saturated fat intake, vasectomy, and geographical region, there was a two thirds reduction (odds ratio = 0.35 , 95% CI 0.16-0.78, p = .03).

Ref: *J Natl Cancer Inst* 1998;90:1219-1224

Study two: ATBC study

Subjects: 29,133 subjects in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study.

Method: Case-control with 9 years of follow-up.

Results: There was no significant association baseline selenium levels and prostate cancer during

Ref: *Cancer Epidemiol Biomarkers Prev*, 1998;7:335-40

Study three: Randomised controlled trial

Subjects: 974 men with a history of either a basal cell or squamous cell carcinoma, of which 843 had initially normal levels of prostate-specific antigen.

Method: They were randomised to receive either selenium supplementation (200 µgm/day) or placebo for a mean of 4.5 years treatment and 6.5 years follow-up.

Results: There was a two-thirds reduction in the secondary endpoint of prostate cancer incidence in the supplemented compared with placebo group.

In those subjects who had normal PSA levels at the outset of intervention, the reduction was even greater - after a 2 year treatment lag the relative risk was 0.26 (p=0.009).

The authors also reported significant health benefits for other secondary endpoints, including total cancer mortality, and the incidence of total, lung and colorectal cancer. Because of these findings, the blinded phase of the trial was concluded early.

Ref: *Br J Urol* 1998;81:730-4

Comments

The evidence that selenium is linked to prostate cancer is really quite strong. It includes a number of epidemiological studies and laboratory work showing feasible mechanisms by which the association might work.

This is part of a wider body of evidence that is quite convincing in showing that prostatic cancer is a disease with strong nutritional influences. Potentially preventive nutrients include: reduced fat intake, higher vitamin E, selenium and soy protein. A lesser benefit is also suggested with intake of vitamins D and C (for a recent review, see ¹).

As prostate cancer is the second most common cause of cancer death amongst men, the prospect of nutritional prevention has drawn enormous interest from researchers in the last 5 years. Unfortunately, there have been few controlled clinical trials reported so far.

The first two studies add to the epidemiological evidence, but with contradictory results. This highlights one of the difficulties in this area of research, which is in establishing a good method of assessing tissue selenium levels. The use of toenail clippings has perhaps allowed the Harvard research team to find significant results where the ATBC study was not able to.

The third study is the first solid clinical trial evidence we have had on the use of selenium supplements in

prostate cancer prevention. It is a follow up result to the skin cancer prevention trial by researchers from Cornell University, which was prematurely aborted when it was found that the incidence of other types of cancer than skin cancer were significantly reduced by selenium supplementation.

This latest publication confirms that selenium intake does indeed have a powerful impact on prostate cancer, as well as colorectal, lung and overall cancer rates. Although selenium was disappointing in the secondary prevention of recurrent skin cancer, the impact on prostate cancer is worthy of close and careful follow-up.

However, as studies with vitamin A have shown, in the area of nutritional cancer prevention it is not always easy to move from the promising epidemiological, laboratory and early clinical trials to clear clinical recommendations. One of the issues that needs to be addressed is the appropriate form and dose of the nutrient.

In the case of selenium, laboratory work has suggested that different chemical forms of selenium may have differing antitumor activity. Selenium is also a nutrient with potentially toxicity in overdose. Hence we definitely require more clinical trials before the role of selenium supplementation in prostatic cancer can be said to be clearly established.

Reference: 1. J Urol 1999;161:1748-60

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