EARLY CONSUMPTION OF LYCOPENE AND REDUCED INCIDENCE OF PROSTATE CANCER- A SYSTEMATIC REVIEW

Eldhose George[1], Nevin Joseph[1], Alfin Baby[1], Gopikrishnan T.S[1], Anjali Shaju[1], and Merrin Joseph[1]

[1]Nirmala College of Pharmacy

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Abstract

Prostate cancer and benign prostatic hyperplasia (BPH) are two common diseases of the prostate gland. Pharmaceutical drugs are widely used to treat BPH, which enhance symptoms but are also accompanied by side effects such as erectile dysfunction, which have a negative impact on quality of life. Prostate cancer, like other cancers, has a wide range of treatment options. The effectiveness of these prostate cancer therapies is determined by the stage of the disease. While the efficacy of prostate cancer therapies varies, erectile dysfunction, incontinence, and a lower quality of life are all common side effects. Diet and lifestyle factors can be helpful in lowering the risk of cancer, according to preliminary evidence from systematic reviews. Lycopene, a carotenoid found in a variety of red-colored fruits and vegetables, has been shown to have powerful antioxidant and pro-oxidant properties. The existing evidence on the use of lycopene as a prostate disease prevention agent is examined in this chapter.

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Eldhose Elias George[1], Nevin Joseph[1], Alfin Baby[1], Gopikrishnan T.S[1], Anjali Shaju[1] , Dr.Merrin Joseph [2*]

[1] Pharm D Interns, Nirmala College of Pharmacy, Muvattupuzha, Kerala University of Health Sciences, Thrissur, PIN 686661

[2*] Assistant Professor, Department of Pharmacy Practice, Nirmala College of Pharmacy, Muvattupuzha, Kerala University of Health Sciences, Thrissur, PIN 686661

CORRESPONDING AUTHOR:

Dr. Merrin Joseph, Department of Pharmacy Practice, Nirmala College of Pharmacy, Muvattupuzha, Kerala University of Health Sciences, Thrissur, Kerala, India, 686661

E-Mail ID: merrin.nirmalacp@gmail.com

Phone No.: +91 8848264103

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ABSTRACT

Prostate cancer and benign prostatic hyperplasia (BPH) are two common diseases of the prostate gland. Pharmaceutical drugs are widely used to treat BPH, which enhance symptoms but are also accompanied by side effects such as erectile dysfunction, which have a negative impact on quality of life. Prostate cancer, like other cancers, has a wide range of treatment options. The effectiveness of these prostate cancer therapies is determined by the stage of the disease. While the efficacy of prostate cancer therapies varies, erectile dysfunction, incontinence, and a lower quality of life are all common side effects. Diet and lifestyle factors can be helpful in lowering the risk of cancer, according to preliminary evidence from systematic reviews. Lycopene, a carotenoid found in a variety of red-colored fruits and vegetables, has been shown to have powerful antioxidant and pro-oxidant properties. The existing evidence on the use of lycopene as a prostate disease prevention agent is examined in this chapter.

KEY WORDS:

Lycopene, Prostate Cancer, anticancer, carotene, diet, nutraceutical

INTRODUCTION

The prostate gland is a walnut-sized gland situated behind the base of the penis, in front of the rectum, and below the bladder, covering the urethra; it is only found in males, as everybody knows. The prostate gland's primary function is to produce seminal fluid, a liquid found in sperm that protects, supports, and transports sperm. When a cell divides rapidly even after the signal for cell proliferation has been turned off, a tumour or neoplasm is said to have emerged. Prostate Cancer is what occurs when this happens to the prostate gland (PCa). Prostate cancer is the second most widely diagnosed cancer in men worldwide, after lung cancer, and it is also the leading cause of death in men. While three well-established risk factors have been identified: increasing age, race, and heredity, the factors that decide the risk of developing clinical PCa remain unknown. Greater uptake of prostate cancer screening and dietary intake have been suggested as possible explanations for this geographic variation, but there is currently insufficient evidence to back up these claims. Prostate cancer is predominantly a condition that affects men over the age of 65.,[1] which now is the fifth most common cancer when compared with others' incidence. Recent studies show that 1 in 350 men under the age of 50 years will be diagnosed with prostate cancer Frequent urination, sluggish or interrupted urine flow, the need to struggle to empty the bladder, the need to urinate regularly at night, blood in the urine, new onset of erectile dysfunction, pain or burning during urination, which is much less normal, discomfort or pain while sitting, caused by an enlarged prostate, and so on are some of the symptoms and signs of prostate cancer. Prostate cancer is caused by a combination of factors, the most common of which are age and family background. Familial prostate cancer is a form of prostate cancer that runs in families and accounts for about 20% of all prostate cancers. A combination of common genes and shared environmental or lifestyle factors causes this form of prostate cancer to grow. The most dangerous element is age, which has a direct proportionality. Prostate cancer risk rises with age, particularly after the age of 50. Prostate cancer is diagnosed in approximately 60% of men aged 65 and up. Diabetes mellitus,[2] height, weight, and obesity,[3] smoking habit, physical activity,[4] body mass index (BMI),[5] and vasectomy are among the other factors. Routine examinations, such as a PSA test every 3 to 6 months or a DRE at least once a year, or a prostate biopsy within 6 to 12 months, followed by a biopsy every 2 to 5 years, can help diagnose or prevent prostate cancer. PSA is the most widely used diagnostic test of all of these since the correlation is well established and accepted; that is, it rises with age.[6]

Radical prostatectomy (robotic aided or laparoscopic), radiotherapy (external beam or brachytherapy), androgen therapy, or active monitoring or observation alone are all options for prostate cancer care. Erectile dysfunction, urinary incontinence, blood loss, infection, and a detrimental effect on quality of life through psychosocial aspects are all common adverse events associated with these procedures (apart from active surveillance). Because of the scarcity of randomised controlled trials in this area, it is generally difficult to say that one treatment is obviously superior to another.[7] Androgen deprivation therapy (ADT), radiation therapy (RT), ablative therapies, chemotherapy, and recently emerging immunotherapies are all nonsurgical treatments for prostate cancer. Depending on the clinical situation, these methods may be used individually or in combination.[8]

METHODS

PUBMED and SCIENCEDIRECT database and bibliographies of retrieved articles were searched. Studies investigating the relationship between Lycopene and Prostate Cancer were included in the review. Potential sources of heterogeneity between studies were explored and publication bias was evaluated.

DISCUSSION

DIET AND LIFESTYLE MODIFICATIONS IN PROSTATE CANCER

According to the World Cancer Research Fund (WCRF), a high fruit and vegetable intake serve to minimise cancer risk (World Cancer Research Fund/American Institute for Cancer Research 2007). This suggestion was based on the premise that most cancers would not be detectable until years after the initial DNA damage has occurred, with diet and metabolism as potential moderators (World Cancer Research Fund/American Institute for Cancer Research 2007). The World Cancer Research Fund/American Institute for Cancer Research expert panel concluded that foods containing lycopene, selenium, vitamin E, and soy have the ability to protect against cancer (World Cancer Research Fund/American Institute for Cancer Research 2007). The current findings from systematic studies of randomised clinical trials examining the anti-neoplastic efficacy of selenium, vitamin E, zinc, and betacarotenes, they concludes that there is no definitive evidence to support the argument that these drugs deter or reduce prostate cancer incidence.. Lycopene is a carotenoid present in red-pigmented fruits and vegetables such as tomatoes, strawberries, and watermelon. Unlike other member of the carotenoid family, like beta-carotene, lycopene has been shown to have good antioxidant and pro-oxidant effects, which could be useful in shielding DNA from oxidation and cancer-related mutationsSeveral mechanisms by which lycopene can protect against cancer have been proposed. Lycopene is thought to prevent cancer cells from propagating during the G0-G1 cell cycle process. The association of androgen steroid hormones that promote the biological activity of lycopene in reducing the expression of 5-alpha reductase-1 has been related to the inhibition of prostate cancer cell development. Upregulation of tumour suppressor proteins and enhanced gap-junctional intercellular connectivity through the insulin-like growth factor (IGF) 1 pathway have also been proposed as potential preventive mechanisms. Prostate cancer (PCa) occurrence varies widely by region, owing to dietary variations. As previously reported using animal models, nutrients such as fat, protein, carbohydrates, vitamins (vitamin A, D, and E), and polyphenols can influence PCa pathogenesis and progression; however, clinical trials have reported mixed results for almost all nutrients. These nutrients' effects can be manifested through a variety of pathways, including inflammation, antioxidant effects, and sex hormone action. PCa risk is also influenced by dietary trends such as the Western and Prudent patterns. According to recent research, the intestinal microbiota plays a role in tumorigenesis in some organs. Dietary structure and way of life have a strong and significant impact on gut bacteria. In human trials, the concentration of unique gut bacteria increased in PCa patients. Although there are few research on the topic, diet and nutrition can have an impact on PCa, which may be regulated by the gut microbiota. A dietary pattern intervention may help to avoid PCa. Thus, a dietary pattern-based intervention may aid in the prevention of PCa.[9]

LYCOPENE- ITS ROLE, MECHANISM AND EFFECT IN PCa

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. 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. Only one of the before and after studies reported a significant reduction in Lycopene for the Prevention and Treatment of Prostate Disease 111 pain—with the same study reporting a significant improvement in LUTS. A systematic review of observational studies identified 11 case–control and 10 cohort studies investigating lycopene as a preventive agent for prostate disease. Pooled analysis of the case–control and cohort studies demonstrated little benefit from lycopene supplementation in the prevention of prostate cancer. 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. 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. No adverse events were reported across the systematic reviews regarding ingestion of lycopene.

Lycopene is a bright red carotenoid (a carotenoid without Vitamin A activity) hydrocarbon found in tomatoes and other red fruits and vegetables, such as red carrots, watermelons, grapefruits, and papayas with sufficient and ample antioxidant and anti-cancer properties. Lycopene has been linked to many other health benefits which ranges from heart health to protection against sunburns and so on. The health related effects were known from early 1990s. Test-tube studies which lasted till 2016 as per those early data showed that the nutrient may slow down the growth of breast and prostate cancers by limiting tumour growth. This 23-year study in more than 46,000 men carefully examined the link between lycopene and prostate cancer in more detail. And they found that men who consumed at least two servings of lycopene-rich tomato sauce per week were 30% less likely to develop prostate cancer than those who ate less than one serving of tomato sauce per month [10]

Another double-blind placebo-controlled study concluded that after 28 days of using lycopene juices, the concentration of lycopene in serum increased to 80.2 % which was higher when compared with the placebo. This result leads to a conclusion that lycopene reduces DNA damages, oxidative stress, and risk of disease [11]. The analytical results of a study men population who were newly diagnosed with prostate cancer who received lycopene twice a day for 3 weeks, showed that lycopene effectively decreases the risk and growth of prostate cancer cells.

Lycopene's ability to prevent cancer is mediated by a number of direct mechanisms, including signal regulation, cell cycle arrest, induction of apoptosis, and changes in enzymes and antioxidants, all of which prevent cancer cells from spreading, invading, and angiogenesis[12-14]. Lycopene decreases or suppresses the carcinogenic effects of Rb (retinoblastoma protein) and p53 (tumour protein p53) proteins on phosphorylation, and arrests the cell cycle by inhibiting the expression of cyclin D1 in the G0/G1 phases, according to new research [15]. Lycopene has been shown to inhibit the growth of normal human PrEC (prostate epithelial cells) in cell culture medium and to affect the cell junction between cancer cells in in vitro studies [15]. Higher serum levels of IGF-1 (Insulin-Like Growth Factor 1) are linked to prostate and breast cancer, and lycopene can slow cell cycle progression by interfering with IGF-1 mitogenic pathways [16, 17]. Lycopene has been shown to regulate the differentiation of intrathymic T cells, which can suppress tumour cell development in SHN virgin mice models[18]. Lycopene inhibited the phosphorylation of GSK-3 (glycogen synthase kinase-3), AKT, and ERK1/2 (extracellular signal-regulated protein kinases 1 and2), which interfered with PI3K (phosphatidylinositol-3-kinase)/AKT and MAPK (mitogen-activated protein kinase)/ERK signalling pathways in in-vitro studies on HT-29 cells (human colon cancer cell line). Lycopene also resulted in significant reduction of nuclear proteins such as AP-1 (Activator protein-1) and beta-catenin [19]. Lycopene inhibited cell proliferation and induction of apoptosis in PC3 cells by lowering the expression of AKT2 and increasing the expression of miR let-7f1 (mi-croRNA Lethal-7) [20]. Evaluations of the effects of lycopene and beta-carotene on AtT20 cells (Musmusculus pituitary tumour) have shown a negative relation to regulating the aggressive form of AtT20 cells. These substances can lower the expression of ACTH (Adrenocorticotropic hormone) and Skp2 (S-phase kinase-associated protein2) while increasing the expression of p27kip1 (Cyclin-dependent kinase inhibitor) and phosphorylated connexin 43. Lycopene can block the inter-cellular gap junction communications and thus regulate cancer progression [21, 22] as these Gap Junction communication of cancer cells are responsible for invasion and allows a metastatic type of cancer.

FUTURE OF LYCOPENE

It appears that there is no substantial evidence to support or refute the argument that lycopene is successful

in the prevention and treatment of prostate disease, based on evidence from clinical and laboratory research (be it BPH or prostate cancer). In a pooled study of observational trials, a high intake of lycopene was linked to a substantial reduction in prostate cancer incidence. While it has been proposed that a daily intake of 6 mg is adequate to maintain lycopene's antioxidant properties, the optimal daily intake remains uncertain.. The most frequent dosage of lycopene used in recorded RCTs was 15 to 30 mg, but this higher dose was not linked to a reduction in the occurrence of BPH or prostate cancer. However, since the meta-analysis is focused on only two articles, the evidence base on this topic is small.Furthermore, RCT follow-up times have been brief in the past, spanning from four weeks to two years. Conversely, retrospective data suggests a slight but substantial reduction in the prevalence of prostate cancer in men who consume a large amount of lycopene..In case–control and cohort research, though, drawing such optimistic inferences from qualitative evidence should be done with caution due to the possibility of memory and reaction bias, as well as conflicting results. In the United States, it is projected that more than half of customers take dietary supplements on a daily basis, with this number increasing to more than 70% for those over the age of 70. Supplementing with lycopene does not seem to cause damage, but it does have certain benefits. And it may be claimed that the latent harm is the expense of purchasing a therapy that has not been shown to be beneficial, given the vast number of people who purchase those supplements. The methodological consistency and dosage of studies that looked at the benefits of lycopene for the prevention and treatment of prostate cancer differed. Given the scarcity of clinical data, a well-designed RCT with long-term participant follow-up is urgently needed to assess the effectiveness of lycopene in the prevention and treatment of prostate disease.

Several studies have looked into the anti-cancer effect, non-toxicity, efficacy, and preventive or therapeutic functions of lycopene. We gathered data on lycopene's anti-cancer, anti-progressive, and apoptotic effects on prostate cancer in the current review. Clinical trials show that this adjunctive dietary can be used indefinitely to treat various types of cancers, including prostate cancer in men. In both in-vivo and in-vitro studies, lycopene was found to effectively inhibit prostate cancer cell progression and proliferation, arrest in-cell cycle, and trigger apoptosis.. Lycopene has also been shown to be able to modulate signalling channels and their proteins in the treatment and prevention of prostate cancer.[23]Tomato extracts are linked to a lower risk of prostate cancer when consumed often.·[24] Tomatoes are thought to play a minor role in the treatment of prostate cancer. To decide the form and quantity of tomato products that have the potential to prevent prostate cancer, further research is required.·[25]

CONCLUSION

In conclusion, our dose–response meta-analysis found a significant linear dose–response relationship between lycopene intake and PCa risk, but a significant nonlinear dose–response relationship between circulating concentrations and PCa risk. To substantiate these hypotheses in populations with high lycopene intake and circulating concentrations, more high-quality study evidence is required..[26]

ABBREVIATIONS

PCa: Prostate Gland Carcinoma

BPH: Benign Prostate Hyperplasia

ADT: Androgen deprivation therapy

RT: Radiation therapy

IGF: Insulin-like growth factor

RCT: Randomised Control Trial

Rb: retinoblastoma protein

PrEC: prostate epithelial cells

ERK1/2: extracellular signal-regulated protein kinases 1 and2

PI3K: phosphatidylinositol-3-kinase

MAPK: mitogen-activated protein kinase

AP-1: Activator protein-1

miR let-7f1: mi-croRNA Lethal-7

ACTH: Adrenocorticotropic hormone

Skp2 : S-phase kinase-associated protein2

CONFLICT OF INTEREST

Authors have no conflict of interest to declare.

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