بسم الله الرحمن الرحيم

مريم بنت عيسى

عليه السلام

واستغفر الله
Benign Prostatic Hyperplasia

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BPH is a common disorder that increases in frequency progressively with age in men older than 50 years. It is a condition that occurs when the prostate enlarges, potentially slowing or blocking the urine stream.
Clinical Manifestations

- increased frequency of urination, nocturia, hesitancy, urgency, and weak urinary stream. These symptoms typically appear slowly and progress gradually over a period of years.
Clinical Manifestations

Obstructive symptoms:
Urinary hesitancy
urine dribbles out of penis
Sense of incomplete emptying

Irritative signs:
Nocturia,Urgency ,Frequency

Complication:
Chronic kidney disease
Gross hematuria
Urinary incontinence
Recurrent tract infection
Bladder stone
a normal prostate gland in an adult man weighs 4 to 20 g.

The prostate has two major functions: 
(a) To secrete fluids that make up a portion (20%–40%) of the ejaculate volume;  
(b) To provide secretions with possible antibacterial effect related to its high concentration of zinc
The prostate is a male reproductive gland that produces the fluid that carries sperm during ejaculation. Aging decreases in testicular androgen production in the aging male. Testosterone is converted to dihydrotestosterone by 5-alpha-reductase.
The cause of BPH is unclear most hypotheses are based on hormonal and aging processes.

The prostate gland comprises 3 types of tissue:

- **Epithelial or glandular**
  
  Produces prostatic secretions. These secretion are delivered into the urethra during ejaculation and contribute to the ultimate ejaculate volume. Androgens stimulate epithelial tissue growth.

- **Stromal or smooth muscle**
  
  Is embedded with $\alpha_1$-adrenergic receptors

- **Capsule**
Phathophysiology

BPH commonly results from both static and dynamic.
Static: Gradual enlargement of prostate
Dynamic: agents or situations that α-adrenergic tone and constrict the gland smooth muscle.
Androgen

Testosterone 5-alpha-reductase activity (type 2) dihydrotestosterone

Estrogen

Prostatic stromal cells contain estrogen receptors, and the concentrations are lower in hyperplastic than in normal prostatic tissue. Increase in the estrogen/androgen ratio in prostatic tissue, especially in the stroma.
Clinical Manifestations

Mild  Asymptomatic
      Peak urinary flow rate 10ml/s
      Postvoid residual urine volume 25-50ml

Moderate  Obstructive voiding symptoms and irritative voiding symptoms

Severe  More complication of BPH
Clinical Manifestations

**Obstructive symptoms:**
Urinary hesitancy
urine dribbles out of penis
Sense of incomplete emptying

**Irritative signs:**
Nocturia, Urgency, Frequency

**Complication:**
Chronic kidney disease
Gross hematuria
Urinary incontinence
Recurrent tract infection
Bladder stone
<table>
<thead>
<tr>
<th>AUA Symptom Score Sheet</th>
<th>Not at all</th>
<th>Less than 1 time in 5</th>
<th>Less than half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
<th>Your score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incomplete emptying</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Over the past month, how often have you had a sensation of not emptying your bladder completely after you finish urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Over the past month, how often have you had to urinate again less than two hours after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>Intermittency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Over the past month, how often have you found you stopped and started again several times when you urinated?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>Urgency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Over the last month, how difficult have you found it to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>Weak stream</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Over the past month, how often have you had a weak urinary stream?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>Straining</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Over the past month, how often have you had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>Nocturia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Over the past month, many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>Quality of life due to urinary symptoms</strong></td>
<td>Delighted</td>
<td>Pleased</td>
<td>Mostly satisfied</td>
<td>Mixed – about equally satisfied and dissatisfied</td>
<td>Mostly dissatisfied</td>
<td>Unhappy</td>
<td>Terrible</td>
</tr>
<tr>
<td>If you were to spend the rest of your life with your urinary condition the way it is now, how would you feel about that?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

**Total score:** 0-7 Mildly symptomatic; 8-19 moderately symptomatic; 20-35 severely symptomatic.
Diagnosis

- Medical history
- Physical examination
- Laboratory tests
  - Blood urea nitrogen (BUN)
  - Prostate specific antigen (PSA)
Diagnosis

- Physical examination
  A digital rectal examination should be done to assess prostate size and consistency and to detect nodules, indurations, and asymmetry, all of which raise suspicion for malignancy.

- Urinalysis
  to detect urinary infection and blood, which could indicate bladder cancer or calculi.
Diagnosis

- Serum prostate specific antigen (PSA)
  
The specificity of the serum PSA assay in men with obstructive symptoms is less than in asymptomatic men.

  Prostate cancer can cause obstructive symptoms, although the presence of symptoms is not predictive of prostate cancer.

  Measurements of serum PSA may be used as a screening test for prostate cancer in these men with BPH, preferably in men between the ages of 50 to 69 years and before therapy for BPH is discussed.
Diagnosis

- **Post-void residual urine volume**
  
  Determined by in-out catheterization, radiographic methods, or ultrasonography.

  Normal men have less than 12 mL of residual urine.

  In addition to being a possible indicator of BPH, a large residual volume is probably associated with increased risk of infection and is a precursor to bladder decompensation.
Diagnosis

- Serum A high serum creatinine
  may be due to bladder outlet obstruction or to underlying renal or prerenal disease; it also increases the risk for complications and mortality after prostatic surgery.
untreated BPH can cause acute urinary retention, recurrent urinary tract infections, hydronephrosis, and even renal failure.

Age, symptoms, urinary flow rate and prostate volume are risk factors for acute urinary retention.
Watchful waiting and behavioral modification
Medical Management
Surgical Management
SELF-CARE

- Urinate when you first get the urge. Also, go to the bathroom when you have the chance, even if you don't feel a need to urinate.
- Avoid alcohol and caffeine, especially after dinner.
- Don't drink a lot of fluid all at once. Spread out fluids throughout the day. Avoid drinking fluids within 2 hours of bedtime.
- Try NOT to take over-the-counter cold and sinus medications that contain decongestants or antihistamines. These medications can increase BPH symptoms.
- Keep warm and exercise regularly. Cold weather and lack of physical activity may worsen symptoms.
- Learn and perform Kegel exercises (pelvic strengthening exercises).
- Reduce stress. Nervousness and tension can lead to more frequent urination.
Treatment

- 5α-Reductase Inhibitors
- Alpha-1-adrenergic antagonists
Treatment

- $\alpha$-Adrenergic antagonists do not decrease prostate volume or PSA levels.
- $\alpha$-Adrenergic antagonists are associated with less sexual dysfunction than are $5\alpha$-reductase inhibitors.
- $\alpha$-Adrenergic antagonists which is faster acting and more effective than a $5\alpha$-reductase inhibitor.
A 5α-reductase inhibitor is a good first-choice agent in patients with a significantly enlarged prostate (>40 g) who cannot tolerate the cardiovascular adverse effects of α1-adrenergic antagonists.

In patients at risk for developing complications of BPH, specifically patients with an enlarged prostate gland greater than 40 g and an elevated PSA ≥1.4 ng/mL, combination drug therapy with an α1-adrenergic antagonist and a 5α-reductase inhibitor is more beneficial than single drug therapy.
Alpha-1-adrenergic antagonists Five long-acting alpha-1-antagonists, terazosin, doxazosin, tamsulosin, alfuzosin, and silodosin have been approved by the Food and Drug Administration in the United States for treatment of the symptoms of BPH. Prazosin, a short-acting alpha-1-antagonist, is generally not used for BPH, due to need for frequent dosing and the potential for more cardiovascular side effects.

Mechanism Alpha-1-adrenergic antagonists such as terazosin act against the dynamic component of bladder outlet obstruction. Prostatic tissue contains two types of alpha-adrenergic receptors: alpha-1 and alpha-2. Alpha-1 receptors are abundant in the prostate and base of the bladder, and sparse in the body of the bladder. The density of these receptors is increased in hyperplastic prostatic tissue. Alpha-1-adrenergic antagonists target alpha-1A receptors (largely in prostatic smooth muscle) and alpha-1D receptors (largely in bladder detrusor smooth muscle).
Terazosin, doxazosin, and alfuzosin are second-generation α-adrenoergic antagonists. They antagonize peripheral vascular α1-adrenoergic receptors in addition to those in the prostate. Therefore, their adverse effects include first-dose syncope, orthostatic hypotension, and dizziness. Alfuzosin is less likely to cause cardiovascular adverse effects than other second-generation agents.

To minimize orthostatic hypotension and first-dose syncope with terazosin and doxazosin, patients should be slowly titrated to a maintenance dose and should take these drugs at bedtime.
Treatment

- differ in terms of duration of action and dosage formulation.
- prazosin requires dosing two to three times per day, terazosin, doxazosin, and alfuzosin offer more convenient once-daily dosing. Because prazosin requires twice to thrice-daily dosing and has significant cardiovascular adverse effects, it is not recommended in the current
<table>
<thead>
<tr>
<th><strong>Dose titration schedule to reduce orthostatic effects</strong>[^1]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Terazosin standard (appropriate for most patients)</strong></td>
</tr>
<tr>
<td>Days 1 to 3</td>
</tr>
<tr>
<td>Days 4 to 14</td>
</tr>
<tr>
<td>Weeks 2 to 6</td>
</tr>
<tr>
<td>Weeks 7 and thereafter</td>
</tr>
<tr>
<td><strong>Terazosin rapid (for selected patients)</strong></td>
</tr>
<tr>
<td>Days 1 to 3</td>
</tr>
<tr>
<td>Days 4 to 14</td>
</tr>
<tr>
<td>Weeks 2 to 3</td>
</tr>
<tr>
<td>Weeks 4 and thereafter</td>
</tr>
<tr>
<td><strong>Doxazosin (immediate release)</strong></td>
</tr>
<tr>
<td>Days 1 to 3</td>
</tr>
<tr>
<td>Days 4 to 14</td>
</tr>
<tr>
<td>Weeks 2 to 6</td>
</tr>
<tr>
<td>Weeks 7 and thereafter</td>
</tr>
<tr>
<td><strong>Doxazosin (extended release preparation only)</strong></td>
</tr>
<tr>
<td>Days 1 to 21</td>
</tr>
<tr>
<td>Week 4 and thereafter</td>
</tr>
</tbody>
</table>

**Uroselective Alpha-1 receptor antagonists**[^2]•

<table>
<thead>
<tr>
<th>Antagonist</th>
<th>Initial and maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alfuzosin</td>
<td>10 mg</td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>0.4 mg</td>
</tr>
<tr>
<td>Silodosin</td>
<td>8 mg</td>
</tr>
</tbody>
</table>

BPH: benign prostatic hyperplasia.

*Titrate dose as tolerated and as needed for effect. Oral administration for all medications is once daily at bedtime. Peak effect of a given dose on BPH symptoms may not be fully evident until 4 to 6 weeks, if therapy is interrupted for three or more days, reinitiate at lowest dose and re-titrated according to schedule.

• Due to lower risk of orthostatic hypotension and syncope, uroselective agents do not require gradual dose titration. Oral administration for all medications is once daily at bedtime.


Treatment

- Reduces dynamic factor
  - Blocks $\alpha_1$-adrenergic receptors in prostatic stromal tissue
    
    Alfuzosin (UroXatral) → 10 mg PO daily
    Terazosin (Hytrin) → 1-10 mg PO daily
    Doxazosin (Cardura) → 1-8 mg PO daily

- Blocks $\alpha_1$-1A receptors in the prostate
  
  Tamsulosin (Flomax) → 0.4-0.8 mg PO daily
Terazosin

- Oral: Initial: 1 mg at bedtime, increasing as needed; most patients require 10 mg day. If no response after 4-6 weeks of 10 mg/day, may increase to 20 mg/day.

- ADVERSE REACTIONS
  - postural hypotension, dizziness, somnolence, nasal congestion/rhinitis, and impotence
Terazosin

- **CONTRAINDICATIONS**
  
  Hypersensitivity to quinazolines (doxazosin, prazosin, terazosin) or any component of the formulation; concurrent use with phosphodiesterase-5 (PDE-5) inhibitors including sildenafil (>25 mg), tadalafil, or vardenafil

- **WARNINGS / PRECAUTIONS**
  
  - Angina: Discontinue if symptoms of angina occur or worsen
  - Orthostatic hypotension/syncope
Tamsulosin (Flomax®)

- Tamsulosin, the only third-generation $\alpha$-adrenergic antagonist, is selective for prostatic $\alpha_1A$ receptors. Therefore, tamsulosin does not cause peripheral vascular smooth muscle relaxation.

- Tamsulosin is a good choice for patients who cannot tolerate hypotension; have severe coronary artery disease, volume depletion, cardiac arrhythmias, severe orthostasis, or liver failure; or are taking multiple antihypertensives. Tamsulosin is also suitable for patients who want to avoid the delay of dose titration or to avoid dosing only at bedtime.

- Caution is needed to avoid potential drug interactions. Tamsulosin decreases metabolism of cimetidine and diltiazem. Carbamazepine and phenytoin increase catabolism of $\alpha$-adrenergic antagonists.
Tamsulosin (Flomax®)

Oral: tamsulosin should be taken on an empty stomach because food decreases the drug’s bioavailability and reduces the peak

- The onset of peak action is quick, in the range of 1 week, and only a minority of patients will require up-titration to a higher daily dose.

- No decreases in blood pressure or increases in heart rate have been reported in normotensive patients, the elderly, subgroups of patients with well-controlled hypertension, or those with uncontrolled hypertension.
Tiredness and asthenia, ejaculatory dysfunction, flu-like symptoms, and nasal congestion are the most common dose-related adverse effects of tamsulosin.
Tamsulosin (Flomax®)

- WARNINGS / PRECAUTIONS
  - Angina: Discontinue if symptoms of angina occur or worsen
  - Orthostatic hypotension/syncope
  - Priapism:
  - Sulfonamide allergy
to avoid α1-adrenergic antagonists for 4 hours after taking a dose of one of these phosphodiesterase inhibitors. The exception is tadalafil, which can be taken together with tamsulosin 0.4 mg.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Half-Life (h)</th>
<th>Usual Daily Dosage</th>
<th>Time to Peak Effect on BPH Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prazosin (Minipress)</td>
<td>2–3</td>
<td>2–10 mg in two to three divided doses</td>
<td>2–6 weeks</td>
</tr>
<tr>
<td>Terazosin (Hytrin)</td>
<td>11–14</td>
<td>1–10 mg as a single dose; maximum 20 mg</td>
<td>2–6 weeks</td>
</tr>
<tr>
<td>Doxazosin (Cardura)</td>
<td>15–19</td>
<td>1–4 mg as a single dose; maximum 8 mg</td>
<td>2–6 weeks</td>
</tr>
<tr>
<td>Doxazosin GTS (Cardura XL)</td>
<td>15–19</td>
<td>4 or 8 mg as a single dose, maximum 8 mg</td>
<td>Several days</td>
</tr>
<tr>
<td>Alfuzosin (Uroxatral)</td>
<td>14–15</td>
<td>10 mg as a single dose</td>
<td>Several days</td>
</tr>
<tr>
<td>Tamsulosin (Flomax)</td>
<td>14–15</td>
<td>0.4 or 0.8 mg as a single dose</td>
<td>Several days</td>
</tr>
</tbody>
</table>
Treatment

5α-Reductase Inhibitors

- 5α -Reductase inhibitors are the only agents approved for BPH by (FDA) that interfere with the stimulatory effect of testosterone. These agents slow disease progression and decrease the risk of complications.

- Compared with α-adrenergic antagonists, 5α -reductase inhibitors have the disadvantages of requiring 6 months to maximally shrink an enlarged prostate, being less likely to induce objective improvement, and causing more sexual dysfunction.
Treatment

- $5\alpha$ -Reductase inhibitors reduce serum PSA levels by 50%. Therefore, PSA should be measured at baseline and, for monitoring purposes, subsequent measurements should be doubled.

- $5\alpha$ -Reductase inhibitors are in FDA pregnancy category X and are therefore contraindicated in pregnant females. Pregnant and potentially pregnant women should not have contact with semen from men receiving $5\alpha$ -Reductase inhibitors.
Treatment

Reduces static factor
Blocks 5α-reductase enzyme

Finasteride (Proscar)
Dutasteride (Avodart)

Blocks dihydrotestosterone at its intracellular receptor

Bicalutamide (Casodex)
Finasteride

- Benign prostatic hyperplasia (Proscar®): Oral: 5 mg/day as a single dose; clinical responses occur within 12 weeks to 6 months of initiation of therapy; long-term administration is recommended for maximal response

- Male pattern baldness (Propecia®): Oral: 1 mg daily

- Female hirsutism (unlabeled use): Oral: 5 mg/day
Finasteride

- **CONtraindications** — Hypersensitivity to finasteride or any component of the formulation; pregnancy; not for use in children

- **WARNings / Precautions**
  Special handling: Hazardous agent: Use appropriate precautions for handling and disposal. Women/pregnancy: Women can absorb the active ingredient through the skin and should always use caution whenever handling. Pregnant women or women trying to conceive should not handle the product; finasteride may negatively impact fetal development.
<table>
<thead>
<tr>
<th></th>
<th>$\alpha_1$-Adrenergic Antagonists</th>
<th>$5\alpha$-Reductase Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreases prostate size</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Halts disease progression</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Peak onset</td>
<td>1–6 weeks</td>
<td>3–6 months</td>
</tr>
<tr>
<td>Efficacy</td>
<td>++</td>
<td>++ (in patients with enlarged prostates)</td>
</tr>
<tr>
<td>Frequency of dosing</td>
<td>1–2 times per day, depending on the agent</td>
<td>Once per day</td>
</tr>
<tr>
<td>Decreases prostate-specific antigen</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Sexual dysfunction adverse effects</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Cardiovascular adverse effects</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
Treatment

Reduces static factor

Flutamide (Eulexin) 100-250 mg PO t.i.d.
Leuprolide (Lupron) 7.5 mg IM monthly or 22.5 mg IM every 3 months
Nafarelin 400 mcg SC daily
Treatment

- **OTHER STRATEGIES**: Patients with BPH should avoid medications that can exacerbate symptoms or induce urinary retention. These include anticholinergic medications such as sedating antihistamines, and adrenergic agents such as decongestants.

- Behavioral modifications may be helpful. These include avoiding fluids prior to bedtime or before going out, reducing consumption of mild diuretics such as caffeine and alcohol, and double voiding to empty the bladder more completely.
Antimuscarinics

Some men with have obstructive symptoms, such as frequency, urgency, and incontinence, related to an overactive bladder. Bladder contractions are stimulated by acetylcholine effects on muscarinic receptors in smooth muscle of the bladder.

Use of antimuscarinic agents should be restricted to men with low post-void residual volumes.
- Tolterodine for reduction of urgency episodes and frequency.
- Oxybutynin has direct antispasmodic effects and inhibits the action of acetylcholine on smooth muscle. Was superior to tolterodine for reduction of incontinence.
SURGICAL INTERVENTION

- Prostatectomy, performed transurethrally or suprapubically, is the gold standard for treatment of patients with moderate or severe symptoms of BPH and for all patients with complications.
The choice of a specific surgical procedure is usually based on the severity of your symptoms and the size and shape of your prostate gland.

**Transurethral resection of the prostate (TURP):** This is the most common and most proven surgical treatment for BPH. TURP is performed by inserting a scope through the penis and removing the prostate piece by piece.

**Transurethral incision of the prostate (TUIP):** This procedure is similar to TURP, but is usually performed in men who have a smaller prostate. It is usually performed without the need for a hospital stay. Like TURP, a scope is inserted through the penis until the prostate is reached. Then, rather than removing the prostate, a small incision is made in the prostate tissue to enlarge the opening of the urethra and bladder outlet.

**Simple prostatectomy:** An open prostatectomy is usually performed using general or spinal anesthesia. An incision is made through the abdomen or perineum (the area behind the scrotum). Only the inner part of the prostate gland is removed. The outer portion is left behind. This is a lengthy procedure, and it usually requires a hospital stay of 5 to 10 days.
The primary therapeutic outcome of BPH therapy is restoring adequate urinary flow without causing adverse effects.

Outcome depends on the patient's perception of effectiveness and acceptability of therapy. Objective measures of bladder emptying (e.g., uroflowmeter and postvoid residual urine volumes) are also useful after 6 to 12 months of 5α-reductase inhibitor therapy or 3 to 4 weeks of α-adrenergic antagonist therapy.

Laboratory tests (e.g., BUN, creatinine, PSA) and urinalysis should be monitored regularly. In addition, patients should have an annual digital rectal examination. If PSA does not decrease by 50% after 6 months of 5α-reductase inhibitor therapy, the patient should be evaluated for prostate cancer.
BPH is not believed to be a risk factor for prostate cancer, although studies have come to conflicting results.

Prostate cancer & BPH

BPH occurs primarily in the central or transitional zone of the prostate, while prostate cancer originates primarily in the peripheral part of the prostate.
از توجه شما متشکرم
finasteride often suppresses the hematuria