

MINIREVIEW ARTICLES

Dietary Selenium and Prostate Cancer Prevention: A Brief Review

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ABSTRACT

Evidence suggests that the trace nutrient selenium may reduce the risk of prostate cancer. There is, however, a need to prove that intake of high but not toxic levels of selenium can prevent the disease in the general population, and to conduct further relevant study.

Key words: Selenium - Prostate cancer - Prevention

INTRODUCTION

Prostate cancer has been the common visceral malignancy in men for the past decade, causing more than 30,000 deaths in the United States in the year 2000 alone (1). The incidence of prostate cancer varies widely around the world, with by far the highest rates in the US and Canada (2). Since the 1960s, there has been a gradual increase in the incidence of prostate cancer in many countries, notably the countries with comparatively low incidence in the past such as India, Japan and China (2,3). The dramatic increase in the prostate-specific antigen (PSA) based screening regimens, widely practiced in recent years, together with the relatively stable mortality rates and treatment-associated morbidity, has promptly stimulated interest in finding ways to prevent this disease.

Selenium is an essential trace nutrient, needed for the activity of the enzymes glutathione peroxidase, which protects cellular constituents including DNA from oxidative damage (4), and type 1, 5'-deiodinase, which catalyzes the conversion of the thyroid hormone thyroxine to 3,3',5-triiodothyronine (5). In many studies using animal models, selenium has been shown to protect against the action of certain carcinogens (6). It has been postulated that the mechanisms by which selenium generates its anticarcinogenic effects constitute an essential part of the cellular enzyme glutathione peroxidase as well as acting as an agent that inhibits cell proliferation and protein synthesis (7,8). In humans, evidence for cancer-protective effects of selenium was initially obtained by means of ecological and correlational studies. In the United States, lower death rates caused by some types of cancer have been observed in areas with higher selenium contents in the soil (9,10). Statistically significant inverse associations between low levels of serum selenium and the risk of various cancers were also noted (11). The strongest evidence for the potential efficacy of selenium as an anticancer agent came from a double blind, placebo-controlled cancer prevention trial reported by Clark et al in 1996 (12), in which 200 µg of selenium was given daily

to patients with histories of skin cancer. In this report, selenium supplementation did not protect against the development of recurrent skin cancers as a primary endpoint, but was inversely associated with the incidence of mortality from total prostate, lung, and colorectal cancers.

A substantial amount of selenium in the diets is present in proteins as selenoaminoacids. In food items made up of meat, fish, and internal organs of animals, selenocysteine is the form of selenium in selenoproteins, whereas selenomethionine is found in plants such as wheat and other cereal crops (13). The typical dietary intake of selenium in the United States is estimated at about 100 µg/day and the Recommended Daily Allowance for adults is at 50-70 µg (14). This has revitalized old questions by some scientists that selenium intakes in the US and elsewhere may be too low, and cancer mortalities in the United States and other Western industrialized nations would decline significantly if the dietary selenium intakes were increased (15). Although high levels of selenium are toxic to humans (16) and there are concerns about raising selenium contents in the diet or taking selenium as a supplement to the diets (17), a daily intake of selenium up to 400 µg, which is relatively high, is considered to be safe (18).

RECENT REPORTS ON SELENIUM AND PROSTATE CANCER

Following the landmark Clark Report (12), there have been several reports on the antitumorigenic effects of selenium. Although some studies show no association between selenium and the development of cancer or inconclusive results (19), the investigations have generally supported the anticancer effects of selenium for at least some cancers. The association of low levels of selenium and the incidence of prostate cancer appears to be relatively strong. The followings are some relevant reports published in the last 5 years.

Yoshizawa et al (20) reported in 1998 a nested case-control prospective study in the United States where they investigated the association between the risk of prostate cancer and prediagnostic level of selenium in toenails, a measure of long-term selenium intake. After about 5 years during which 181 new cases of advanced prostate cancer had been reported, they concluded that higher selenium intakes, resulting in higher level of toenail selenium (mean = 0.96 µg/g compared to 0.82 µg/g in the controls; $p \leq 0.05$) significantly reduced the risk of prostate cancer.

Nomura et al (21) reported in 2000 on a nested case-control study of a cohort of 9,345 Japanese-American men in Hawaii who were examined between 1971 and 1977. A blood specimen was obtained from each and the serum was frozen. After a surveillance period of more than 20 years, 249 cases of prostate cancer were identified, and the stored sera and matched controls were measured for selenium levels. There was a difference in the levels of selenium which was 129.9 ng/ml in cases and 134.1 ng/ml in controls ($p=0.02$). However, they found an inverse association between serum selenium levels and cancer incidence mainly in current or past cigarette smokers rather than in nonsmokers, and expressed the need for caution in the interpretation of their findings.

Brooks et al (22) in 2001 reported on a case control study conducted in Baltimore, Maryland, US, in which 52 cases of prostate cancer and 96 matched controls were analyzed for plasma selenium. It was concluded that low plasma selenium was associated with a 4 to 5-fold increased risk of prostate cancer.

Several large-scale investigations concerning selenium and prostate cancer are currently underway. For example, Kline et al (23) design a randomized, perspective, double blind study to determine whether selenium and vitamin E alone and in combination can reduce the risk of prostate cancer among healthy men. The study is a 2x2 factorial study of 32,400 men in the United States with nonsuspicious digital rectal examination (DRE) and serum PSA level of 4 ng/ml or less. The study supplements are 200 µg L-selenomethionine, 400 mg racemic α-tocopheryl acetate, and an optional multivitamin containing no selenium or vitamin E. The primary endpoint for the trial will be the clinical incidence of prostate cancer as determined by a recommended routine clinical diagnostic work up, including yearly DRE and serum PSA level. Enrollment for the study began in 2001 with the final results expected in 2013.

NUTRITION AND PROSTATE CANCER

In an international survey of the correlation of the incidence and mortality rates of prostate cancer and the dietary practices in 42 countries using the cancer rates provided by the International Agency for Research on Cancer (IARC) and the food supply data provided by the Food and Agriculture Organization (FAO), it was found that among the food items examined, milk was most closely correlated ($r = 0.711$) with the incidence of prostate cancer, followed by meat and coffee (24). Therefore there is reason to believe that nutrition is an important factor that influences the incidence and mortality rates of prostate cancer together with other determinants such as race (25). Although the incidence rates of prostate cancer in many Asian countries are relatively low compared to those in the United States and Europe, there has been a growing concern that this disease may become a problem in the near future due to the ongoing westernization of lifestyle and dietary practices (3). In a recent Thai study to determine the prevalence of prostate cancer in elderly Thai men in an urban community, it was found that more than 0.75 per cent of the subjects presented symptoms of prostate cancer. The prevalence of abnormal DRE and PSA was 8.7 and 17.3 per cent respectively. These findings were comparable with those of similar studies in the Western countries (26, 2, 3).

CONCLUSION

The findings of the studies appear to validate the beneficial role of selenium as a preventive agent against prostate cancer. However, more data are required to prove that intake of relatively high but not toxic levels of selenium can prevent prostate cancer in the general population. Further relevant investigations in different parts of the world with racial and environmental differences should be conducted.

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บทคัดย่อ

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ธาตุซีลีเนียมในอาหารและการป้องกันการเกิดมะเร็งของต่อมลูกหมาก

หลักฐานทางการศึกษาวิจัยเบื้องต้นชี้ให้เห็นว่า ธาตุซีลีเนียมซึ่งเป็นสารอาหารที่ร่างกายต้องการในปริมาณน้อย อาจมีคุณสมบัติป้องกันการเกิดมะเร็งของต่อมลูกหมากได้หากบริโภคในปริมาณที่เหมาะสม ดังนั้น เพื่อให้สามารถนำผลการศึกษาไปใช้ประโยชน์ได้อย่างกว้างขวาง จึงควรมีการศึกษาคุณสมบัติการต้านมะเร็งต่อมลูกหมากในประชากรกลุ่มเสี่ยงต่าง ๆ รวมถึงการศึกษาด้านพิษวิทยาและทางด้านชีววิทยาที่เกี่ยวข้องอื่น ๆ ของแร่ธาตุนี้ให้มากขึ้น

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