



Can we prevent prostate cancer?



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BACKGROUND

Prostate cancer is the second leading cause of cancer deaths among men. It is common in Australia, New Zealand, North America and North West Europe, but rare in Asia, Africa and South America.

OBJECTIVE

This article reviews the role of chemopreventive agents for prostate cancer. The available evidence strongly suggests that dietary changes and supplementation with a variety of micronutrients, vitamins and trace elements may reduce the incidence and mortality of prostate cancer.

DISCUSSION

Epidemiologic observations reveal lower cancer rates in those with diets rich in fruits, vegetables, vitamins, and a number of specific foods. This available data is adequate to clinically apply the role of various factors to possibly reduce the incidence of prostate cancer.

Prostate cancer ranks as the second leading cause of death among men after lung cancer. In Australia alone, over 10 000 men are diagnosed with prostate cancer each year, and over 2600 Australian men die of the disease.¹ No definite aetiopathological factors have been found. However, there appears to be a connection with living in a developed country, eating certain types of foods and being of certain racial origin.² Based on a Medline search, we review the possible reported factors that affect the incidence of prostate cancer. This will enable general practitioners to have a scientific basis on which to give advice to patients asking about what can be done to prevent the disease.

Prevention of prostate cancer

Despite the differing rates of clinical prostate cancer in east and western populations, autopsy studies have revealed a similar frequency of microfocal cancer among Japanese and white North American and European men.³ It has been demonstrated that there is a significant increase in clinically evident prostate cancer among Japanese and Asian men who migrated to the United States compared to those who remained in their country of origin.⁴ This suggests that

environmental and nutritional factors have a role in stimulating the growth of latent, microfocal cancer in men who move from an area of low clinical incidence to an area of high clinical incidence.^{5,6}

Diet

There is emerging evidence⁷ that a diet consisting of the following food groups or supplements may help reduce the risk of prostate cancer (*Table 1*).

Saw palmetto

Saw palmetto (*Serenoa repens*) is derived from the Arecaceae palm, native to the West Indies and the Atlantic coast of North America. It is widely used to treat lower urinary tract symptoms caused by benign prostate enlargement. Saw palmetto has a mild oestrogenic effect that counteracts testosterone. It is important for the treating physician to rule out prostate cancer before initiating the use of this compound as it is still not known whether saw palmetto delays the onset of prostate cancer or masks the prostate specific antigen (PSA) level. It is also preferable to have a baseline PSA value and digital rectal examination before starting treatment with this compound.

While saw palmetto is used for lower urinary tract symptoms, there is no evidence that it protects against, or has a direct role, in the treatment of prostate cancer.^{8,9}

Vitamin C

Vitamin C is the major water soluble antioxidant found in citrus fruits and juices, green peppers, cabbage, spinach, broccoli, kale, melons, kiwi fruit, and strawberries. It acts as a free radical scavenger, resulting in the inhibition of malignant transformation in vitro and a decrease in chromosome damage induced by carcinogens.¹⁰ It has recently been shown that ascorbic acid could be a potent anticancer agent for prostate cancer cells.¹¹

Vitamin E

Vitamin E is found in vegetable extracts, seed oil, whole grains, wheatgerm and green leafy vegetables. D-alpha tocopherol is the most potent antioxidant of the vitamin E group, protecting cell membranes from free radical injury.^{12,13} The link between vitamin E, its antioxidant properties and prostate cancer risk, is not entirely clear. However, one study showed that vitamin E supplements did reduce the rate of prostate cancer, as well as death due to cancer.¹⁴ Smokers have a lower blood vitamin E level and this correlated with an increased risk of prostate cancer.¹⁵ Furthermore, taking vitamins C, E, and zinc may be protective against prostate cancer.¹⁶ One study that measured the immune response in healthy elderly individuals, found that doses of 200 IU per day were beneficial. To maximise the effect of vitamin E, particularly d-alpha tocopherol, 400–800 IU per day is acceptable.^{17,18} However, high concentrations of vitamin E can adversely affect those with vitamin K associated blood coagulation disorders, including those on warfarin.¹⁹

Selenium

Selenium is a trace element found in soil. It is a powerful antioxidant present in grains, seeds, vegetables, seafood, liver, and kidneys.²⁰ The risk of prostate cancer has been found to be double in those with low

Table 1. The evidence of dietary factors on the risk of developing prostate cancer

- Vitamin C is the major water soluble antioxidant resulting in inhibition of malignant transformation in vitro and a decrease in chromosome damage induced by carcinogens
- Vitamin E, most likely through its antioxidant activity, may be helpful in prostate cancer prevention, with a recommended dose of 500 IU/day
- The risk of prostate cancer doubles in those with low serum selenium levels as compared with subjects having higher levels
- EGCG found in green tea, inhibits the growth of prostate cancer cells and destroys them in high concentrations
- Isoflavonoides found in green tea, betacarotene in oranges and red/dark green vegetables, and lycopene from tomato skins have been found to lower the risk of developing prostate cancer
- A diet low in saturated fat is recommended
- Use of anabolic steroids and occupational exposure to cadmium are likely to lead to an increased risk

serum selenium levels as compared with patients having higher levels.²¹ Further studies have revealed that selenium supplementation in the diet was related to a lower incidence and mortality from prostate cancer.^{22,23} Selenium works synergistically with vitamin E and together they help neutralise free radicals. A recommended dose is 200 µg per day,²⁴ with toxic effects occurring above 750 µg per day.

Soy products

Asian men have a lower risk of prostate cancer compared to men on a primarily western diet. This may be because Asians tend to eat more soy products (active ingredient isoflavonoides, a mild, plant based phyto-oestrogen). Animal studies have also shown the benefit of soy products in inhibiting prostate cancer. The evidence however, is not as definitive with human trials. Increasing the soy content in the diet to replace dairy products may be helpful. There is no evidence to suggest this would be harmful.^{25–28}

Green tea

Green tea (*Camellia sinensis*) has been shown in epidemiological studies to be associated with a decreased risk of prostate cancer. This beverage, commonly drunk in Japan and

China where mortality from prostate cancer is significantly low, is gaining popularity in the west for its powerful antioxidant polyphenols. The principle polyphenol in green tea, EGCG (epigallocatechin-3-gallate), inhibits the growth of prostate cancer cells, and in high concentrations, destroys them. In light of this, drinking green tea could be potentially helpful in protecting against prostate cancer.^{29–31}

Others

Betacarotene is present in oranges and red or dark green leafy vegetables.³² Lycopene is a carotenoid antioxidant most commonly found in tomato skins (processed tomatoes) and has been found to lower the risk of prostate cancer.^{33,34} Consuming tomato sauces such as those found in pasta, ketchup and soup appears to be better than eating raw tomatoes.

Risk factors for prostate cancer

Prostate cancer is more common in older men. Autopsy studies have shown that prostate cancer was present in 20% of men aged 20–29 years, 30% in men over 50 years, and 70% of men aged 80–89 years. While these studies revealed the presence of cancer, a significant number were microscopic and may not have led to malignancy.^{35–37}

A diet high in saturated fat from animal

Table 2. Lifestyle and dietary recommendations to prevent prostate cancer

- Certain nutrients and supplements, along with increasing fruit and vegetable intake and decreasing animal produce, can reduce the incidence and mortality from prostate cancer
- A diet consisting of 5–8 servings of fruits and vegetables, low/no animal fat, and an adequate intake of tomato sauces, soy and green tea is recommended
- A diet low in saturated fat is recommended

origin and dairy products, as well as other foods from animal sources such as red meats and liver can potentially transform a latent cancer into an aggressive one.^{38–40} Fat is proposed to affect prostate cancer cells by increasing the circulating level of testosterone,^{41,42} free radical activity,⁴³ and the carcinogenic effects of arachidonic acid,^{44–46} a metabolic end product. Currently, it is reasonable to conclude that a high fat diet, especially one containing animal fat, is a significant risk factor for prostate cancer.⁴⁷

Long term use of anabolic steroids, leading to high levels of testosterone, increases the risk.⁴⁸ Exposure to cadmium, commonly used in the mining and printing industries, has been found to be carcinogenic for prostate cells.⁴⁹

Unproven factors

Cigarette smoking

Cigarette smoking increases the risk of numerous cancers. Surprisingly, there is no clear evidence that cigarette smoking increases the risk of prostate cancer.^{50,51}

Alcohol

There is no link between the level of physical activity⁵² or the amount of alcohol consumed and prostate cancer.⁵³

Vasectomy

At present, it is difficult to ascertain if there is a cause and effect relationship between vasectomy and prostate cancer.^{54–57}

Finasteride

A recent study⁵⁸ of 18 882 men revealed that finasteride reduced the cumulative risk of prostate cancer compared to placebo (18%

vs. 24%). However, in those who did get prostate cancer while on finasteride, 37% had more aggressive cancers compared to 22% in the placebo group. The editorial comment raised the concern that this finding was not attractive as a potential chemopreventive agent because in the placebo group, cancer was detected four times as often as expected; in 24.4% rather than 6% of the men. Furthermore, the relative rate of high grade cancers and the absolute number of such cancers were greater in the finasteride group than in the placebo group.

Calcium

Two studies have shown a link between increased calcium intake, particularly from dairy products, and a higher risk of prostate cancer; but a definite link remains unclear.^{59,60}

DFMO

The preventive role of difluoromethylornithine (DFMO), involved in polyamine synthesis, is not yet known.⁶¹

Alternative therapies

Between 27% and 55% of men may use treatments outside conventional medical therapy, commonly consisting of dietary changes and herbal and nutritional supplements.⁶² Advice to patients on nutritional supplements must be based on current evidence.^{63,64} This is not always an easy task when many of the treatments have not been conventionally trialed, or the identity and amount of the ingredients are not as readily identifiable as conventional prescription medications.

If alternative supplements are to be taken, it is always preferable to have a product that

at least complies with the Therapeutic Goods Administration and pharmaceutical guidelines adhering to good manufacturing practice.

The commonly available vitamin supplements of vitamin D,⁶⁵ zinc,⁶⁶ garlic,⁶⁷ and modified citrus pectin⁶⁸ (obtained from peel and pulp of citrus fruits) still have unproven roles.

The Memorial Sloan Kettering Cancer Centre has a website dedicated to herbal products (www.mskcc.org/aboutherbs).

Conclusion

There is strong evidence to suggest that certain nutrients and supplements, along with dietary changes, can reduce the incidence and mortality from prostate cancer (*Table 2*). More needs to be learnt about the environmental and dietary aetiology of prostate cancer, and indeed many other cancers. It appears that this issue is unlikely to involve one micronutrient, but rather an appropriate 'blend' of micronutrients at their 'therapeutic' doses.⁶⁹

To continue to believe that a careful well balanced diet will be enough to prevent some cancers and chronic degenerative diseases may not acknowledge the available evidence. The reality is that most people do not consume an optimum amount of all vitamins and antioxidants by diet alone. There is already a growing amount of data present in our medical literature to help us give appropriate and scientifically based advice to our patients and ourselves.

Conflict of interest: none declared.

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