

Serum Selenium and the Risk of Prostate Cancer

Chelsea Stancoff-Hon* and John Carter, PhD.

Department of Physician Assistant, College of Health Professions

Abstract. *Introduction:* The purpose of this study is to investigate the relationship of serum selenium levels and the risk of developing prostate cancer. It has been documented that antioxidants reduce the incidence of cancer by eradicating free radicals that damage DNA, thus increasing the risk of cancer. Selenium is a component of the antioxidant enzyme glutathione peroxidase, whose role in cancer prevention has been controversial in the last 40 years. *Methodology:* A systematic review of evidence-based literature was performed utilizing the following search engines: MEDLINE FirstSearch, ArticleFirst, dissertations, and Paper's First and a bibliographic search of selected articles. MeSH (medical subject heading terms) and text words utilized in this study include: serum, selenium, prostate, neoplasia, risk, nutrition, adenocarcinoma, male, prostatic intraepithelial neoplasm, and prostatic neoplasia. *Results:* The results of the evidence-based literature results are consistent with the epidemiologic studies available at this time. The best quality evidence suggests that higher selenium levels decrease a man's risk of developing prostate cancer. However, because of unaccounted for confounders including family history of prostate cancer and educational level, it is not recommended that providers prescribe selenium as preventive medicine combating prostate cancer. Nevertheless, individuals who have a higher intake of selenium may benefit from its protective effects.

1. Introduction

A systematic, evidence-based literature review was performed looking for an association between the risk of prostate cancer and serum selenium in men of different races, cultures and regions. Prostate cancer is the most common cancer in American men. It is also the second leading cause of cancer death, after lung cancer; however, the etiology of the disease is unknown. The prevalence of microscopic or latent prostate tumors is similar in most countries, but clinical prostate cancer morbidity and mortality are extremely different in various geographic regions among various ethnic or racial groups [1,2]. The epidemiology of prostate cancer is quite complicated because there are few recognized risk factors. Risk factors which may be relevant include: family history, age, country, race, testosterone deficiency, and diet [3].

Prostate cancer may be found as nodules in the prostate at the time of a digital rectal exam (DRE). Most prostate cancers are diagnosed, due to the elevation of serum prostate specific antigen (PSA). PSA is a glycoprotein produced in the cytoplasm of benign as well as malignant prostatic cells; its level correlates to the amount of prostate tissue, benign or malignant [3].

Antioxidants are nontoxic compounds that have been shown to reduce the incidence of cancer. Their function is to eradicate free radicals that damage DNA, which in turn can cause cancer. The most widely known, highly effective antioxidants include vitamin E, Beta-carotene, and lycopene. Selenium is an element in the antioxidant enzyme glutathione peroxidase; its role in cancer prevention has been somewhat controversial over the last 40 years. Selenium has many functions in the body. It is present in the active site of many enzymes which may encourage apoptosis of cancer cells; it improves the body's immune system by causing the formation of natural killer cells, it restrains the prostaglandins that cause inflammation, and it may induce P450 enzymes in the liver that detoxify carcinogenic molecules. Lastly, selenium, at high doses can decrease the rate of tumor growth in humans [1].

2. Experiment, Results, Discussion, and Significance

The design of this study is a systematic review of evidenced-based medicine. A review of the literature was done using a combined search of MEDLINE FirstSearch, ArticleFirst, dissertations, and Paper's First using the following subjects: *serum AND selenium AND prostate cancer, prostate cancer AND risk AND selenium, prostate cancer AND nutrition AND selenium, prostate AND adenocarcinoma AND selenium, prostatic intraepithelial neoplasm AND selenium, male AND selenium AND risk AND neoplasm,prostatic neoplasia AND selenium, male AND selenium.*

Other searches were performed using the same search terms but in the following search engines: Cambridge Scientific Abstracts (CSA), Info Trac Web, LexisNexis Academic, SilverPlatter Web SPIRS, Wilson Web and Complementary and Alternative Medicine (CAM) on PubMed.

Potentially missed articles were searched in the reference section of each obtained article and from reviews of this topic. All applicable articles were then retrieved based on consensus among authors and searching the reference lists of those articles for potentially relevant articles.

Articles were used from the years 1977-2005. There were no articles on this subject found before the year 1977, thus the reason for this start date.

Inclusion and exclusion criterion were used to select which studies would be incorporated in this evidenced-based literature review. Men between the ages of 45 and 75, that currently had not been diagnosed with any other type of cancer besides prostate cancer at the onset of the trial, and the evidence level of the article had to be a Level 1 or Level 2 article to be included in this review. Exclusion criterion used included African American men, because of their higher rates of prostate cancer, articles that were low in evidence and those articles that used selenium in a cocktail of nutrients or antioxidants.

Three levels of evidence were used to classify each study. Level 1 evidence is based on randomized controlled trials and large meta-analysis studies. Studies that are considered to be Level 2 studies are nonrandomized controlled studies, clinical cohort studies, and case-controlled studies with non-biased selection of study participants. Level 3 includes case series, and non-controlled case studies.

The results of this systematic review of the literature are consistent with the results of other epidemiologic studies. A majority of the studies suggest that higher serum selenium levels decrease a man's risk of developing prostate cancer. There were four Level 1 studies that showed a protective effect of selenium and eleven Level 2 studies that shared those same results. The strength of the association was similar for both cohort studies and case-control studies. The literature also showed a dose-response trend. The men with the lowest amount of serum selenium had the highest incidence of cancer.

Weaknesses in the Literature:

There needs to be a larger number of randomized controlled trials to decide the exact role of selenium and selenium supplementation in developing prostate cancer. The potential for confounding is present in each of the Level 2 studies. Each of these studies included control for potential confounders such as age, race and geography. However, there were two very important confounders that were unaccounted for: the first is family history of prostate cancer and the second was education level. Those men with higher education levels may be more health conscious and use dietary supplementation of antioxidants as a preventative measure for all types of cancer including prostate cancer.

Gaps in the Literature:

Currently there is research under way to determine the amount of supplemental selenium that should be recommended to provide a protective effect against contracting prostate cancer.

3. Conclusion

To date, the Level 1 evidence-based literature supports the protective effect of selenium in the risk of developing prostate cancer. There are also eleven good quality Level 2 studies that support this theory. However, the possibility of confounding factors that may have skewed the result cannot be excluded.

The SELECT trial is an ongoing randomized trial designed to answer whether selenium has a protective role in preventing prostate cancer [4]. Until the publication of these results, it is not recommended that clinicians prescribe selenium for prostate cancer prevention. However, those who have an elevated intake in selenium may benefit from its protective effects.

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