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## Daphal Supriya

Department of Pharmaceutics,  
Gourishankar Institute of  
Pharmaceutical Education &  
Research, Limb, Satara,  
Maharashtra, India

## Patil Anup

Department of Pharmaceutics,  
Gourishankar Institute of  
Pharmaceutical Education &  
Research, Limb, Satara,  
Maharashtra, India

## Charge Varsha

Department of Pharmaceutics,  
Gourishankar Institute of  
Pharmaceutical Education &  
Research, Limb, Satara,  
Maharashtra, India

## Correspondence

### Daphal Supriya

Department of Pharmaceutics,  
Gourishankar Institute of  
Pharmaceutical Education &  
Research, Limb, Satara,  
Maharashtra, India

## Benign prostatic hyperplasia with respect to diet

### Daphal Supriya, Patil Anup and Gcharge Varsha

#### Abstract

Benign Prostatic hyperplasia is not a cancerous, but it is a condition in a men in which prostatic gland enlarged. In which the gland pinches the urethra, so that the bladder becomes thicker, eventually bladder becomes weaker and lose the ability to empty completely. Usually it begins between the age of 30 -50 years. Testosterone is converted into Dihydrotestosterone in presence of 5- $\alpha$  reeducates inhibitor. Therapy with a 5 - $\alpha$  reeducates inhibitor markedly reduces the DHT content of prostate and in turn reduces the prostate volume. Generally low volume conc. of Testosterone is found in a Benign Prostatic Hyperplasia. Anatomically the median lobe is usually enlarged in BPH. The anterior lobe has little in the way of glandular tissue and is seldom enlarged carcinoma of the prostate typically occurring in posterior lobe. In Benign Prostatic Hyperplasia majority of growth occur in the TZ, In addition to this of classic areas, the peripheral zone of the prostate is also involved to a lesser extent. The clinical diagnosis of BPH is based on the history of Lower Urinary Tract Symptoms (LUTS), a digital rectal examination, and exclusion of other causes. The degree of LUTS does not necessarily correspond to the size of the prostate. The dynamic component of the BPH is controlled by a sympathetic nervous system i.e. Androgenic receptor blockers which are commonly used to alleviate these symptoms act by relaxing prostatic smooth muscle. To avoid such conditions some key nutrients will be involved such as Saw Palmetto, Pyeum, Zinc, Alanine, Glutamic acid /Glycine, Selenium, Starch. The explored possible diet and adaption of healthy life style will prevent the progression of BPH.

**Keywords:** dihydrotestosterone, carcinoma, 5- $\alpha$  reeducates inhibitor, sympathetic nervous system

#### 1. Introduction

Benign prostatic hyperplasia—also called BPH—is a condition in men in which the prostate gland is enlarged and not cancerous. Benign prostatic hyperplasia is also called benign prostatic hypertrophy or benign prostatic obstruction The prostate goes through two main growth periods as a man ages. The first occurs early in around age 25 and continues during most of a man's life. Benign prostatic hyperplasia often occurs with the second growth phase.<sup>[1]</sup> As the prostate enlarges, the gland presses against and pinches the urethra. The bladder wall becomes thicker. Eventually, the bladder may weaken and lose the ability to empty completely, leaving some urine in the bladder. The narrowing of the urethra and urinary retention—the inability to empty the bladder completely—cause many of the problems associated with benign prostatic hyperplasia. <sup>[2]</sup> The prostate is a walnut-shaped gland that is part of the male reproductive system. The main function of the prostate is to make a fluid that goes into semen. Prostate fluid is essential for a man's fertility. The gland surrounds the urethra at the neck of the bladder. The bladder neck is the area where the urethra joins the bladder. The bladder and urethra are parts of the lower urinary tract. The prostate has two or more lobes, or sections, enclosed by an outer layer of tissue, and it is in front of the rectum, just below the bladder. The urethra is the tube that carries urine from the bladder to the outside of the body. In men, the urethra also carries semen out through the penis. The cause of benign prostatic hyperplasia is not well understood; however, it occurs mainly in older men. Benign prostatic hyperplasia does not develop in men whose testicles were removed before puberty. For this reason, some researchers believe factors related to aging and the testicles may cause benign prostatic hyperplasia. Throughout their lives, men produce testosterone, a male hormone, and small amounts of estrogen, a female hormone. As men age, the amount of active testosterone in their blood decreases, which leaves a higher proportion of estrogen. Scientific studies have suggested that benign prostatic

prostatic hyperplasia may occur because the higher proportion of estrogen within the prostate increases the activity of substances that promote prostate cell growth.<sup>[2]</sup> Another theory focuses on dihydrotestosterone (DHT), a male hormone that plays a role in prostate development and growth. Some research has indicated that even with a drop in blood testosterone levels, older men continue to produce and accumulate high levels of DHT in the prostate. This accumulation of DHT may encourage prostate cells to continue to grow. Scientists have noted that men who do not produce DHT do not develop benign prostatic hyperplasia. Men with the following factors are more likely to develop benign prostatic hyperplasia:

- age 40 years and older
- family history of benign prostatic hyperplasia
- medical conditions such as obesity, heart and circulatory disease, and
- type 2 diabetes
- lack of physical exercise

Benign prostatic hyperplasia (BPH), also called benign enlargement of the prostate (BEP or BPE), adenofibromatous hyperplasia and benign prostatic hypertrophy (technically incorrect usage), is a benign (noncancerous) increase in size of the prostate. BPH involves hyperplasia of prostatic stromal and epithelial cells, resulting in the formation of large, fairly discrete nodules in the transition zone of the prostate. BPH involves hyperplasia (an increase in the number of cells) rather than hypertrophy (a growth in the size of individual cells), but the two terms are often used interchangeably, even among urologists. Although prostate specific antigen levels may be elevated in these patients because of increased organ volume and inflammation due to urinary tract infections, BPH does not lead to cancer or increase the risk of cancer<sup>[3]</sup>.

Prostatitis is a swelling of the prostate gland, usually caused by infection. The patient feels urgent needs to urinate frequently and has a burning sensation during benign prostatic hypertrophy (BPH) is an enlargement prostate among men after 50 years of age.<sup>[4]</sup> Among other considerations, a metabolite of testosterone called dihydrotestosterone is thought to contribute to the enlargement of the prostate in BPH. The condition is not malignant or inflammatory, but may lead to obstruction of the urethra, interfering with the flow of urine. This can increase frequency of urination, the need to urinate during the night, pain, and urinary tract infections. Since the main function of the prostate is to produce the seminal fluid, a man with BPH can become sterile, although his libido is not necessarily affected. On the other hand, the male with prostate problems often has serious problems with his sex life, primarily because of the urine retention situation and possible low grade infection<sup>[5]</sup>.

Conventional medical treatment may include antibiotics, drugs that inhibit the conversion of testosterone into dehydrotestosterone, sitz baths, bed rest, regular sexual release, massage of the prostate, avoiding alcohol and drinking excessive fluids, urinating as soon as the urge occurs, and surgery—in some cases. Alternative medical treatment may involve the use of herbs and key nutrients, including

Saw Palmetto, Pygeum, Zinc, Alanine/Glutamic Acid/Glycine, and Selenium.

BPH changes occur inevitably with advancing age but BPH disease, which we define as a life altering urinary condition requiring medical intervention, is predictable and preventable. BPH disease is most often associated with prostate enlargement (volume more than 30 ml). As BPH disease progresses, it is often associated with decreased urinary flow, worsening urinary symptoms and long-term complications, most notably AUR and the need for surgery. The concept of BPH disease prevention has evolved in the last 15 years, stimulated in large part by the advent of effective medical therapy in the early 1990.<sup>[5]</sup>

## 2. Signs and symptoms

BPH is the most common cause of lower urinary tract symptoms [LUTS], which are divided into Storage, voiding and symptoms which occurs after urination<sup>[6]</sup>. Include the need to urinate frequently, waking at night to urinate, urgency (compelling need to void that cannot be deferred) involuntary urination, including involuntary urination at night, or urge incontinence (urine leak following a strong sudden need to urinate).<sup>[7]</sup> Voiding symptoms include urinary hesitancy (a delay between trying to urinate and the flow actually beginning), intermittency (not continuous),<sup>[8]</sup> involuntary interruption of voiding, weak urinary stream, straining to void, a sensation of incomplete emptying, and terminal dribbling (uncontrollable leaking after the end of urination, also called post-micturition dribbling)<sup>[9, 10, 11]</sup>.

These seem- *Benign prostatic hyperplasia* atoms may be accompanied by bladder pain or pain while urinating, called dysuria<sup>[12]</sup>. Bladder outlet obstruction (BOO) can be caused by BPH. Symptoms are abdominal pain, a continuous feeling of a full bladder, frequent urination, acute urinary retention (inability to urinate), pain during urination (dysuria), problems starting urination (urinary hesitancy), slow urine flow, starting and stopping (urinary intermittence), and nocturia. BPH can be a progressive disease, especially if left untreated. Incomplete voiding results in residual urine or urinary stasis, which can lead to an increased risk of urinary tract infection. Symptoms can vary throughout the day with mild symptoms after standing or walking and more pronounced symptoms after lying down.<sup>[13]</sup>

## 3. Causes

DHT can act in an autocrine fashion on the stromal cells or in paracrine fashion by diffusing into nearby epithelial cells. In both of these cell types, DHT binds to nuclear androgen receptors and signals the transcription of growth factors that are mitogenic to the epithelial and stromal cells<sup>[14]</sup>. DHT is ten times more potent than testosterone because it dissociates from the androgen receptor more slowly. The importance of DHT in causing nodular hyperplasia is supported by clinical observations in which an inhibitor of 5 $\alpha$ -reductase such as finasteride is given to men with this condition. Therapy with a 5 $\alpha$ - reductase inhibitor markedly reduces the DHT content of the prostate and, in turn, reduces prostate volume and BPH symptoms. Testosterone promotes prostate cell proliferation, but relatively low levels of serum testosterone are found in patients with BPH. One small study has shown that medical castration lowers the serum and prostate hormone levels unevenly, having less effect on testosterone and dihydrotestosterone levels in the prostate<sup>[15]</sup>.

Studies indicate that dietary patterns may affect

development of BPH, but further research is needed to clarify any important relationship. Studies from China suggest that greater protein intake may be a factor in development of BPH. Men older than 60 in rural areas had very low rates of clinical BPH, while men living in cities and consuming more animal protein had a higher incidence. On the other hand, a study in Japanese- American men found a strong association with alcohol intake, but a weak association with beef intake. In a large prospective cohort study in the US (the Health Professionals Follow-up Study), investigators reported modest associations between BPH (men with strong symptoms of BPH or surgically confirmed BPH) and total energy and protein, but not fat intake. There is also epidemiological evidence linking BPH with metabolic syndrome (concurrent obesity, impaired glucose metabolism and diabetes, hypertriglyceridemia, low-density cholesterol and hypertension). Benign prostatic hyperplasia is an age-related disease. Disrepair-accumulation aging theory suggests that development of benign prostatic hyperplasia is a consequence of fibrosis and weakening of the muscular tissue in the prostate. The muscular tissue is important in the functionality of the prostate, and provides the force for excreting the fluid produced by prostatic glands. However, repeated contractions and dilations of myofibers will unavoidably cause injuries and broken myofibers. Myofibers have low potential of regeneration; therefore collagen fibres need to be used to replace the broken myofibers. Such misrepairs make the muscular tissue weak in functioning, and the fluid secreted in glands cannot be excreted completely. Then, the accumulation of fluid in glands increases the resistance of muscular tissue during the movements of contractions and dilations, and more and more myofibers will be broken and replaced by collagen fibres. Progressive fibrosis of muscular tissue and accumulation of fluid are important causes for the expanding of the prostate in benign prostatic hyperplasia [16, 17].

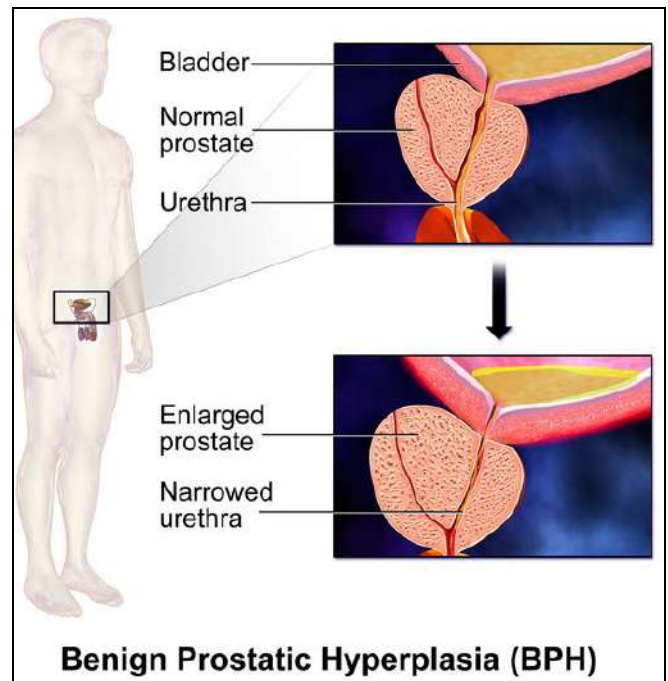
#### 4. Path physiology

Anatomically the median lobe is usually enlarged in BPH. The anterior lobe has little in the way of glandular tissue and is seldom Enlarged (Carcinoma of the prostate typically occurs in the posterior lobe – hence the ability to discern an irregular outline per rectal examination). The earliest microscopic signs of BPH usually begin between the age of 30 and 50 years old in the PUG, which are posterior to the proximal urethra.<sup>[18]</sup> In BPH, the majority of growth occurs in the TZ.<sup>[18]</sup> In addition to these two classic areas, the peripheral zone (PZ) of the prostate is also involved to a lesser extent.

#### 5. Diagnosis

BPH is diagnosed using the American Urological Association Symptom Index (AUA-SI), the internationally validated counterpart, the International Prostate Symptom Score (I-PSS)<sup>[19]</sup>, and more recently the UWIN score (urgency, weak stream, incomplete emptying, and nocturia).<sup>[20]</sup> An IPSS score <7 is “mildly symptomatic” and does not usually require pharmacotherapy. Screening and diagnostic procedures for BPH are similar to those used for prostate cancer<sup>[21]</sup>. The clinical diagnosis is based on a history of LUTS, a digital rectal exam, and exclusion of other causes. The degree of LUTS does not necessarily correspond to the size of the prostate. The differential diagnosis includes other

diseases of the bladder, urethra, and prostate such as bladder cancer, urinary tract infection, urethral stricture, urethral calculi (stones), chronic prostatitis and prostate cancer. Rectal examination (palpation of the prostate through the rectum) may reveal a markedly enlarged prostate, usually affecting the middle lobe. Blood tests are often performed to rule out prostatic malignancy. Elevated prostate specific antigen (PSA) levels need further evaluation, such as reinterpretation of PSA results, in terms of PSA density and PSA free percentage, rectal examination and transrectal ultrasonography. These combined measures can provide early detection. Ultrasound examination of the testicles, prostate, and kidneys is often performed, again to rule out malignancy and hydronephrosis<sup>[21]</sup>.



#### 6. Effect of age on BPH

Prostatic growth is believed to begin at approximately age 30. An estimated 50% of men have histologic evidence of BPH by age 50 and 75% by age 80; in 40–50% of these men, BPH becomes clinically significant.<sup>[4]</sup> BPH was one of the ten most prominent and costly diseases in men older than 50 years of age in a study in the United States.

Benign prostatic hyperplasia (BPH) is a common disease of older men, characterized by overgrowth of the prostatic epithelium and fibro muscular tissue of the transition zone and per urethral area and by obstructive and irritative lower urinary tract symptoms. Autopsy data indicate that anatomic or microscopic evidence of BPH is present in 40% and 90% of men aged 50–60 and 80–90 y, respectively. More than 200 000 transurethral resections of the prostate for BPH are performed annually in the United States. The etiology of BPH is unclear, but it appears to represent a multifactorial process involving both mechanical and dynamic components. Enlarged prostate, a mechanical or static component of BPH, is influenced mainly by androgens and can be pharmacologically treated with 5<sub>α</sub>-reductase inhibitors to block intraprostatic conversion of testosterone to the more potent dihydrotestosterone (DHT). Lower urinary tract symptoms due to a heightened tone of the prostatic smooth muscle, the dynamic component of BPH, are controlled by the sympathetic nervous system. \_1-

Adrenergic receptor blockers, which are commonly used to alleviate these symptoms, act by relaxing prostatic smooth muscle [18].

## 7. Food which prevents BPH

### High-protein diet

An 8-year study of 3523 men with BPH cited that total protein intake is positively associated with BPH, with the association being slightly stronger for animal protein intake than for vegetable protein intake.

Therefore at this time, ingesting excess animal protein as a means to increase total protein intake is not recommended. Instead, high-quality, plant-derived and cold water fish-based protein sources in moderate amounts are probably reasonable choices until we know more about the relationship of protein intake and BPH [22].

### Fruits and vegetables

Fruits and vegetables contain high levels of substances that can fight inflammation, including antioxidants, polyphenols, vitamins, minerals, and fibres. Vegetables appear to have an important role in preventing BPH. In a study – the Prostate Cancer Prevention Trial – 4770 participants were evaluated. The investigators found a significantly lower risk of BPH among men who consumed at least four servings of vegetables daily compared with those who ate less than one serving daily. Plant proteins combined with aerobic exercise may be even more beneficial for prostate health than is protein from animal foods, such as meat, poultry, and eggs. Barnard and Aronson reported that daily aerobic exercise along with a low-fat, high-fibre diet consisting of whole grains, fruits, and vegetables can reduce factors associated with BPH (e.g. estradiol/testosterone ratio, insulin) [23]. Many high-fibre plant foods, such as whole grains, lentils, and beans, are also high in protein.

### Lycopene

In a randomized, double-blind, placebo-controlled trial, it was found that lycopene, a component found in tomatoes, may inhibit BPH progression and may ameliorate symptoms in patients at a dose of 15 mg/day for 6 months. Lycopene supplements are safe and well tolerated. Lycopene does not selectively interfere with prostate-specific antigen (PSA) levels, which is important to allow early detection of prostate cancer during long-term supplement intake [24].

### Green tea

Green tea has components that are attributed to potent antioxidants called catechins, known as epigallocatechin-3-gallate (EGCG), which have been shown to destroy certain bacteria and viruses, enhance the immune system, and combat several forms of cancer. EGCG seems to be useful for the management of BPH and other hormone-related abnormalities. One caution to remember about green tea is that it contains caffeine, although at a much lower level than does coffee, and somewhat less than black tea. Caffeine is a diuretic and can stimulate the bladder, causing an urgent need to urinate. On average, one cup of green tea has 25 mg of caffeine, whereas black tea has nearly twice as much. The decaffeinated version is also available [25].

### Control of androgen action by fatty acids and green tea [epigallocatechin-3-gallate]

In the early 1960s, we found that androgens can rapidly

enhance RNA synthesis in target organs, such as the ventral prostate of rats, suggesting that androgens act by modulating gene expression. Subsequent studies have shown that in target organs, testosterone, the major androgen produced by the testis circulating in the blood, is converted by 5 $\alpha$ -reductase to 5 $\alpha$ -dihydrotestosterone (DHT), binding to a specific nuclear androgen receptor (AR). [25] The DHTAR complex, apparently in conjunction with other chromosomal proteins, then regulates the synthesis of specific RNA and modulates cellular activities and organ functions. This research and that of other investigators also showed that mutations in the genes for 5 $\alpha$ -reductase or the AR are responsible for androgen-insensitivity syndromes in humans and animals. The molecular steps required for androgen action provide two effective methods for control of Testosterone-regulated responses:

- The use of a 5 $\alpha$ -reductase inhibitor to suppress DHT production, and
- The use of anti-androgens to block the interaction of DHT with the AR.

Both methods are now being utilised as therapies for androgen-related disorders. Synthetic inhibitors of the reductase have been prepared by pharmaceutical companies. The synthetic 4-aza-steroid, finasteride, is now prescribed as Proscar (Merck & Co., Whitehouse Station, New Jersey, US) for benign prostatic hyperplasia and as Propecia (Merck & Co., Whitehouse Station, New Jersey, US) for male pattern baldness.

### Zinc

The human prostate gland contains a higher level of zinc than most other tissues. There seems to be a decrease in zinc levels in plasma and prostate tissue in men with BPH (and prostate cancer) as compared to normal prostate [26].

Zinc has demonstrated to relieve LUTS probably due to its ability to inhibit 5-alpha-reductase and/or by its ability to inhibit prolactin. Prolactin has been shown to increase the uptake of testosterone by the prostate, thereby leading to increased levels of dihydrotestosterone (DHT) by providing more substrate. Studies have indicated that proper zinc status in men may help with BPH as well as prostate cancer as shown by this preclinical study. [26] Shown zinc to have a possible protective role in a randomized trial of 4770 participants. BPH was assessed over 7 years and was defined as medical or surgical treatment or repeated elevation (>14) on the International Prostate Symptom Score questionnaire. Although the association between zinc and BPH in this study is compelling, the Food Frequency Questionnaire performs poorly in assessing associations between diet, nutrition macromolecules and micromolecules, and disease. Excessive consumption of zinc supplement of more than 100mg per day may significantly increase the risk of advanced prostate cancer [27].

### Alcohol

Although only beer raises prolactin levels, higher alcohol intake may be associated with BPH. In a 17-year study of 6581 men in Hawaii, it was noted that an alcohol intake of at least 25 oz/month was directly correlated with the diagnosis of BPH. The association was most significant for beer, wine, and sake, and less for distilled spirits. Most other recent studies confirm a protective effect of alcohol towards

BPH but higher LUTS [28]. A met analysis of 19 published studies], incorporating 120 091 men, observed up to a 35% decreased likelihood of BPH among men who drank daily, but an increased risk of LUTS [29].

### Vitamin D

Kristal *et al.* showed vitamin D supplementation was associated with reduced risk of BPH, but the dosage was imprecise. The association in this 4770-participant trial was observed only among men who used both multivitamins and single vitamin D supplements. There were no associations of supplement use with BPH risk, with the exception of a trend for decreasing BPH risk with increasing dose of supplemental vitamin D. Although this study lacked data on frequency, dose, and duration of vitamin D use, the results are intriguing enough to support further research that will address whether vitamin D alone will have any benefit for BPH. Mechanism of how vitamin D may have a favourable effect on BPH is by attaching the molecule vitamin D receptors on the prostate and bladder, and inhibiting prostate growth, lowering excessive contractility, and reducing inflammation [23, 30].

### Starch

A case-control study of 1369 patients with BPH and 1451 controls demonstrated a direct association between starch consumers and BPH. The main sources of starch in this population were white bread, pasta, and rice. Starch may be responsible for a glycemic response that is compensated for by an increase in serum insulin and insulin-like growth factor. Elevated insulin-like growth factor levels, possibly mediated by dihydrotestosterone, are thought to stimulate the development of BPH. No association was found for sugars from fruit, which have a lower glycemic index, than does bread [31].

### Saw palmetto

The extracts from the berries of saw palmetto are the most popular herbal products used to treat symptomatic BPH. Saw palmetto is native to Florida, and has been shown to significantly improve the signs and symptoms of BPH in numerous older clinical studies. One examination of 21 randomized controlled trials involving a total of 3139 men (including 18 double-blind trials) demonstrated that men treated with saw palmetto experienced decreased urinary tract symptom scores, less nocturia [19], better urinary tract symptom self-rating scores, and peak urine flow improvements compared with men receiving placebo. This analysis also showed that matched up with men receiving the DHT inhibitor finasteride (Proscar), [32] men treated with saw palmetto had similar improvements in urinary tract symptom scores with less adverse effects compared to the group on finasteride. The mechanism of action is related to inhibition of DHT binding to both the cytosolic and nuclear androgen receptors, inhibition of 5-alpha-reductase and interference with intra prostatic estrogen receptors. As a result of this multitude of effects, most of the results have been excellent in randomized trials. A randomized, placebo-controlled, dose-escalation trial indicates no benefit from saw palmetto consumption compared to placebo with 369 participants.

Palmetto berries are helpful in reducing inflammation of the prostate in cases of benign prostate hypertrophy

1. Saw palmetto inhibits the action dihydrotestosterone

2. The compound thought to be responsible (in part) for the enlargement of the Prostate.

In sub-hypertrophied cases, it may also reduce swelling to some degree, but in case of true hypertrophy it is not known whether the herb brings relief by decreasing gland size or by reducing pain and swelling. It also increases the bladder's ability to contract and expel urine. Saw Palmetto extract is so effective in treating benign prostatic hyperplasia (BPH), that it had been compared in research to the prescription drug Proscar. During the course of a three year study involving 309 men, Saw Palmetto extract was associated with a significant increase in urinary flow rate and a 50 percent decrease in residual urine volume. Furthermore, improvement in quality of life was reported "which reflected in the over 80 percent good to very good efficacy judgment's." By comparison, Proscar showed a 30 percent decrease in symptom scores over three years, but urine flow improved only slightly, and residual urine volume was almost unchanged [33]. Only one-third of the treated patients had "clinically relevant improvement," and only after six months. Clearly, Saw Palmetto extract offers superior symptomatic relief in BPH.

### Rye pollen extract (cernilton)

Cernilton is a water-soluble pollen fraction phytotherapeutic rye grass pollen. One review analyzed the specific effects of Cernilton and suggested that it improved [34] subjective symptoms including nocturia, but no significant improvement in urodynamic measures was product whose extract originates from observed when compared with placebo. The Cernilton studies are challenged by short duration low number of participants, and the lack of updated data [34].

### Beta-sitosterol

Beta-sitosterol is one of the several phytosterols (plant sterols) with chemical structures similar to that of cholesterol. Beta-sitosterol is widely distributed in the plant kingdom and found in pecans [35].

### Saw palmetto

Pumpkin seeds. A review of beta-sitosterol studies included for double-blind trials of 519 men, duration of which was between 4 and 26 weeks. [36] Beta-sitosterol improved symptom scores by 35%, peak flow rate improved symptom scores by 35%, peak flow rate by 34%, and reduced postvoid residual volume by 24%. Their long-term effectiveness, safety, and ability to prevent BPH complications are not known.

## 8. Intakes of energy and macronutrients and the risk of benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common disease of older men, characterized by overgrowth of the prostatic epithelium and fibromuscular tissue of the transition zone and periurethral area and by obstructive and irritative lower urinary tract symptoms. [37] Autopsy data indicate that anatomic or microscopic evidence of BPH is present in 40% and 90% of men aged 50–60 and 80–90 y, respectively. More than 200 000 transurethral resections of the prostate for BPH are performed annually in the United States.

The etiology of BPH is unclear, but it appears to represent a multi factorial process involving both mechanical and

dynamic components. Enlarged prostate, a mechanical or static component of BPH, is influenced mainly by androgens and can be pharmacologically treated with 5 $\alpha$ -reductase inhibitors to block intra prostatic conversion of testosterone to the more potent dihydrotestosterone (DHT). Lower urinary tract symptoms due to a heightened tone of the prostatic smooth muscle, the dynamic component of BPH, are controlled by the sympathetic nervous system.  $\alpha$ -1-Adrenergic receptor blockers, which are commonly used to alleviate these symptoms, act by relaxing prostatic smooth muscle [38]. Dietary and nutritional factors may have an effect on BPH etiology through a variety of mechanisms, but the literature on this topic is sparse (7–10). The absolute amount and composition of macronutrients may influence sympathetic nervous system energy intake may elevate sympathetic nervous system activity and concentrations of testosterone. In addition, the macronutrient composition of the diet may be important. In particular a high consumption of unsaturated fatty acids may contribute to lipid peroxidation of the cell membrane and of the components and fluidity of cell membranes, which may affect 5 $\alpha$ -reductase activity [38]. One group noted age-related changes in the fatty acid composition of the prostate epithelium and stroma in men with BPH. Because the literature on relations between macronutrient intakes and BPH risk is limited, we examined the relation.

### 9. Dietary Patterns, Supplement Use, and the Risk of Symptomatic Benign Prostatic Hyperplasia

Benign prostatic hyperplasia (BPH) is one of the most common medical conditions in older men. Estimates of BPH prevalence range from 40 percent to 50 percent at 50 years of age to as high as 80 percent for men aged 70 years. Both the high prevalence of BPH and the associated costs of medical care (approximately 4 billion dollars per year in the United States) strongly motivate research to better understand the causes of BPH and identify modifiable risk factors to prevent or delay the disease [39]. The current literature on BPH risk factors is limited. Most reports have been based on case series, cross-sectional association, or hospital-based case-control studies, and few studies have examined the risk of incident BPH using case definitions that reflect current medical practice and validated symptom. Symptomatic BPH is caused by two components: enlargement of the prostate and heightened tone in prostate smooth muscle, both of which can obstruct urinary flow. Although the pathogenesis of BPH is not well understood, age-related changes in hormonal and other growth-regulatory factors are likely cause of cellular proliferation. Thus, dietary patterns that alter the hormonal milieu, such as a high-fat diet, or other regulator factors, such as insulin-like growth factors, could conceivably affect BPH risk. Prostate muscle tone is controlled by the sympathetic nervous system, which is directly affected by many diet-related factors. BPH may also be caused or exacerbated by chronic inflammation and subsequent oxidative damage and thus dietary factors such as  $\omega$ -3 fatty acids, polyunsaturated fats, and antioxidants may also affect risk. Clearly, there are many mechanisms whereby dietary patterns Here, we give results of a prospective cohort study examining the 7-year incidence of symptomatic BPH among men participating in the Prostate Cancer Prevention men aged 55 years or older. Here, we give results of a prospective cohort study examining the 7-year incidence of symptomatic BPH among

men participating in the Prostate Cancer Prevention Trial (PCPT). Data from the PCPT include rigorous assessment of both the symptoms and treatment of BPH, as well as extensive information on diet and other lifestyle factors that may affect BPH risk [40]. This report examines whether dietary pattern supplement use, and alcohol consumption affect the risk of incident, symptomatic BPH in a population diet high in total fat were associated with increased risk of symptomatic BPH and that diets high in protein and alcohol were associated with decreased risk. In analyses of foods, high vegetable consumption was associated with lower risk, and high red meat consumption was associated with increased risk. There were no associations of antioxidant nutrients, including supplemental vitamin E and selenium or total vitamin C, with risk. Dietary but not supplemental zinc was associated with reduced risk, and use of vitamin D supplements was associated with reduced risk. Finally, there was a suggestion that high intake of lycopene, but not other carotenoids, was associated with reduced risk. Before discussing the consistency of our findings with those in the published literature, it is important to note that research on dietary patterns and BPH is very limited.

Most reports are from small case-control studies in which cases were men undergoing surgical treatment or from cross-sectional studies examining associations of lower urinary tract symptoms with current diet or serum micronutrient concentrations. Two studies used a longitudinal design to examine true BPH incidence, using either surgery or the combination of medical and surgical treatment plus the development of severe lower urinary tract [41]. Symptoms as BPH endpoints. For dietary assessment two studies used one used serum micronutrients, and the rest collected limited information on specific foods or food groups. Given these differences in study design, BPH endpoints, and dietary assessment methods, inconsistencies in findings across studies are expected. Our finding that total fat was associated with increased BPH risk, with no evidence that associations were specific to type of fat, was in part consistent with the two previous studies that have examined macronutrients and BPH risk. In the 6-year period prevalence of BPH associated with high intakes of energy, animal protein, polyunsaturated very small case-control study, reported a non-significant increased risk associated with high intake of polyunsaturated fat. Our finding that regular alcohol consumption was associated with reduced risk was consistent with findings from many studies that have examined this question) and probably due to the effects of alcohol on the production and metabolism of testosterone. We did examine whether the alcohol finding could be attributed to avoiding beverages to reduce symptoms; however, BPH incidence was not associated with consumption of either tea

### 10. BPH is a progressive condition

Longitudinal, community based studies, such as the Olmsted County Study and Baltimore Longitudinal Study of Aging, clearly show that BPH is a gradually progressive disease. These studies show that generally with time in many men living independently in the community with no overt evidence of prostate disease prostate volume increases the urinary flow rate decreases and symptoms worsen. In the Olmsted County Study Rhodes *et al.* used repeat ultrasound measures in a 7-year period and found that average prostatic growth rates were 1.6% yearly in men between ages 40 and



79 years Another important finding in this study was that the percent growth of the prostate yearly depends on baseline volume, in that the larger the prostate at baseline, the greater the percent of growth every year thereafter. Similar findings were also reported in men participating in the Baltimore Longitudinal

Study of Aging. Thus, while prostate volume correlates poorly with symptoms and urinary flow at any given time point, the larger the prostate, the greater the likelihood of future clinical deterioration. The progressive appearance of complications of BPH disease e.g. bleeding, infection stones and AUR, is more important than symptoms and flow from a medical standpoint. As a discrete event that is uniformly recorded and coded, AUR serves as an index of BPH disease severity and numerous studies have focused on this serious event in regard to the progression issue. Barry *et al.* found that the incidence of AUR was 2.5% yearly in symptomatic men under going watchful waiting in urology practices in the United States.<sup>9</sup>In the Health Professionals Follow-Up Study the annual few symptoms incidence of AUR was 0.5%, which increased sharply when patient age and BPH diagnosis were added factors. In community based studies of randomly selected older men Jacobsen *et al.* found that the incidence of AUR years of life. The incidence of AUR in this population exceeded that of stroke, heart attack and hip fracture in similar men. Men in the Olmsted County Study men living in the community of Olmsted County, Minnesota. Thus, AUR is not purely a symptom driven event symptoms are important risk factors, even men with few antecedent symptoms have AUR. This fact has important implications for prophylactic treatment for BPH in men with but a large prostate <sup>[42]</sup>.

### 11. PSA and BPH disease risk

AUR or surgery in placebo treated men with PSA to what extent does serum PSA (prostate volume) foretell the natural history of the disease process, i.e BPH outcomes? Roehrborn *et al.* helped answer this question for symptoms, flow rate, AUR and the need for surgery in men treated with placebo during 4 years in PLESS. Of 881 men treated with placebo for 4 years worsening of symptoms and urine flow developed only in those with a prostate volume exceeding 40 ml and PSA 1.4 ng/ml or greater. In men with prostate volume and PSA below these thresholds appreciable disease progression did not occur. Furthermore, this study showed no significant improvement in symptom score for men with PSA lower than 1.4 ng/ml, when they were treated with a 5ARI, suggesting that fine stride had a limited effect on symptoms in men with a smaller prostate. In fact, a sustained placebo response was noted for symptoms and urine flow. The investigators concluded that with regard to symptoms and uro flow, “men with PSAs less than 1.4 ng/ml do not have clinically progressive BPH.” With regard to AUR and need for surgery, outcomes paralleled symptom-flow data, except some progression was noted even in the lowest PSA stratum. The 4-year incidence literati lower than 1.4 ng/ml (lowest tertile) was 7.8%, whereas the incidence in men with PSA greater than 3.3 ng/ml (highest tertile) was 19.9%. The investigators concluded, “There is a very strong relationship between baseline prostate volume and serum PSA in predicting the incidence of BPH related surgery or AUR during 4 years. When spontaneous vs found. A similar relationship between baseline PSA and the risk of clinical progression of BPH

was observed in MTOPSA. The higher the PSA, the greater the risk of clinical progression, symptom deterioration (greater than 4-point increase progression was defined as the first occurrence of a 4-point increase from baseline in the AUA symptom index score AUR, renal insufficiency, recurrent urinary tract infection or urinary incontinence. Men with PSA greater than 1.4ng/ml were considered to be at increased risk for BPH disease progression. Data from 2 large, longitudinal studies of community dwelling men, that is the Olmsted County Study and Baltimore Longitudinal Study of Aging, also support a relationship between prostate volume and the risk of AUR. In the Olmsted County Study the risk of AUR was 3 times greater in men with a prostate volume of more than 30 ml compared with that in men with a prostate volume of less than 30 ml. In the Baltimore Longitudinal Study of Aging Wright *et al.* found that the relative risk of “prostate enlargement” to greater than 75% of normal for age could be stratified by baseline PSA. For example, 50 to 59-year-old men had a 5 to 9-fold increase in the 10-year risk of prostate enlargement if baseline PSA exceeded 0.8 to 1.70 ng/ml compared with men with baseline PSA lower than 0.5 ng/ml. of BPH clinical manifestations and, thus, the predictive value of PSA as a marker for BPH disease progression appears to be independent of symptoms. Carter *et al.* recently analyzed data from the Baltimore Longitudinal Study of Aging and reported that PSA was not a useful predictor of the development of symptoms, which stands in contrast to other studies. Most men in this study had few symptoms and low PSA and, therefore, stratification of outcomes in this analysis may have been blunted. Finally, in an exhaustive analysis of data on more than 3,700 placebo treated men in randomized BPH trials world wide predictor of subsequent AUR and spontaneous AUR, studied separate of great interest in this landmark study was the fact that a sophisticated decision matrix incorporating 110 clinical variables was no better at predicting AUR than PSA alone. While other variables, such as symptoms severity or the degree of urine flow impairment, may be independent risk factors, they contribute little to the power of PSA for predicting BPH disease progression in its most severe form. PSA is a valuable surrogate of prostate volume and an important predictor of BPH disease progression <sup>[43]</sup>. Currently voiding symptoms remain a key to the implementation of treatment in individuals but serum PSA is the most important factor for predicting disease progression. Men with an enlarged prostate are at greatest risk for BPH disease progression regardless of symptom status. We propose using PSA greater than 1.5 ng/ml to identify men at risk for BPH disease progression because this cutoff is easily remembered, conservative for selecting men likely to receive benefit and generally reflective of prostate enlargement (more than 30 ml) in 60 to 69-year-old men

### 12 Aris can decrease the risk of BPH disease progression

Although the etiology of BPH is complex and influenced by a number of factors, prostate growth is primarily regulated especially DHT. Testosterone is converted to DHT by 2 isoenzymes of 5 AR, A and B). The 2 isoenzymes (types 1 and 2) are found in the prostate and they affect cell proliferation. Type 2 predominates in normal and BPH tissue, while type 1 is more prevalent in prostate androgen receptor to form a DHT-androgen receptor complex. This

causes a cascade of intracellular events that leads to gene expression, and the production of growth and signaling factors that regulate cell division and proinflammatory factors in the prostate [44]. DHT has approximately 5-fold greater affinity for androgen receptors than does testosterone and, therefore, DHT has a greater role in regulating prostate growth. The 2 widely available 5ARIs for BPH are finasteride (Proscar®) and dutasteride (Avodart®), which were approved by the United States Food and Drug Administration in 1992 and 2002, respectively, “for the treatment of symptomatic BPH in men with an enlarged prostate.” Finasteride inhibits the type 2 5AR isoenzyme and dutasteride inhibits 5AR isoenzyme types 1 and 2. According to the Food and Drug Administration approved labels each drug induces marked DHT suppression through the inhibition of 5AR, decreases prostate volume, increases urinary flow and relieves BPH related symptoms. Dutasteride administration appears to induce more profound DHT suppression than finasteride, an action that may be important during long treatment intervals. Finasteride and dutasteride are also approved to decrease the risk of AUR and the need for BPH related surgery. The net risk decrease provided by 15% MTOPS demonstrated that finasteride but not the  $\alpha$ -blocker doxazosin decreased the incidence of AUR and surgery during 5.5 years. While the risk decrease in men with symptomatic BPH is now well documented, a growing body of evidence suggests that a risk decrease may also be possible in men with asymptomatic

BPH. As detailed prostate enlargement, which is mediated primarily by DHT and manifests as increased serum PSA, is associated independently of symptoms with the risk of AUR and need for surgery. Despite the standardization afforded by the International Prostate Symptom Score symptoms are subjective, while prostate volume determinations are objective. Since PSA as a surrogate marker of prostate volume is the variable that is most predictive of AUR or surgery PSA should be seriously considered in decisions about BPH disease prevention [45].

## Discussion

In the review we explored possible diet intake can prevent progression of disease, also adopting healthy life style, major BPH Progression found in aged people 60, so those people should adopt healthy life style and healthy eating to reduce risk of BPH.

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