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TOPIC PAPER

The effect of diet on BPH, LUTS and ED

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Abstract

Objective Benign prostatic hyperplasia (BPH) and erectile dysfunction (ED) are common conditions that increase in the aging population. Several environmental factors have been linked to the development and progression of BPH and ED. Several studies have shown potential direct and indirect influences of several micronutrients and macronutrients on the risk of developing these conditions. We reviewed the available published literature of the effect of diet on BPH and ED.

Methods A comprehensive search was performed to identify studies that evaluated how diet affected males with BPH and ED. Searches were run on July 5th, 2018 in the following databases: Ovid MEDLINE®; Ovid EMBASE; and The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL). There were no language restrictions, publication date restrictions, or article type restrictions on the search strategy.

Results We retrieved a total of 1670 results across all databases. After removing any duplicated results, 2 independent reviewers screened a total of 1325 citations. A total of 35 articles were selected for inclusion in this review. Diet is an important factor affecting the risk of development of BPH and ED. Several studies have shown the effect of dietary interventions for BPH and ED.

Discussion A better understanding diet and its relative effects on the development, treatment and prevention of these diseases are an important area of further research for the given aging male population.

Keywords Diet · BPH · ED · LUTS

Introduction

Benign prostatic hyperplasia (BPH) and erectile dysfunction (ED) are common conditions that increase in the aging population [1–9]. BPH is characterized by the increased proliferation of epithelial and stromal cells in the transitional zone of the prostate [1, 10]. Eventually, BPH results in compression of the urethra, known as bladder outlet obstruction (BOO) and can present as lower urinary tract symptoms (LUTS) [10]. Furthermore, BPH commonly presents with the development of erectile dysfunction (ED) [2, 11]. ED dysfunction is the inability to achieve or maintain an erection sufficient for a satisfactory sexual intercourse [11]. ED may be multifactorial and results from psychological, neurological, hormonal, arterial, or cavernosal impairment [12].

Age has been correlated with the incidence of BPH and ED [1–9]. Approximately, 50% of men older than 50 have evidence of BPH, while the proportion of men with BPH increases to > 80% as they approach their eighth decade of life [10, 13]. Several environmental factors have been linked to the development and progression of BPH and ED [10, 11, 14, 15]. Several studies have shown potential direct and indirect influences of several micronutrients and macronutrients on the risk of developing these conditions [10, 11, 14, 15]. In this review, we will review the effect of diet on BPH and ED.

Methods

This review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [7].

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Search strategy

A comprehensive search was performed to identify studies that evaluated how diet affected males with BPH and ED. Searches were run on October 19th, 2018 in the following databases: Ovid MEDLINE®; Ovid EMBASE; and The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL). There were no language restrictions, publication date restrictions, or article type restrictions on the search strategy.

Study selection

We retrieved a total of 1670 results across all databases. After removing any duplicated results, 2 independent reviewers screened a total of 1325 citations. Discrepancies were resolved by consensus. Titles and abstracts were reviewed against pre-defined inclusion/exclusion criteria. Articles considered for inclusion involved RCTs/controlled trials/cohort studies conducted with animal or human males, with BPH or ED. Excluded studies were those that did not access diet in these condition.

We pulled full text to screen for eligibility in a second round for a number of selected studies. We used reference lists for articles selected for inclusion in the study for additional references; an additional xx articles were screened. A total of 35 articles were selected for inclusion in this review.

Diet and BPH/LUTS

Modifiable lifestyle factors have been overwhelmingly associated with the development of BPH [10, 16]. Diet is thought to contribute to various prostatic diseases from BPH to prostate cancer [17, 18]. In a study assessing the influence of diet on prostate cancer development, the incidence of prostate cancer was found to be 26-fold higher in Americans compared to their Chinese counterparts eating a plant-based diet and further found that newly emigrated Chinese–Americans had intermediate incidence rates lower than Americans but higher than those in China [19]. The increase in prostate cancer incidence was associated with dietary fat [19]. The Prostate Cancer Prevention Trial (PCPT), which enrolled over 18,800 men over the age of 55, identified a weak association between BPH and a variety of supplements including lycopene, zinc or vitamin D, but antioxidants had no association with risk for BPH [20]. However, the trial showed a high consumption of fat and red meat or low consumption of protein and vegetables were associated with an increased risk of BPH [20].

Similarly, in a prospective study of 32, 265 men in the health profession, of whom 6092 had BPH, found a reported lower consumption of vegetables in men with BPH compared to their healthy counterparts [21]. Interestingly, fruits (both as a group and specific species such as *Serenoa repens* combined with nettle root *Urtica dioica*) were not correlated with risk for BPH in this and other studies. This finding is echoed in both AUA and EAU guidelines [21–23], which do not support their use in the treatment of BPH. However, in a more recent study of 184 men with BPH and 246 controls, Lagiou et al. interviewed participants and administered a food frequency questionnaire and found over 3 years an inverse relation between reported consumption of fruits containing high levels of β-carotene, lutein or vitamin C and BPH risk [24]. A better understanding of the micro and macro-nutrients providing the beneficial effects of select fruits may prevent or mitigate the onset of BPH.

This same study by Lagiou et al. further showed that high fat-content food such as butter and margarine is associated with an increased risk of BPH [24]. This may be due to the pro-inflammatory effects of a high fat diet, which results in prostate inflammation, hypoxia and tissue remodeling [25]. Nonetheless, flaxseed has been shown to reduce epithelial cell hyperplasia in prostate cell-induced BPH rats [26], suggesting that different fat types and content can differentially affect BPH risk and development (Table 1).

In a randomized, double-blind, placebo-controlled clinical study, Zhang et al. administered placebo, 300, or 600 mg/day of the flaxseed extract secoisolariciresinol diglucoside (SDG) to 87 men with BPH. Over a 4-month period, International Prostate Symptom Score (IPSS) decreased, Quality of Life score (QOL) improved and LUTS grade improved from "moderate/severe" to "mild". These changes show that flaxseed may be of therapeutic value. In fact, the authors concluded that its therapeutic efficacy is comparable to current medical therapies such as α_{1A}-adrenoceptor blockers and 5α-reductase inhibitors [27].

Pumpkin seed extract has been found to have no benefit when compared to placebo after 12 months of use [28]. A study of 1431 men aged 50–80 years were randomized to either pumpkin seed (5 g b.i.d.), capsules with pumpkin seed extract (500 mg b.i.d.) or a placebo group were found to have similar response rate (decrease in IPSS score of > 5 points) [28]. While this could be the result of an absent active compound in the extract, other potential explanations could be the use of a suboptimal dose.

In a prospective study of more than 18,000 men without LUTS at baseline, men with higher body mass index (BMI) as well as a higher total and abdominal fat were more likely to develop LUTS [29]. This suggests that lifestyle modifications, such as diet and exercise, can have a positive impact on LUTS. Other studies [30] have confirmed this link

Table 1 Dietary factors associated with increased, decreased or unchanged risk of BPH or ED development

	Decrease	Increase	Unchanged/unclear
BPH	Flaxseed ($p < 0.0001$) [26] Flaxseed extract (secoisolariciresinol diglucoside) ($p < 0.001$) [27] Fruit [24] Fruits rich in β-carotene (OR 0.87) [21] Fruits rich in lutein (OR 0.83) [21] Fruits rich in vitamin C (OR 0.89) [21] Plants [18] Protein ($p < 0.05$) [20] Vegetables (OR 0.87) [20], (HR = 0.68) [21] Vitamin D ($p = 0.048$) [20]	Lipid ($p < 0.05$) [20] Red meat (HR = 1.38) [20]	Antioxidants [20] Fruits (OR 1.00–1.06) [21] Lycopene ($p = 0.056$) [20] Pumpkin seed extract (OR 1.06) [28] Zinc ($p = 0.310$) [20]
ED	Diet-induced weight loss [37] Flavonoids (RR = 0.89) [47], (OR = 0.93) [48] Flavone (RR = 0.91) [47], (OR = 0.83) [47, 48] High-protein low-fat diet [37] Mediterranean diet ($p = 0.01$) [40], (HR = 0.44) [40, 41] Nuts (> 2 times/week) (OR = 0.41) [49] Vegetables (> once/day) (OR = 0.47) [49]	Decaffeinated coffee (HR = 1.37) [50] Mediterranean diet ($p < 0.05$) [46]	Total or caffeinated coffee (HR = 1.00) [50]

between diet and metabolic syndrome, which increases the risk for LUTS.

Diet and ED

It is estimated that approximately 322 million men will be affected with ED by 2025 [31]. Like BPH, the prevalence of ED increases with age affecting 1–10% of men younger than 40 years of age but 50–100% of men 70 years or older [31]. ED can result from a pro-inflammatory state causing endothelial cell damage and decreased nitric oxide (NO) necessary for an erection [32–35]. In addition to age, risk factors for ED include cardiovascular disease, physical inactivity, obesity, metabolic syndrome and diet [31, 36].

Diet can have profound effects on ED. Diet-induced weight loss in 31 abdominally obese, type 2 diabetic men has been shown to result in rapid improvements of sexual and endothelial function, as measured by International Index of Erectile Function (IIEF-5) score and brachial artery flow-mediated dilatation (FMD) [37]. A high-protein, low-fat diet has been shown to reduce inflammation and maintain the beneficial effects from diet modifications for at least 1 year [37]. This has been confirmed in a high-fat diet-induced vasculogenic mouse model of ED through expressed microRNAs [38] and in a rabbit model of metabolic syndrome that showed that metabolic syndrome results in penile alterations and that it is itself modulated by the farnesoid X receptor (FXR) agonist obeticholic acid (OCA) [39]. These findings suggest that the beneficial effects following dietary modifications may be explained by an altered genome expression, providing a potential explanation for these findings.

Similarly, a prospective study enrolling 555 type 2 diabetic patients with type 2 diabetes randomly assigned to either a Mediterranean or high-fat diet have both shown that adherence to the Mediterranean diet has been shown to decrease the risk of ED, particularly in men with type 2 diabetes [40, 41]. This effect may be due to the anti-inflammatory, metabolic and cardiogenic benefits of the Mediterranean diet [42–44]. This has been confirmed in type-2 diabetic rats (induced by a high-fat diet) who have higher oxidative stress levels in penile but not the systemic vasculature [45].

The effect of flavonoids, and flavone in particular, which is high in nuts have been shown to decrease the risk for ED [47, 48]. In a study of 440 patients including 186 patients with ED, we found that consumption of nuts more than twice

a week and vegetables more than once a day was associated with a decreased risk of developing ED (as assessed by the International Index of Erectile Function) [49].

Conclusions

Diet is an important factor affecting the risk of development of BPH and ED. Several studies have shown the effect of dietary interventions for BPH and ED [39]. A better understanding diet and its relative effects on the development, treatment and prevention of these diseases are an important area of research given the aging male population.

Author contributions ME: data collection/management, data analysis, drafting of manuscript, critical revisions. DT: data collection/management, data analysis, drafting of manuscript, critical revisions. DE: data analysis, protocol development, drafting of manuscript, critical revisions. BC: data analysis, protocol development, drafting of manuscript, critical revisions.

Compliance with ethical standards

Conflicts of interest BC is a consultant for Allergan and Boston Scientific.

Research involving human participants and/or animals There were no human participants or animals used in this manuscript. This was a review article.

Informed consent Informed consent was not required in this manuscript. This was a review.

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