MINI-REVIEW

Dietary Agents in Prevention of Prostate Cancer

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Abstract

   Prostate cancer is the second leading cause of internal malignancy among men worldwide, with an annual incidence of 679,000 cases, and an annual mortality load of 220,000 deaths, making it the sixth leading cause of cancer mortality among men. It is generally on the increase. Environmental and lifestyle factors may have an aetiological role in prostate cancer and hence may provide potential targets for future intervention. In fact, because of the disease high prevalence, slowly progressive nature, and long latency prostate cancer is a very good candidate for chemoprevention. Dietary agents have gained considerable attention as chemopreventive agents against prostate cancer. The methodology for this review included computerized literature searches of the PubMed database using the keywords "chemoprevention of prostate cancer" from 1992 to 2007 . This mini-review examines the influence of plant-derived dietary agents for which articles reported statistically significant effects in the management of prostate cancer.

Key Words: Prostate cancer - dietary agents - chemoprevention

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Introduction

   Prostate cancer is the second leading cause of internal malignancy among men worldwide, with an annual incidence of 679,000 cases, and an annual mortality load of 220,000 deaths, making it the sixth leading cause of cancer mortality among men (Parkin et al., 2005). There are substantial ethnic differences in both incidence and mortality rates between regions. The highest rates found in North America and Western Europe and the lowest rates occurring in Asian populations (Gronberg, 2003). Environmental and lifestyle factors may have an aetiological role in prostate cancer, and hence may provide potential targets for future intervention.

   The term chemoprevention is defined as the pharmacologic intervention with a natural or synthetic compound to reverse or suppress carcinogenesis in its early or premalignant stages so as to prevent the development of invasive cancer (Khuri et al., 1999). The ideal therapeutic intervention would arrest disease progression during the latency period and decrease the incidence of clinical disease (Mohanty et al., 2005). Chemoprevention for prostate cancer increased in the last decade because of the disease high prevalence, slowly progressive nature, and long latency so prostate cancer is the best model for chemoprevention (Kelloff et al., 1999). For prostate cancer, there are significant risk factors; androgen hormone and other risk factors include modifiable factors (diet, obesity, and screening history) and nonmodifiable factors (age, race, family history, and the presence of certain genetic polymorphisms). Strategies for developing prevention clinical trials for prostate cancer have focused primarily on prevention by hormonal modulation and through the use of natural and synthetic bioactive food components. Although clinical trials of androgen-insensitive prostate cancer cell lines also have been conducted investigating bioactive food components (Greenwald, 2004). Dietary agents have gained considerable attention as chemopreventive agents against prostate cancer. Several studies have focused on the antioxidant and nonantioxidant effects of various dietary substances in the prevention of prostate cancer.

   The development of chemoprevention strategies against prostate cancer will have a huge impact, both medically and economically. Large-scale clinical trials suggest that some dietary agents such as selenium, lycopene, soy isoflavones, green tea, vitamins D and E are effective in preventing prostate cancer (Gupta, 2007). The methodology for this review included computerized literature searches of the pub med database using the keyword "chemoprevention of prostate cancer" from 1992 to 2007 years. This review will examine significance of plant-derived dietary agents which articles had statistical value in the management of prostate cancer.

Lycopene

   Lycopene is a red-orange carotenoid found primarily in tomatoes and tomato-derived products (tomato sauce, tomato paste and ketchup), watermelon, guava, pink grape fruit and red vegetables. There is mixed epidemiologic evidence that lycopene consumption is associated with a

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lower risk of prostate cancer. Lycopene inhibits the growth of benign and malignant prostatic epithelial cells in vitro (Giovannucci, 1999; Obermuller-Jevic et al., 2003). Lycopene has many effects like anti-proliferative insulin-like growth factor-1 inhibition, differentiation and apoptosis, connexin and gap junctional intercellular communication and it is antioxidant activation plays role in carcinogenesis inhibition.

Mohanty undertook a study to use lycopene as a chemopreventive agent in the treatment of HGPIN for preventing prostate cancer from developing in this vulnerable group of patients. A total of 40 patients with HGPIN were randomized into 2 groups: one received 4 mg lycopene twice a day for one year, and the other was periodically followed up one year. PSA level in the treated group A decreased for a mean level of 6.07–3.5 ng/ml, while in the control group B, it increased from a mean value of 6.55 to 8.06 ng/ml. This initial small trial has shown that lycopene is an effective chemopreventive agent in preventing HGPIN from becoming prostate cancer (Mohanty et al., 2005).

Health Professionals Follow-Up Study demonstrating that lycopene intake was associated with a significant decrease risk of prostate cancer (RR=0.84,95% Cl 0.73-0.96, p=0.003) and greater reduction in risk for extraprostatic disease (Kirsh et al., 2006).

Green Tea

Green tea has been suggested as a prostate cancer preventative based on epidemiologic observations of a low incidence of prostate cancer among Japanese and Chinese populations with a high dietary intake of green tea (Klein, 2005). Also green tea has an oestrogenic activity. In vivo experiments in transgenic adenocarcinoma of the mouse prostate (TRAMP) model have demonstrated that IGF-I/IGFBP-3 signalling pathway is a prime pathway for green tea polyphenol-mediated inhibition of prostate cancer that limits the progression of cancer through inhibition of angiogenesis and metastasis (Adhami VM et al., 2004). The cancer chemopreventive effects of green tea are associated to its major polyphenolic constituent, epigallocatechin-3-gallate (EGCG) (Saleem et al., 2003).

Vitamin E

Vitamin E is an essential, fat-soluble vitamin compounds which is present in the diet in two forms, gamma-tocopherol and alpha-tocopherol, the most active form (Rodriguez et al., 2004). Vitamin E functions as the major lipidsoluble antioxidant in cell membranes. It is a chain-breaking free-radical scavenger and specifically inhibits lipid peroxidation, a biological activity relevant to carcinogen-induced DNA damage (McCall et al., 1999). It acts as a potent antioxidant, cause G1 cell cycle arrest; prevent oxidation and peroxidation of membrane phospholipids while it may also affect androgen concentrations (Hartman et al., 1999). In animal studies it was shown that dietary supplementation of vitamin E slows down prostate cancer growth due to its ability to inhibit androgen signalling (Siler et al., 2004).

In the study of the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC Study), it was reported that men who received 50 μg daily vitamin E (α-tocopherol) and β-carotene 20 mg daily supplements had a 41% decrease in prostate cancer mortality and a 36% decrease in incidence (Heinonen et al., 1998).

Another randomized, double blind, placebo-controlled cancer prevention trial, the β-Carotene and Retinol Efficacy Trial (CARET), suggest to the epidemiologic evidence that α-tocopherol may prevent prostate cancer. Low serum levels of α-tocopherol were associated with a higher risk of prostate cancer (Goodman et al., 2003).

Selenium

Selenium (Se) is an essential element occurring in both organic and inorganic forms. The organic form is found predominantly in grains, fish, meat, poultry, eggs, and diary products and enters the food chain via plant consumption (Klein, 2005). Selenium has several structural and enzymatic roles. It is the main constituent of glutathione peroxidase which is an antioxidan enzym. Selenium works early in the carcinogenic pathway by blocking cell proliferation, promoting apoptosis and inducing antioxidant enzymes (Klein et al., 2004).

Male participants in the Nutritional Prevention of Cancer Trial who received 200 μg/d of selenium supplements (as selenized yeast) had a 63% reduced risk of prostate cancer incidence (Clark et al., 1998).

The Selenium and Vitamin E Cancer Prevention Trial (SELECT) was designed as one of the largest prostate cancer prevention trial, uses a randomized, prospective, double-blind study design (Klein et al., 2003). SELECT is a phase III trial of selenium (200 μg/day from L-selenomethionine) and/or vitamin E (400 IU/day of all _-tocopheryl acetate) supplementation for a minimum of 7 years (maximum of 12 years) in non–African American men at least 55 years of age and African American men at least 50 years of age a DRE not suspicious for cancer, serum PSA≤4 ng/ml, and normal blood pressure (Shukla et al., 2005; http://www.nci.nih.gov/select). Randomization will be equally distributed among four study arms (selenium + placebo, Vitamin E + placebo, selenium +Vitamin E, and placebo + placebo). This trial will permit detection of a 25% reduction in the incidence of prostate cancer for selenium or Vitamin E alone, with an additional 25% reduction for the combination of selenium and Vitamin E compared to either agent alone. The study will be ended in 2013 (http://www.nci.nih.gov/select).

Isoflavonoids

Isoflavonoids are polyphenolic compounds that are ubiquitously present in foods of plant origin especially in leguminosae and soybean that have estrogen-like activity (Williams et al., 2004). Soybeans are important nutrition source for East Asian People who are at low risk for prostate cancer.

The effects of isoflavonoids inhibit benign and malignant prostatic epithelial cell growth, downregulate

Table 1. Sources of Dietary Agents and Chemoprevention Mechanisms

Agent	Sources	Chemoprevention mechanisms
Lycopene	Tomato,watermelon, guava, pink grape	Antioxidant activation, IGF-1 inhibition, promoting apopitozis
Isoflavonoids	Soybean, legumes, green tea	Inhibit cell growth, down-regulate androgen, estrogen-like activity
Vitamin E		Antioxidant activation, inhibits androgen signaling
Selenium	Fish, meat, eggs	Induce antioxidant enzymes, promote apoptosis, inhibit cellgrowth

androgen-regulated genes, increases serum testosterone levels, and reduce tumor growth in some animal models (Hedlund et al., 2003; Yu et al., 2003). Also it was noticed that Japanese mmale plasma total isoflavenoid levels are 7–110 times higher than in Finnish men. A prospective study demonstrated that frequent consumption (>1/day) of soy milk was associated with a 70% reduction in the risk of developing prostate cancer (Jacobsen et al., 1998).

Vitamin A and Vitamin D

A relation of prostate cancer risk with calcium, vitamin D, vitamin A and phosphorus has been suggested, but remains controversial. However, additional prospective studies in this field are needed (Klein, 2005).

Conclusions

Epidemiological studies have suggested that diet and nutrition are critical determinants of prostate cancer risk. Its high rate of occurrence and long lead time to clinically significant disease make prostate cancer an ideal disease for pharmacologic or nutritional chemoprevention. The data remains compelling in regards to the potential for a variety of nutrients to potentially prevent the development and progression of prostate cancer. Changing dietary intake is an effective treatment method which has a major impact on disease-associated cost, morbidity, and mortality for prevention of prostate cancer.

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