Complementary therapies in prostate cancer

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The authors look at some of the many complementary therapies and alternative medicines used by patients with prostate cancer, and conclude that more research is needed to assess their safety and efficacy.

Prostate cancer accounts for 25 per cent of new cancer diagnoses and is the second most common cause of cancer-related death in men in the UK.[1] Prostate cancer commonly has a long latent period to clinically overt disease and radical treatments carry significant side-effects. In addition, the treatment regimens of active surveillance and watchful waiting (either at diagnosis or at biochemical recurrence) can make patients worry about the prevailing inactivity.

WHAT IS COMPLEMENTARY THERAPY AND ALTERNATIVE MEDICINE?

Complementary therapy and alternative medicine (CAM) is defined as 'a group of diverse medical and healthcare systems, practices and products that are not generally considered part of conventional medicine'. [2]

Prostate cancer has thus been an ideal focus for CAM, to attempt to prevent prostate cancer, to shrink early prostate cancer, to control recurrent prostate cancer, or to alleviate symptoms caused by prostate cancer itself or the treatment thereof. The very long time spans involved, especially in preventive trials, have made sound research difficult.

Figure 1. Many dietary supplements and nutraceuticals can be purchased without consultation in the larger supermarkets

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CAM is increasingly popular and it is important for doctors to understand what therapies their patients may obtain elsewhere, and why patients may choose CAM (Figure 1). Up to 80 per cent of prostate cancer patients use some form of CAM.[3]

LITERATURE SEARCH

We conducted a literature search of the Allied and Complementary Medicine (AMED), Excerpta Medica (EMBASE) and National Library of Medicine (MEDLINE) databases for complementary therapy/alternative medicine/herbal medicine/plant extract/herbaceous agent and prostate cancer. We included significant references within the articles identified. The earliest articles date back to 1991. Interest in the subject has since increased exponentially – as have publications.

WHAT CAM ARE USED IN PROSTATE CANCER?

CAM are either biological or mind/body therapies. The biological therapies may be more familiar to doctors at first, but there are many other therapies. Box 1 shows CAM used in prostate cancer. We will discuss the most commonly used modalities in the West, *ie* several biological therapies, exercise and prayer. Most users use more than one CAM.

BOX 1. Complementary therapies and alternative medicine used in prostate cancer

BIOLOGICAL THERAPIES

*Dietary supplements/nutraceuticals**

- Antioxidants: lycopene, vitamin A, vitamin E, selenium, polyphenols, flavonoids
- Multivitamins
- Vitamin D
- Zinc
- Chinese herbal medicine
- Numerous plant extracts

Dietary systems

- Vegetarianism/plant-based diet
- Low fat diet

Nutritional foods

- Tomatoes/tomato products
- Green tea
- Soy
- Pomegranate juice
- Saw palmetto

MIND/BODY THERAPIES

- Meditation/yoga/tai chi/relaxation training/music therapy
- Exercise
- Acupuncture
- Chiropractic care/massage
- Guided imagery
- Spiritual healing
- Spirituality/faith/prayer

*Dietary supplements that contain a concentrated form of a presumed bioactive substance originally derived from a food, but now presented in a non-food matrix, and used to enhance health in dosages exceeding those obtainable from normal foods.[4]

LIMITATIONS OF THE EVIDENCE

Many plant extracts are being tested in the laboratory for their effect on prostate cancer cell lines, without supporting *in vivo* studies. We will focus on CAM with evidence from studies involving patients with prostate cancer. These studies still tend to be small, short, not randomised and not placebo controlled, although some large studies have now been conducted on selected dietary supplements. The evidence therefore remains largely indicative rather than providing any compelling proof. Until more evidence becomes available, the efficacy, safety and quality of any biological agent marketed for prostate cancer prevention and/or treatment still needs to be questioned. Currently, 44 ongoing trials with dietary interventions in prostate cancer are registered at clinicaltrials.gov.[5]

Robust studies on mind/body therapies are even more challenging; evidence is largely anecdotal with case reports and some observational evidence. Only for exercise and acupuncture could we find any clinical trials.

POTENTIAL PROBLEMS WITH SUPPLEMENTS

There are three potential problems with dietary supplements/nutraceuticals.[4,6] First, the dosage of the claimed active ingredient may vary considerably from that advertised on the packaging (0–150 per cent); the claimed active ingredient may be entirely absent. Second, combination preparations are common, and there may be any number of other undisclosed ingredients, including active pharmacological agents (*eg* hormones) and even known toxins (*eg* lead). Third, the specific health claims made may have no evidence at all.

REASONS FOR USING CAM[7–10]

Many men state that they simply want to do what they can to prevent or control the cancer and improve their own survival. Many CAM promise just this: good results without side-effects. Additional commonly stated reasons are that CAM:

- makes patients feel better
- gives an element of control
- helps patients cope with the diagnosis and the side-effects of conventional treatment
- improves quality of life.

Some patients are convinced that their choice of CAM will cure the cancer on its own, often believing that only holistic approaches can work, and that conventional therapy would interfere with their healing.[11]

Many CAM users do not disclose their CAM treatment unless specifically asked and many would like more information on CAM.

Individual reasons or beliefs do not appear to be associated with any one CAM in particular. However, CAM users believe in the safety and efficacy of their chosen CAM, regardless of any objective evidence. This belief can be very specific, with users considering other CAM as 'sham'.

Use of CAM is frequently triggered by the cancer diagnosis, but declines with time; higher-effort therapies are more frequently discontinued. Often the patient justifies this by saying it did not work or did not suit them. Other reasons for stopping CAM are cost, advice from doctor, friends and family, and rarely side-effects from the CAM.[9]

PATIENT FACTORS[7,10]

Most CAM users are young and well educated. Biological CAM are more common among Caucasians, whereas mind/body therapies are more frequently chosen by ethnic minorities. Patients with previous negative experiences or severe side-effects of conventional treatment are also more likely to choose CAM.

INDIVIDUAL THERAPIES

Lycopene, tomatoes and tomato products

In a western diet, lycopene is found mainly in tomatoes (Figure 2); its concentration is higher in processed tomatoes. It is a powerful antioxidant and is found in high concentrations in the healthy prostate. Lycopene supplements are as bioavailable as lycopene derived from processed tomatoes in the diet (Figure 3). Evidence from observational studies suggests a lower incidence of aggressive prostate cancer and slower progression of prostate cancer in people with higher intake.[12,13] One small randomised trial supports these findings.[14] More research is needed.

Selenium and vitamin E

The antioxidants selenium and vitamin E had both shown promise in observational studies and interventional trials, prompting the largest trial into CAM in prostate cancer – the Selenium and Vitamin E Cancer Prevention Trial (SELECT). This was designed to quantify the advantages of selenium and vitamin E (alone and in combination); 35 000 healthy men were recruited, but the trial closed early because of a failure to show any decrease in the incidence of prostate cancer. Moreover, concerns were raised about possible increases in prostate cancer (vitamin E-only group) and diabetes (selenium-only group). Therefore, selenium and vitamin E can no longer be widely recommended.[4,15]

Figure 2. Tomatoes contain lycopene, a powerful antioxidant found in the healthy prostate

Figure 3. Lycopene tablets. There is some evidence that a higher lycopene intake may lead to a lower incidence of aggressive prostate cancer and slower progression of the disease

It is possible that vitamin E has a protective effect only in smokers, as found in three previous large trials.[3]

Pomegranate juice

Pomegranate juice is a very potent antioxidant; initial evidence suggests a potential to reduce prostate-specific antigen doubling time in biochemical recurrence.[16] Caution is indicated as the juice inhibits CYP3A enzymes and can interact with medications.[6] More research is needed.

Polyphenols, flavonoids, green tea, soy, plant-based diet, vegetarianism

Polyphenols and flavonoids are found in fruit, vegetables and green tea. Epidemiological evidence shows reduced prostate cancer incidence in Asia compared with western countries, and migration studies confirm an increased risk for Asians adopting a western diet and lifestyle. The 'magic' component could be green tea, soy, a plant-based diet/vegetarianism, other lifestyle factors or any combination of these.

Initial evidence suggests that soy isoflavones may prevent prostate cancer and reduce prostate cancer growth; green tea may reduce incidence. Trials are largely observational; a recent meta-analysis suggests a true risk reduction with soy products;[17] results for green tea have been inconsistent, but one small randomised controlled trial showed a risk reduction.[18] More research is needed.

Small interventional trials have shown weight loss and changes in hormone levels as a result of adopting a plant-based diet; stabilisation of recurrent prostate cancer is claimed. It is unknown whether any disease-modifying effect resulted from the diet itself or the changes in weight and hormone balance.[19] There is no association between total fruit and vegetable intake and incidence of prostate cancer.[20]

Vitamin D

There is limited observational evidence that vitamin D levels may reduce the incidence of aggressive prostate cancer. Elderly men, especially those on hormone treatment, have an increased risk of fractures, and any calcium or vitamin D deficiencies should be corrected regardless of any direct anticancer effect. One placebo-controlled randomised clinical trial suggests a survival advantage for high-dose intermittent vitamin D during chemotherapy for prostate cancer. This still needs confirmation in a fully powered trial.[21]

Other dietary therapies

The available evidence suggests/confirms little or no benefit from multivitamins/multiminerals, vitamin A, vitamin C, calcium, zinc, flaxseed, low-fat diet, Chinese herbs or saw palmetto in prostate cancer prevention or control.[4,6,22–24] Zinc may be detrimental.[6] Saw palmetto is detrimental when given with radiotherapy.[25]

Exercise

Exercise has obvious effects – reducing weight, which in turn positively affects hormonal balance,[19] and increasing fitness, which increases physical functioning.[26] In addition, observational studies and small interventional trials[27,28] have shown decreased fatigue (during radiotherapy or androgen deprivation) and increased quality of life with regular exercise. These effects are reversed upon termination of the exercise regimen. A large cohort study (47 000 health professionals)[29] identified an association between vigorous exercise in men over 65 years and lower Gleason grade at diagnosis, less advanced prostate cancer at diagnosis and a lower risk of fatal prostate cancer.

Spirituality/faith/prayer[11]

Spirituality is a common coping strategy, reducing anxiety and distress and improving quality of life, but it can also have the opposite effect. Spirituality can itself be influenced by the experience of prostate cancer.

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KEY POINTS

- **Up to 80 per cent of prostate cancer patients use complementary therapy and alternative medicine (CAM)**
- **CAM is marketed to prevent prostate cancer, shrink or contain prostate cancer, or alleviate side-effects of conventional treatment**
- **CAM includes biological as well as mind/body therapies**
- **Evidence is limited and often inconsistent for most CAM modalities**
- **The best available evidence of effectiveness is for lycopene, soy products and exercise**
- **Patients have high confidence in CAM**
- **CAM is used not solely for cure, but also as a coping strategy**
- **Patients frequently do not disclose their use of CAM unless specifically asked**

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