



## A Review on Benign Prostatic Hyperplasia

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### ABSTRACT

Benign prostatic hyperplasia is the enlargement of prostate gland mainly seen in men aged above 50 years. It has been observed that 8 out of 10 men having prostate enlargement. It is mainly caused due to over growth of benign glandular tissue and leads to the constriction of urethra and decreased urine output. Diagnosis for BPH involves Obligatory and optional evaluation. The main risk factor for BPH is age. BPH is clinically manifested as obstructive LUTS (lower urinary tract symptoms) and irritable LUTS (lower urinary tract symptoms). Treatment for BPH depends on number of factors like age, prostate size, and severity of symptoms. Alpha-1 Adrenergic receptor antagonist decreased lower urinary symptoms and increased flow rates of urine in men with symptomatic BPH but do not reduce the long term risk of urinary retention. 5 alpha reductase inhibitors decrease the production of dihydrotestosterone with in the prostate which results in decreased prostate volume, increased peak urinary flow rate, improvement of symptoms, and decreased risk of acute urinary retention. Combination therapy involves 5 alpha reductase inhibitors and alpha adrenergic blockers it is effective in patients having LUTS with prostatic enlargement. Anticholinergics and phosphodiesterase inhibitors were also used in the management of BPH. Medication therapy is used in all the three stages but it only delays surgery in patients with severe BPH.

### Key words:

Prostate enlargement,  
LUTS, 5Alpha reductase inhibitors,  
Alpha adrenergic blockers.

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## INTRODUCTION:

### PROSTATE GLAND

Prostate gland is the part of male reproductive system it is of walnut size and weighs about one ounce. The prostate is present below the urinary bladder and in front of rectum. It goes around the tube called urethra which carries urine from bladder out through penis. The main work of prostate is to produce semen. Sperm is produced in the testicles and it moves through urethra during ejaculation at this time the fluid from prostate and seminal vesicles moves into urethra. This semen goes out through urethra and through penis.

### BENIGN PROSTATIC HYPERPLASIA:

Benign prostatic hyperplasia is also called as BPH. It is a condition seen in men in which enlargement of prostate gland is seen but non cancerous. BPH is also called as benign prostatic hypertrophy or benign prostatic obstruction. Growth of prostate observed in two main periods of life as the men ages. First period occurs in early puberty. The second phase begins at the age of 25 and continue throughout the man's life. BPH is mostly observed in second growth phase of prostate. As the prostate enlarges, it presses against and tightens urethra. The bladder wall becomes thicker. Finally the bladder weakens and loses its ability to empty completely, cause to remain some urine in bladder. Narrowing of urethra, urinary retention and incomplete emptying of bladder may cause many problems associated with benign prostatic hyperplasia<sup>1</sup>.

## PATHOGENESIS OF BPH:

The prostate gland consists of two types of tissues epithelial tissue, stoma tissue and capsule. Epithelial tissue also known as glandular tissue and produces prostatic secretions. During ejaculation these secretions are released into urethra and bring about total ejaculate volume. Epithelial tissue growth is triggered by androgens. Stromal tissue is also known as smooth muscle tissue is fixed with alpha 1 adrenergic receptors. these receptors are stimulated by nor epinephrine and causes contraction of smooth muscle which results in an extrinsic compression of urethra, narrowing of urethral lumen, and decreased urinary bladder emptying. The capsule or outer shell consists of fibrous connective tissue and smooth muscle which is also fixed with neither alpha 1 adrenergic receptors when stimulated with nor epinephrine contracts around the urethra. Testosterone is the important testicular androgen in males. these androgens are converted by 5 alpha reductase in target cells to dihydrotestosterone. 2 types of 5 alpha reductase enzymes are present Type 1 is localized to sebaceous glands in the frontal scalp, liver and skin. DHT produced at this target tissues causes acne and increased facial and body hair. Type 2 is localized to the prostate, genital tissue and hair follicles of the scalp. In the prostate DHT induces the growth and enlargement of gland<sup>2</sup>.

**CIRCULATING TESTOSTERONE**

5-reductase type 2



Dihydrotestosterone (DHT)



Binds To Nuclear Androgen Receptor



Regulate the Expression Of Genes Which Aid In Growth and Survival of Epithelium and Stroma

Fig 1: Pathogenesis of BPH

**CLINICAL PRESENTATION:**

Patients with BPH present with number of signs and symptoms. The symptoms of BPH can be divided into two categories Obstructive and Irritable.

Obstructive symptoms also known as prostatism or bladder outlet obstruction result when dynamic or static factor reduce bladder emptying. Patient report urinary hesitancy, straining and a weak urine stream. Urine dribbles out of the penis and the urinary bladder always feels full; even after patient have voided. Some patients state that they need to press their bladder to force out the urine. In severe cases patient go into urinary retention .when bladder emptying is not possible, in these cases suprapubic pain can result from bladder over distension .Approximately 50to 80% of patients have irritative voiding symptoms which result from long standing obstruction at the bladder neck. Patient complains of urine urgency and frequency and Nocturia which significantly reduces quality of life. Symptoms of BPH vary over time, symptoms may improve remain stable or worsen spontaneously. Obstructive and irritative voiding symptoms and their impact on a patient's quality of life are referred to as lower urinary tract symptoms. Another presentation for BPH is silent prostatism patients have obstructive and irritable voiding symptoms but adopt to them and do not voluntarily complain about them such patients do not present for medical treatment until complication of BPH disease arouse or a spouse bring in a symptomatic patient for medical care<sup>3</sup>.

**MALE LUTS ARE CLASSIFIED AS FOLLOWS:**

**Obstructive LUTS:** It is usually caused due to the stenosis of bladder neck or prostate symptoms include hesitancy, weak stream, and urinary retention, straining and incomplete emptying. **Irritable LUTS:** It may be caused due to overactive bladder or tumour in the bladder. Symptoms include urgency, frequency, Nocturia, suprapubic pain. Generally, the symptoms observed in early BPH are slow urinary stream and feeling of incomplete voiding. If the male patients present with urge incontinence and urinary urgency it should be consider that we are dealing with advanced BPH that they have developed bladder this function<sup>4</sup>.

**DIAGNOSIS:****OBLIGATORY EVALUATION:****MEDICAL HISTORY:**

History should be collected from the patient because there are several class of drugs which may cause LUTS and other co

morbid conditions that contribute to symptoms or any previous history of surgical procedures that may increase risk of urethral stricture<sup>5,6</sup>.

**ASSESSMENT OF SYMPTOMS BY USING I-PSS (INTERNATIONAL PROSTATIC SYMPTOM SCORE):****About the I-PSS**

The International Prostate Symptom Score (I-PSS) based on the answers to seven questions Related to urinary symptoms and one question related to quality of life. Each question Related to urinary symptoms allows the patient to select one out of six answers based on severity of the particular symptom. The answers are assigned from 0-5. The total score ranges from 0-35 (asymptomatic to severe condition). Question eight related to the patient's perceived quality of life. The first seven questions of the I-PSS are identical to the questions appearing on the American Urological Association (AUA) Symptom Index which currently

**CATEGORIZES SYMPTOMS AS FOLLOWS:**

- A score of 0 to 7 indicates mild symptoms
- 8 to 19 indicates moderate symptoms
- 20 to 30 indicate or suggest it as severe condition.

A study was conducted in a territory care hospital. 100 outpatients of age above 51 years were selected and the patients were priorly diagnosed by using history of the patient, Digital rectal examination, and physical examination lateron the severity is assessed by using international prostatic symptom score. Patients having LUTS with BPH are selected for the study and the patients having DM, BP, and other co morbidities are excluded. in this study patients having moderate symptoms were evaluated followed by severe symptoms. The results of this study have proved that IPSS saves as a good instrument for symptom assessment.

- **DIGITAL RECTAL EXAM:** In this test the physician or doctor inserts his figure into rectum to examine the enlargement of prostate gland.
- **URINE TEST:** Urine Analysis of the sample was done to rule out the infection or any other condition that cause similar symptoms.

**OPTIONAL EVALUATION:**

**CYTOSCOPY:** In this test the physician inserts a thin tube having camera at the end called cystoscope through the opening of the urethra at the tip of penis. The camera is helpful to visualize the prostate and bladder. Before doing this test patient is given anaesthesia.

**TRANS ABDOMINAL ULTRASOUND:** This test is used to measure the size of prostate and the amount of urine left in bladder after urination.

**PROSTATIC SPECIFIC ANTIGEN:** If the elevated levels of PSA in blood are observed it may be an indicator of prostate cancer.

**MRI:** The entire view of the prostate is provided by this test.

**BLOOD TEST:** To rule out Kidney problems.

**POST VOID RESIDUAL VOLUME TEST:** This test was done to measure the amount of urine left in bladder after urination it can be done by using ultrasound or by inserting catheter into bladder after urinate.

**24 HOUR VOIDING DAIRY:** Recording the frequency and volume of urine. This test may be helpful if 1/3<sup>rd</sup> of patients morning output occurs during nighttime<sup>7</sup>.

**INTERNATIONAL PROSTATE SYMPTOM SCORE (I-PSS)**

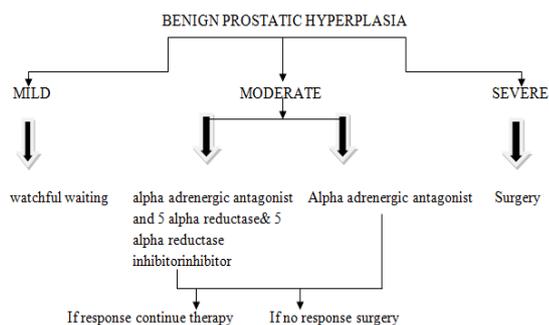
<b>In the past month</b>	<b>Not at all</b>	<b>Less than 1 in 5 times</b>	<b>Less than half the time</b>	<b>About half the time</b>	<b>More than half the time</b>	<b>Almost always</b>	<b>Your score</b>
1. Incomplete emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. Frequency How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. Intermittency How often have you have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
	None	1 Time	2 Times	3 Times	4 Times	5Times	
7. Nocturia How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
<b>TOTAL I-PSS SCORE</b>							

**SCORE 1-7 MILD 8-19: MODERATE 20-35: SEVERE**

<b>QUALITY OF LIFE DUE TO URINARY SYMPTOMS</b>	<b>Delighted</b>	<b>Pleased</b>	<b>Mostly satisfied</b>	<b>Mixed</b>	<b>Mostly dissatisfied</b>	<b>Unhappy</b>	<b>Terrible</b>
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6

## TREATMENT GUIDELINES:

For the management of BPH AUA guidelines are used as main tool in the United States. According to AUA guidelines BPH patients should be encouraged to maintain a healthy lifestyle by high intake of fresh fruits, vegetables and regular physical exercises and quit smoking. Specific treatment options include pharmacological therapy and surgical intervention phototherapy is also recommended along with medications during treatment with BPH. In mild BPH conditions these patients are treated by watch full waiting which entails having the patient return for reassessment at yearly intervals. Behavioural modifications include restricting fluids close to bed time, minimization of caffeine, alcohol intake, and frequent emptying of bladder during awake. During each visit physician should assess the patient risk of acute renal retention by evaluating the prostate size using PSA as a surrogate marker. During moderate or severe conditions patient should be offered with specific treatment by drug therapy with an alpha adrenergic antagonist or 5 alpha reductase inhibitor or a combination of an alpha adrenergic antagonists and 5 alpha reductase inhibitor or planned for surgery. Patient with severe complications TURP surgery or minimal invasive surgical procedure is performed. Drug therapy only delays aggravation of patient symptoms<sup>8</sup>.



## TREATMENT OPTIONS:

BPH is a common condition seen in older men and lots of treatment options available for this condition. Selection of treatment option based on age, severity of symptoms and other co morbid conditions.

Treatment involves

- Lifestyle modification and watchful waiting
- Treatment using medications
- Surgery plan

## LIFESTYLE CHANGES:

The physician recommends lifestyle changes for those patients whose symptoms are mild or slightly troubled.

- Intake of fluids should be reduced while going out in public or while going to sleep.
- Avoid taking alcohol and caffeinated beverages.
- Treating the constipation problem
- Monitoring the use of medications such as decongestants, antihistamines, antidepressants and diuretics.
- Exercising pelvic floor muscles<sup>1</sup>.

## MEDICAL TREATMENT:

### ALPHA BLOCKERS

Alpha blockers are first line drug for the men having BPH with symptomatic bother. Alfuzosin, doxazosin, Tamsulosin and terazosin are the drugs used for LUTS secondary to BPH. All the above four drugs having same action and efficacy but the selection depends on patient co morbidity condition side effects and tolerance. Alpha adrenergic receptors are present throughout the body and maintain the smooth muscle tone. These Alpha-receptors are divided into sub types in that Alpha1 a receptor is present in bladder neck and prostate. Clinical trials of BPH alpha blockers have shown rapid symptom improvement but Alpha blocker monotherapy is not a best option when the patient was at a risk of disease progression. Based on Alpha 1 subtype alpha blockers are divided into non uroselective and uroselective.

### NON UROSELECTIVE DRUGS:

Doxazosin, terazosin, alfuzosin. Before giving non uroselective drugs like doxazosin and terazosin dose titration is needed because higher the dose higher the efficacy and more chance in lowering the blood pressure and other possible side effects for Doxazosin starting dose is 1mg and can be titrated to a maximum dose of 8mg. Alfuzosin does not require any dose titration. Terazosin starting dose 2mg and can be titrated to a maximum dose of 10mg.

### UROSELECTIVE DRUGS:

Tamsulosin and silodol does not require any dose adjustment. Alpha blockers work by blocking the sympathetic nerve endings at the bladder neck and relieve the patient symptoms. These drugs do not prevent the progression of disease so these drugs are given to patients who are having trouble by their symptoms only but not symptoms score alone. Before giving medication patient should be informed regarding efficacy and possible side effects of drugs. Patient taking alpha blockers should be given a trial course for not more than two to four weeks to see the effectiveness and possible side effects. If the patient agrees by the results of the drug then it can be prescribed as long term treatment. The patient should be advised to take the medications when ever needed so that it may be more cost effective.

### ADVERSE DRUG REACTIONS:

Hypotension, giddiness and possibility of falls<sup>10, 11, 12, 13</sup>. In 50 to 59 years BPH patients when the drug Alpha blocker Terazosin is prescribed it shows its action up to 31% during management of BPH and LUTS. Another Alpha blocker Tamsulosin shows its action up to 43%, Alpha blocker Doxazosin shows its action up to 18%, alpha blocker Alfuzosin shows its action up to 8%. In 60 to 69 years patients when the following alpha blocker drugs are prescribed Terazosin works up to 31%, Tamsulosin works up to 42%, and Doxazosin works up to 21%, Alfuzosin works up to 6%. In 70 to 79 years patients when the following alpha blockers are prescribed Terazosin shows its action 34%, Tamsulosin action 37%, Doxazosin action 23%, Alfuzosin action 6%. In 80 to 89 years patients when the following alpha blockers are prescribed Terazosin action 41%, Tamsulosin action 36%, Doxazosin action 19%, Alfuzosin action 4%.

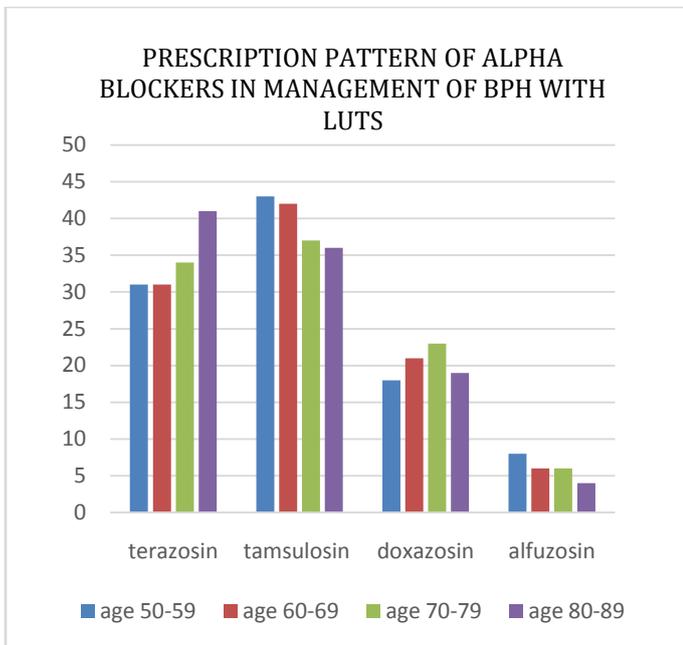


Fig: 3 Prescription patterns of Alpha blockers in management of BPH with LUTS

### 5-ALPHA REDUCTASE INHIBITORS:

The growth of prostate depends on androgen and mediated predominantly by dihydro testosterone which is produced from testosterone by the action of 5 alpha reductase. Two types of 5alpha reductase isoenzymes are present type 1 present in liver and skin and type 2 mainly in prostate. The two main drugs used are finasteride and dutasteride. However Dutasteride inhibit or block both isoenzymes and finasteride selective for only type2 isoenzyme. As dutasteride inhibits both isoenzymes the concentration of dihydrotestosterone in serum is reduced more than that of finasteride (95% vs 75%) and intraprostatic testosterone is reduced more by dutasteride than finasteride (94% vs80). Before starting 5 Alpha reductase inhibitors the patient should be informed about the possible side effects such as gynaecomastia (1%) ejaculatory dysfunction (1-5%), erectile dysfunction (5-8%), decreased libido (5%) [8]. these two drugs are mostly used and they work by preventing the conversion of testosterone to 5 hydroxytestosterone which stimulates BPH. Men having prostate weight >30 grams and PSA >1.5 micro gm/litre. These class of Drugs are believed to reduce static intrusive constituent of BPH with increase in urine flow rate (1.6-2.2ml/sec)and decreases symptom score. Finasteride have shown to reduce urinary tract symptoms and increase urine flow. In older patients these classes of drugs were prescribed only in severe conditions to reduce the need for surgery. 5alpha reductase inhibitors shrink the size of adenoma but does not alter the shape of enlarged prostate. So due this in some patients having prostatic lobes no result is observed and surgery is planned. Benefit to this therapy can be identified by DIGITAL rectal examination and Trans rectal ultra sonography.

### ADVERSE DRUG REACTIONS:

Sexual dysfunction<sup>9, 14, 15,16,17,21,</sup>

### COMBINATION THERAPY:

5Alpha reductase inhibitors and Alpha adrenergic blockers: this combination is effective in the patients having LUTS with prostatic enlargement. In clinical trials it has proved that

combination therapy have significantly improved the patient symptoms score and peak urinary flow when compared to monotherapy. Combination therapy reduces the symptomatic disease to advanced stage. Combination therapy and or 5Alpha reductase inhibitors monotherapy decrease the risk of urinary retention and prostate surgery. Doxazosin and Finasteride combination have shown decrease in IPSS and increased urine output more benefit to patient is observed while taking these drugs in combination than monotherapy. Similar results were observed for dutasteride and tamsulosin. Patient taking alpha blockers have an option to discontinue after 6 to 8 months when the patient was treated successfully if reoccurrence of symptoms observed again therapy was started<sup>9,16 20,23,</sup>

### ROLE OF ANTICHOLINERGICS:

Work by blocking muscular receptor within the detrusor muscle resulting in relaxation. These are given in the condition of over active bladder and symptoms of urinary urgency, frequency and urge incontinence. More improvement observed when anticholinergics and alpha receptor antagonist are used for BPH patients with irritable LUTS and post voidal residual volume. Caution is needed when these agents were considering in men having history of spontaneous urinary retention and increased residual urine volume because historically these drugs are contraindicated in patients with BPH because of concern about urinary retention. Men having PVR<200ml anticholinergic drugs do not increase the risk of urinary retention<sup>9, 21, 22,</sup>

### PHOSPHODIESTERASE INHIBITORS:

Phosphodiesterase isoenzymes 4 and 5 were presenting prostate gland for regulating smooth muscle tone. Drugs like sildenafil and tadalafil inhibit these isoenzymes and have shown improvement in symptoms and quality of life in patients with LUTS. But now these agents were not recommended for the patients with symptomatic BPH related LUTS.

### CONCLUSION:

By giving Alpha adrenergic antagonist patients are relieved from symptoms but they don't reduce prostate size. Alpha reductase inhibitors are indicated for patients in moderate to severe having prostate size more than 40g. They decrease the disease progression and risk of complications and thereby decrease the need for surgical intervention. Combination therapy with alpha adrenergic and alpha reductase inhibitors is effective in patients with severe symptoms. Alpha reductase inhibitors have delayed onset of action when compared to alpha adrenergic receptor antagonists which is undesirable for patients having troublesome symptoms.

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