Lycopene for the Prevention and Treatment of Prostate Disease

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Abstract

Benign prostatic hyperplasia (BPH) and prostate cancer are common diseases of the prostate gland. BPH is commonly treated by pharmaceutical products, which commonly improve symptoms but are often off-set by adverse events including erectile dysfunction, which affect quality of life. Similarly, a variety of treatment options exist for the treatment of prostate cancer. The applicability of these prostate cancer treatments is reliant on stage of disease. Whilst effectiveness of prostate cancer treatments may vary, common adverse effects include erectile dysfunction, incontinence and lower quality of life. Early evidence from systematic reviews has suggested that diet and lifestyle factors may be beneficial in reducing the risk of cancer. Lycopene, a member of the carotenoid family, found commonly in red pigmented fruit and vegetables has been established as having strong antioxidant and pro-oxidant properties. This chapter examines the current evidence on the use of lycopene as a preventive agent for prostate disease.

Contents

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1 What is Prostate Disease?

Benign prostatic hyperplasia (BPH) and prostate cancer are common diseases of the prostate gland. Both BPH and prostate cancer are generally recognised as common diseases that affect men as they age. BPH is defined as a non-malignant enlargement of the prostate gland that causes resistance and obstruction of the urethra, leading to lower urinary tract symptoms (LUTS) (Wilt and Ishani 1998; McVary et al. 2011). Symptoms commonly include increased urinary frequency, nocturia, urinary incontinence, and trouble with voiding (slow and/or weak stream and sense of incomplete emptying of the bladder) (Coyne et al. 2009).

Approximately 50 % of men aged over 50 years of age will experience BPH-related symptoms, rising to 90 % of men aged over 80 years (Berry et al. 1984; Schwarz et al. 2008). After lung cancer, prostate cancer is the most commonly diagnosed cancer in men worldwide, and a leading cause of mortality in men (Jemal et al. 2011). Prostate cancer incidence varies worldwide, with prostate cancer incidence the highest in developed countries across Europe, North American and Australia (Jemal et al. 2011). Greater uptake of prostate cancer screening and dietary intake have been postulated as potential reasons for this geographical variability, although limited evidence currently exists to substantiate these suggestions (Ilic et al. 2013).

2 How is Prostate Disease Treated?

BPH is primarily treated by pharmaceutical products such as alpha-blockers and 5-alpha reductase inhibitors. Evidence from systematic reviews indicates that when used in combination, or alone, such pharmaceutical interventions may improve urine flow, nocturia and quality of life (Tacklind et al. 2010; Wilt et al. 2008). These benefits are offset by adverse events associated with these pharmaceutical interventions including increased rates of erectile dysfunction, decrease in libido, hypotension and dizziness (Tacklind et al. 2010; Wilt et al. 2008). Surgical intervention via a transurethral resection of the prostate (TURP) is successful in treating BPH and LUTS in 75 % of men, but is also associated with greater morbidity than pharmaceutical intervention including blood loss, infection and erectile dysfunction (Hoffman et al. 2000).

A variety of prostate cancer treatments are available including radical prostatectomy (robotic assisted or laparoscopic), radiotherapy (external beam or brachytherapy), androgen therapy or active surveillance or observation alone (Heidenreich et al. 2011). However, the applicability of each therapy is reliant upon the stage of disease—for example, active surveillance may be utilised when the cancer is localised to the prostate gland and is assessed as non-aggressive, but not in more aggressive tumours (i.e. Gleason 8+). Common adverse events associated with these treatments (apart from active surveillance) include erectile dysfunction, urinary incontinence, blood loss, infection and negative impact upon quality of life through psychosocial aspects (Heidenreich et al. 2011).

3 Can Diet and Lifestyle Changes Prevent Prostate Disease?

The World Cancer Research Fund (WCRF) reported in 2007 that a high fruit and vegetable intake may be beneficial in reducing the risk of cancer (World Cancer Research Fund/American Institute for Cancer Research 2007). This recommendation was based on the assumption that most cancers will only become identifiable years after the initial DNA damage has occurred; with diet and nutrition possible modifying factors (World Cancer Research Fund/American Institute for Cancer Research 2007). The WCRF expert panel concluded that foods that contain lycopene, selenium, vitamin E and soy have a potential protective role against cancer (World Cancer Research Fund/American Institute for Cancer Research 2007). Current evidence from systematic reviews of randomised controlled trials investigating the anti-neoplastic effects of selenium, vitamin E, zinc and beta-carotenes concludes that there is no conclusive evidence to support the claim that these products prevent or decrease the incidence of prostate disease (Dennert et al. 2011; Stratton and Godwin 2011).

Lycopene is a member of the carotenoid family, found most commonly in fruit and vegetables that contain red pigmentation, such as tomatoes, strawberries and watermelon (Chan et al. 2005). Unlike beta-carotene, another member of the carotenoid family, lycopene has been established as having strong antioxidant and pro-oxidant properties that may be useful in protecting DNA from oxidation and cancer-related mutations (Wertz et al. 2004; Wang 2012).

Several pathways in which lycopene may prevent cancer have been postulated. It has been suggested that lycopene inhibits the propagation of cancer cells at the G0-G1 cell cycle phase (Matsushima et al. 1995). Inhibition of prostate cancer cell growth has been linked with the interaction of androgen steroid hormones promoting the biological action of lycopene in reducing the expression of 5-alpha reductase-1 (Wang 2012). It has also been suggested that prevention may occur through the upregulation of tumour suppressor proteins and increased gap-junctional intercellular communication through the insulin-like growth factor (IGF) 1 pathway (Karas et al. 2000).

4 Can Lycopene Assist in the Prevention and Treatment of Prostate Disease?

A number of systematic reviews on before and after, case–control, cohort and RCTs have been performed—all with varying conclusions about the efficacy of lycopene in the prevention of prostate disease (Haseen et al. 2009; Etminan et al. 2004; Ilic et al. 2011; Ilic and Misso 2012). A systematic review reporting the results of five before and after studies on lycopene for the prevention and treatment of prostate disease identified that three out of the five studies reported a significant decrease in prostate-specific antigen (PSA) levels post-intervention (Haseen et al. 2009). Only one of the before and after studies reported a significant reduction in

Table 1 Results from pooled analysis of case–control and cohort studies for lycopene supplementation in the prevention of prostate cancer

Study type	Number of studies	Pooled relative risk (95 % confidence intervals)
Case–control	7	RR = 0.97 (0.86, 1.09) (low or moderate intake of lycopene) RR = 0.98 (0.83, 1.16) (high intake of lycopene)
Cohort studies	3	RR = 1.00 (0.92, 1.08) (low or moderate intake of lycopene) RR = 0.84 (0.75, 0.95) (high intake of lycopene)
All studies	10	RR = 0.99 (0.93, 1.06) (low or moderate intake of lycopene) RR = 0.89 (0.81, 0.98) (high intake of lycopene)

Data in table adapted from Etminan (Etminan et al. 2004)

pain—with the same study reporting a significant improvement in LUTS (Haseen et al. 2009; Ansari and Gupta 2003).

A systematic review of observational studies identified 11 case–control and 10 cohort studies investigating lycopene as a preventive agent for prostate disease (Etminan et al. 2004). Pooled analysis of the case–control and cohort studies demonstrated little benefit from lycopene supplementation in the prevention of prostate cancer (Table 1) (Etminan et al. 2004). However, a pooled analysis of all observational studies identified in that systematic review suggests a potential benefit in the consumption of high concentrations of lycopene for potentially preventing prostate cancer.

Systematic reviews of RCTs in 2011 and 2012 identified eight RCTs that have investigated the merits of lycopene in the prevention and treatment of BPH and/or prostate cancer (Ilic et al. 2011; Ilic and Misso 2012). Meta-analysis of two studies identified a significant decrease in PSA levels in men allocated to receive lycopene Mean difference (MD) = −1.58 (95 %CI −2.61, −0.55) (Ilic and Misso 2012). Further meta-analysis of two studies within the review identified no significant reduction in the incidence of BPH (RR = 0.92 (95 %CI 0.66, 1.29)) or prostate cancer diagnosis (RR = 0.95 (95 %CI 0.63, 1.44)) between men receiving lycopene supplementation or placebo (Ilic and Misso 2012). No adverse events were reported across the systematic reviews regarding ingestion of lycopene (Haseen et al. 2009; Etminan et al. 2004; Ilic et al. 2011; Ilic and Misso 2012).

5 What is the Future of Lycopene?

Based on evidence from observational and experimental studies, it is apparent that there is no substantial evidence to either support, or refute, the claim that lycopene is effective in the prevention and treatment of prostate disease (be it BPH or prostate cancer). A high intake of lycopene has been associated with a significant decrease in prostate cancer incidence in a pooled analysis of observational studies (Etminan et al. 2004).

The ideal daily intake or lycopene is unknown, although it has been suggested that a daily intake of 6 mg is sufficient to achieve its antioxidant properties (Porrini and Riso 2005). The common dose of lycopene in published RCTs has ranged from 15 to 30 mg, and yet this higher dose of lycopene was not associated with a decrease in the incidence of BPH or prostate cancer. However, the evidence base on this issue is limited as the meta-analysis is based on only two studies. Furthermore, the follow-up period of RCTs to date has been short, ranging from 4 weeks to 2 year follow-up periods (Ilic and Misso 2012). Conversely, the pooled evidence from observational studies would suggest a small, but significant, decrease in the incidence of prostate cancer in men with a high intake of lycopene. However, drawing such positive inferences observational data should be cautiously given the potential for recall and response bias, as well as confounding effects, in case–control and cohort studies.

In the USA, it has been estimated that more than 50 % of consumers regularly consume dietary supplements, with this figure rising to over 70 % of consumers aged above 70 years (Bailey et al. 2011). The evidence would currently suggest that lycopene supplementation does no harm, but it also has limited benefits. Although it could be argued that with the large amounts of consumers buying such supplements, the hidden harm is the cost associated with purchasing a therapy that has no proven benefit. Studies that have investigated the merits of lycopene for the prevention and treatment of prostate disease vary in their methodological quality and dosage. Given the lack of clinical evidence, there is an urgent need for a well-designed RCT, with long-term follow-up of participants, to determine the efficacy of lycopene for the prevention and treatment of prostate disease.

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