Medical treatment of benign prostatic hyperplasia

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INTRODUCTION

Benign prostatic hyperplasia (BPH) increases in prevalence as men age. Urinary symptoms include increased frequency of urination, nocturia, hesitancy, urgency, and weak urinary stream. Treatment includes medical and surgical options.

The medical therapy of BPH will be reviewed here. The clinical manifestations and diagnosis, epidemiology and pathogenesis, and surgical and other invasive therapies of BPH are all discussed separately. (See "Clinical manifestations and diagnostic evaluation of benign prostatic hyperplasia" and "Epidemiology and pathophysiology of benign prostatic hyperplasia" and "Surgical treatment of benign prostatic hyperplasia (BPH)".)

Treatment of lower urinary tract symptoms (LUTS) in men due to etiologies other than BPH is also discussed separately. (See "Lower urinary tract symptoms in males".)

GENERAL CONSIDERATIONS

Lifestyle modifications — Lifestyle modifications and behavioral interventions are first-line treatments for all patients.

Lifestyle modifications include:

- Limiting fluid intake before bedtime or prior to travel
- Limiting intake of mild diuretics (eg, caffeine, alcohol)
- Limiting intake of bladder irritants (eg, highly seasoned or irritative foods)

- Avoiding constipation
- Increasing activity, including regular strenuous exercise
- Weight control

Additional behavioral interventions include:

- Kegel exercises at time of urinary urgency. (See "Patient education: Pelvic muscle (Kegel) exercises (The Basics)".)

- Timed voiding regimens – In patients who exhibit obstructive complaints (ie, decreased force of stream) or who are noted to carry a high post-void residual, instructing them to attempt to empty their bladder based on a time interval rather than by the usual sensations can be effective in reducing lower urinary tract symptoms (LUTS). Requesting that they urinate “by the clock” (every 90 to 120 minutes during the daytime) seems to be effective.

- Double-voiding techniques – Similarly, men who complain of obstructive symptoms may benefit by following one urination by a second attempt at emptying (the double void) within a minute or two of the initial void.

Treatment considerations — Most commonly, treatment is indicated for symptom relief, if lifestyle and behavioral modifications do not suffice. In a smaller subset of men, treatment is need to reverse complications of LUTS/benign prostatic hyperplasia (BPH) such as a rising post-void residual urine, bladder stone, associated hydronephrosis (with or without renal compromise), or recurrent UTI. Symptoms include those of storage (frequency, urgency, and nocturia) and voiding (slow or decreased force urinary stream, straining to void, intermittency, hesitancy, and splitting of the voiding stream). (See "Lower urinary tract symptoms in males".)

We engage patients in a shared decision-making process to choose the preferred treatment after initial evaluation [1]. Patients should be provided with the risk/benefit profile for all treatment options. Symptomatic patients may benefit from medical or surgical treatment. However, patients should generally be trialed on medical management before proceeding to surgical intervention. If patients do not respond adequately to medical management, they should be considered for surgical therapy to relieve obstruction and improve LUTS and overall quality of life.

If medical treatment is considered, the patient should continue lifestyle modifications (see 'Lifestyle modifications' above). During medical treatment, it is recommended that the patient be monitored to assess treatment success and possible adverse events. The time from the initiation of therapy to treatment assessment varies according to the pharmacologic agent

prescribed. If the treatment is successful and the patient is satisfied, yearly follow-ups should be scheduled and include a repeat of the initial evaluation. The follow-up strategy will allow the clinician to detect any changes that have occurred and, more specifically, if symptoms have progressed or become more severe or if a complication has developed that requires surgery. (See "Surgical treatment of benign prostatic hyperplasia (BPH)".)

Men with LUTS/BPH frequently suffer from multiple medical comorbidities. They may use medications that can worsen LUTS (eg, diuretics, anticholinergics) or have drug-drug interactions with medications used for the medical management of LUTS (eg, vasodilator drugs used for the treatment of hypertension and alpha-adrenergic drugs used for LUTS). The clinician should be aware of such iatrogenic causes for worsening LUTS before starting treatment.

When to refer to a urologist — Although primary care clinicians can provide medical therapy for LUTS/BPH, there are some clinical scenarios in which referral to a urologist is appropriate. These include the complications of renal insufficiency, refractory urinary retention, recurrent urinary tract infections, recurrent bladder stones or gross hematuria, rising post-void residual urine volume, and bilateral hydronephrosis with renal functional impairment. In addition, patients with persistent bothersome symptoms after basic management, or those who present with severe symptoms, should be referred to a urologist for possible surgical therapy.

MEDICAL THERAPY FOR SYMPTOM RELIEF

Alpha-adrenergic receptor blockers for most patients — We use alpha-adrenergic receptor blockers as initial pharmacologic agents in most patients with LUTS/BPH. Treatment effects are seen within days.

Bladder outlet obstruction (BOO) is primarily mediated by alpha-1 adrenergic receptors located on prostatic smooth muscle [2], which are upregulated in the stromal glandular hyperplasia seen in BPH. Blocking signaling through the alpha-adrenergic receptors leads to relaxation of the smooth muscle of the bladder neck and the prostatic urethra.

Selective alpha-1 adrenergic receptor antagonists are efficacious in relieving symptoms of BPH but have fewer adverse effects than nonselective blockers [3]. The initially developed selective alpha-1 adrenergic receptor antagonists required twice-daily dosing (prazosin, alfuzosin); however, the extended duration of action of second-generation alpha-1 adrenergic receptor antagonists enables single daily dosing (terazosin, doxazosin, tamsulosin, extended-release alfuzosin, silodosin). The most common treatment regimens for the five alpha-adrenergic receptor blockers approved in the United States are shown in the table (table 1). A controlled-

release tamsulosin tablet is also available in some markets but has not been well studied for treatment of BPH.

Side effects and interactions — The most commonly reported adverse effects of alpha-adrenergic receptor blockers include dizziness (5 to 15 percent) and rhinitis (12 percent) [4]. The agents with greater prostate selectivity (eg, tamsulosin, silodosin) have fewer systemic adverse effects but are associated with a higher frequency of retrograde or anejaculation (8 to 28 percent). Patients prescribed alpha-1 adrenergic blockers should be counseled about the possibility of intraoperative floppy iris syndrome (IFIS). (See 'Intraoperative floppy iris syndrome' below.)

Hypotension is an important potential side effect. Certain agents have a lower risk of hypotension (eg, tamsulosin, alfuzosin, silodosin) than others (eg, terazosin and doxazosin) [5-7]. Because of this, terazosin and doxazosin generally need to be initiated at bedtime (to reduce postural lightheadedness soon after starting the medication), and the dose then titrated up over several weeks. Blood pressures should be monitored in patients who are started on alpha-adrenergic receptor blockers.

The hypotensive effects of terazosin and doxazosin can theoretically be worsened by concomitant use of the phosphodiesterase type 5 (PDE5) inhibitors, particularly sildenafil or vardenafil. Tamsulosin at a dose of 0.4 mg/day does not appear to significantly potentiate the hypotensive effects of sildenafil [8].

Intraoperative floppy iris syndrome — Alpha-1 antagonists, particularly tamsulosin, have been associated with IFIS. IFIS is a surgical condition associated with cataract operations, characterized by a triad of findings: intraoperative miosis despite preoperative dilation, iris prolapse, and a billowing flaccid iris [9]. Although a causal relation between the use of alpha-1 adrenergic blockers and IFIS remains controversial, IFIS is associated with increased rates of iris trauma and posterior capsular rupture during cataract surgery [10].

The American Urological Association guidelines recommend that men with LUTS/BPH for whom alpha blocker therapy is offered should be asked about planned cataract surgery. Men with planned cataract surgery should avoid the initiation of alpha blockers until their cataract surgery is completed. In men with no planned cataract surgery, there are insufficient data to recommend withholding or discontinuing alpha blockers for bothersome LUTS/BPH. Ophthalmologists must make themselves aware, via a medication history, of preoperative alpha blocker use as they can take intraoperative precautions to reduce IFIS complications. (See "Cataract in adults", section on 'Limiting risk of intraoperative floppy iris syndrome'.)

Efficacy — In a meta-analysis of trials with alfuzosin, terazosin, doxazosin, or tamsulosin versus placebo, all agents were found to be more effective than placebo [11].

Terazosin, doxazosin, tamsulosin, alfuzosin, and silodosin appear to have similar efficacy, although there have been few direct comparisons [11-15]. Newer drugs such as silodosin may have greater risk for sexual (altered ejaculation) adverse events (risk ratio [RR] 1.96, 95% CI 1.04-3.71, silodosin versus tamsulosin) compared with older drugs in this class (terazosin, doxazosin, tamsulosin, alfuzosin) [12,15].

In a 2010 meta-analysis, alpha-1 adrenergic antagonists were more effective than 5-alpha-reductase inhibitors for short- and long-term treatment of BPH [16]. (See '5-alpha reductase inhibitors' below.)

Patients with erectile dysfunction — We use PDE5 inhibitors as initial therapy in men with BPH-related symptoms and erectile dysfunction.

Phosphodiesterase type 5 inhibitors — PDE5 inhibitors have been shown in several randomized trials to be beneficial in improving symptom scores in patients with LUTS/BPH, although no significant changes in urine flow rates have been demonstrated [17-19].

Reported adverse effects with PDE5 inhibitors are relatively rare, with the more commonly reported effects consisting of headache, flushing, dyspepsia, nasal congestion, back pain, myalgias, and sinusitis. There is an increased risk of hypotension in patients also using certain alpha-adrenergic blockers. (See 'Alpha-adrenergic receptor blockers for most patients' above.)

A 2018 Cochrane review of 16 randomized trials comparing PDE5 inhibitors with either placebo or alpha blockers in men with LUTS/BPH found that PDE5 inhibitors reduced symptom scores slightly compared with placebo, with a possible increase in adverse events [20]. PDE5 inhibitors were not superior to alpha blockers, and there was no benefit of adding PDE5 inhibitors to therapy for LUTS/BPH with either alpha blockers or 5-alpha reductase inhibitors (5ARIs).

In a trial that compared tadalafil with tamsulosin, the two drugs were comparable in their efficacy in LUTS improvement [21]. Tadalafil 5 mg/day has been approved for use in men with LUTS/BPH in the United States.

These medications are discussed in more detail separately. (See "Lower urinary tract symptoms in males", section on 'Phosphodiesterase 5 inhibitors'.)

Patients with overactive bladder symptoms — Beta-3 adrenergic agonists or anticholinergics can be used for patients in whom OAB symptoms (frequency, urgency, and incontinence) predominate. Lifestyle modifications remain an important component of treatment.

Beta-3 adrenergic agonists — Beta-3 adrenergic agonists are effective in men with concomitant OAB and its urodynamic manifestations: detrusor overactivity. The symptoms attributed to this are urgency, urge incontinence, and frequency.

Beta-3 adrenergic agonists stimulate detrusor beta-3 adrenergic receptors to promote relaxation. Though less abundant than beta-2 adrenergic receptors, beta-3 receptors are more efficacious in promoting relaxation without compromising bladder contractility. Mirabegron and vibegron are available treatments [22]. These medications may be preferred over anticholinergic agents as they do not cause dryness of the mouth.

Meta-analyses of trials have found mirabegron treatment to be more efficacious in reducing urgency and incontinence episodes than placebo and support the use of the medication in men with concomitant BPH [23]. Mirabegron was not associated with an increased incidence of urinary retention. However, blood pressure should be monitored in men receiving beta-3 adrenergic agonists because these drugs can raise blood pressure (see "Lower urinary tract symptoms in males", section on 'Beta3-adrenoceptor agonists'). In a phase 3 trial, Vibegron has shown reductions in micturitions, urgency episodes, and urge incontinence and increased the volume per micturition without a risk of hypertension or need for titration [24].

Anticholinergics — Anticholinergic (antimuscarinic) agents are useful in treating predominantly irritative symptoms due to OAB in men with BPH who do not have an increased post-void residual.

There has been hesitation in utilizing anticholinergics in men with BPH due to the concern that these drugs may increase the risk of acute urinary retention, especially in the setting of BPE with obstruction. Therefore, a post-void residual should be measured prior to initiating treatment with an anticholinergic agent; these drugs should be used cautiously in men with elevated post-void residual (>300 mL).

Anticholinergic (antimuscarinic) agents are also used in combination with alpha-adrenergic blockers in patients with BPH whose irritative symptoms persist after monotherapy with an optimized dose of an alpha-adrenergic blocker. (See 'Combination therapy' below.)

Some of these agents are available in topical/transdermal formulations, although their use is uncommon. Common oral therapeutic dosing is presented in the table (table 2). Common side effects include dry mouth, constipation, dyspepsia, blurred vision, urinary retention, headache, somnolence, and nausea. These effects resulting from cross-reactivity with other cholinergic receptors throughout the body.

Anticholinergics are discussed in detail elsewhere. (See "Lower urinary tract symptoms in males", section on 'Treatment options' and "Lower urinary tract symptoms in males", section on 'Treatment for urodynamically proven OAB'.)

THERAPY TO PREVENT PROGESSION

5-alpha reductase inhibitors — Steroid 5ARIs block the conversion of testosterone (T) to dihydrotestosterone (DHT) and are efficacious in the treatment of LUTS due to prostate enlargement as documented by digital rectal examination (DRE) or transrectal ultrasonography (TRUS). As such, they are used to prevent BPH progression rather than acute symptom treatment. Results from the Medical Therapy of Prostatic Symptoms (MTOPS) study support the utility of 5ARIs in prostates larger than 35 g. The larger the prostate, the bigger the impact of this class of agents [25]. PSA levels can be used as a proxy for prostate volume. Levels below 1.5 ng/mL indicate a prostate that is likely too small to benefit from this treatment. By decreasing the prostatic volume, the static component of benign prostatic enlargement (BPE) is reduced, thereby decreasing the effective BOO. Symptomatic individuals with smaller prostatic volumes may not achieve similar treatment effects.

Steroid 5ARIs may be used alone or in combination with other medications. The reduction in prostatic volume by 5ARIs may take many months, with the maximum effect in symptom relief seen typically after 6 to 12 months of therapy [26]. They have the potential for long-term reduction in prostate volume and a decrease in the need for prostate surgery.

Three isozymes of 5-alpha reductase have been identified: type 1, type 2, and type 3. Finasteride is a selective competitive inhibitor of the type 2 isozyme, whereas dutasteride is a nonselective inhibitor of both type 1 and type 2 isozymes. Both drugs are effective in reducing prostate volume, improving symptoms and urinary flow rates, and reducing the need for surgical intervention. The most common dosing of these medications is presented in the table (table 2). Treatment should be continued indefinitely to prevent symptom relapse [25-30].

Side effects and concerns

Suppression of serum PSA levels — The use of 5ARIs suppresses serum PSA levels by about 50 percent. For this reason, most investigators warn clinicians that a baseline serum PSA should checked prior to using any 5ARIs. The baseline level can be used to determine whether therapy is likely to be effective as described above, and the pretreatment level should be known because 5ARIs lower PSA levels. Thus, clinicians may be lured into a false sense of security if a suppressed PSA is measured after starting 5ARI without consideration as to the impact of drug.

Most experts recommend multiplying PSA value by two in patients receiving long-term (>3 months of continuous treatment) 5ARI therapy. (See "Measurement of prostate-specific antigen", section on 'Medications'.)

Concerns regarding prostate cancer — Two randomized trials, the Prostate Cancer Prevention Trial (PCPT, using finasteride) and the REDUCE trials (using dutasteride), reported a reduced risk of prostate cancer compared with placebo but raised concerns about a possible increased risk of high-grade prostate cancer [31,32]. There was no survival benefit observed with 5ARI treatment in either trial. The apparent increase in the incidence of high-grade cancer may be due to detection bias. These findings led the US Food and Drug Administration (FDA) to recommend evaluation for other urologic conditions, including prostate cancer in patients with BPH being considered for treatment with a steroid 5ARI. This is discussed in detail elsewhere (See "Chemoprevention strategies in prostate cancer", section on '5-Alpha reductase inhibitors'.)

Sexual dysfunction — Sexual dysfunction concurrent with 5ARIs use has been well known since the drug class development. The issue at hand is whether the persistence or emergence of dysfunction following drug cessation even exists. This putative adverse event has been coined “post finasteride syndrome” (PFS). Many have doubts about the mere existence of PFS based primarily on the source and quality of the reports from those supporting this association [33,34].

Most studies supporting PFS are plagued by systematic errors and biases arising from shortcomings in study method and design. These include, for example, the absence of baseline testing, an insufficient or nonexistent control population, no protection against the nocebo effect [35], reporter bias based on awareness of PFS before onset of symptoms, a lack of the use of validated questionnaires, and referral biases of study subjects. Attempting to assess sexual function and depression in a retrospective fashion is a well-described error and prone to severe recall bias [36,37]. These faults permeate nearly the entirety of the PFS literature. Only now are better controlled epidemiological studies emerging which adhere to these fundamental principles, and these fail to support the existence of PFS [38,39]. The results of randomized controlled trials and well-designed, controlled epidemiological studies contain data which do not support the existence of an association between finasteride and persistent sexual dysfunction following drug discontinuation. These controlled studies used more rigorous methods compared with the anecdotal reports of persistence. Additionally, the proposed mechanisms for persistence have not been scientifically established and appear implausible in many circumstances.

Other side effects — 5ARIs may impact fetal development if ingested during pregnancy. Thus, it is important that drug diversion for any reason be avoided. Pregnant females are also

advised to avoid contact with crushed or broken tablets.

Efficacy — In the North American finasteride trial, men with LUTS/BPH who were treated with 5 mg finasteride had a 23 percent reduction in obstructive and 18 percent reduction in nonobstructive symptom scores, an increase in maximal urinary flow rate, and a 19 percent reduction in mean prostatic volume compared with those who took placebo [26].

In the Proscar Long-term Efficacy and Safety Study (PLESS) trial, men taking 5 mg of finasteride had improvements in symptoms and urinary flow rates, as well as a reduction in prostate volume, that were durable over four years [25,27,28]. Finasteride treatment reduced the risk of acute urinary retention and the need for surgical intervention when compared with placebo.

Dutasteride has also been shown in randomized trials and a 2013 meta-analysis to improve symptom scores and maximal urinary flow rates, decrease prostate volume, and reduce the risk of acute urinary retention and need for surgical BPH intervention [29,40]. In a head-to-head comparison of finasteride and dutasteride, no significant difference in prostate volume reduction and improvements in urine flow rates was found between the two drugs [30]. The most commonly reported adverse effects of finasteride and dutasteride include erectile dysfunction, decreased libido, ejaculatory dysfunction, gynecomastia, and breast tenderness.

COMBINATION THERAPY

For certain patients, combination therapy may be appropriate.

Combination of alpha-adrenergic blockers and steroid 5-alpha reductase inhibitors — We use combination therapy with an alpha-adrenergic blocker and a steroid 5ARI in men who have demonstrated prostate enlargement and moderate to severe symptoms of BPH (International Prostate Symptom Score [IPSS] >12). (See "Lower urinary tract symptoms in males", section on 'International Prostate Symptom Score'.)

The VA Cooperative Study, the Prospective European Doxazosin and Combination Therapy (PREDICT) trial, and the Medical Therapy of Prostatic Symptoms (MTOPS) study [41-43] compared finasteride plus doxazosin combination therapy, finasteride monotherapy, doxazosin monotherapy, and placebo, respectively. Combination therapy was associated with a greater reduction in symptomatic clinical progression, episodes of acute urinary retention, incidence of renal insufficiency, recurrent urinary tract infections, and urinary incontinence compared with monotherapy with either agent. Furthermore, when men were stratified for prostate size and PSA, those with larger prostates (>40 mL) and higher baseline PSA (>4.0 ng/mL) showed a more significant reduction in disease progression. The Combination of Avodart and Tamsulosin

(CombAT) trial randomized men with BPH to combination of dutasteride plus tamsulosin, dutasteride alone, or tamsulosin alone. The combination of dutasteride and tamsulosin was superior to monotherapy with either drug in improving BPH symptoms and clinical progression; combination therapy was superior to tamsulosin, but not dutasteride, in reducing the risk of acute urinary retention and surgical intervention, especially for men with prostate volumes ≥30 mL [44].

Combination antimuscarinics or beta-3 adrenergic agonist and alpha blockers — OAB is a chronic symptom syndrome that can affect up to a third of the adult population [45]. Diagnosing OAB in men can be complicated by the presence of the voiding symptoms experienced by men with LUTS/BPH [46]. Recommended pharmacologic treatments for LUTS/BPH include alpha-1 adrenoreceptor antagonists (alpha-1 blockers), although these therapeutics may fail to alleviate urine storage symptoms when they are administered as single agents.

Numerous clinical studies have demonstrated that antimuscarinics are effective and generally well-tolerated treatments for patients with OAB and that they successfully reduce the storage symptoms of frequency, nocturia, and urgency [47-49]. Studies in men have shown that antimuscarinics in combination with alpha-1 blockers can improve OAB-related symptoms [50-52]. However, there are concerns about the tolerability of antimuscarinics due to the risk or occurrence of specific side effects such as dry mouth, urinary retention, and possible dementia [53,54].

Limited data are available on the use of mirabegron in combination in men with underlying LUTS/BPH. In a pilot study, the combination of mirabegron and tamsulosin (TAM+MIRA) was effective and well tolerated in 94 patients with OAB symptoms induced by LUTS/BPH [55]. An investigation (PLUS study) was conducted in North America and Europe to assess the efficacy and safety of mirabegron versus placebo as add-on therapy to alpha-1 blocker treatment for men with ongoing OAB symptoms [56]. TAM+MIRA was statistically superior to tamsulosin plus placebo in reducing the mean number of micturitions/day. Statistically superior results were noted for TAM+MIRA in mean voided volume per micturition and urgency episodes/day but not on symptom severity as measured by the IPSS.

Combination tadalafil and finasteride — A combination pill of finasteride (5 mg) and tadalafil (5 mg) is available and was tested in a short-duration randomized controlled trial against finasteride monotherapy [57]. In their review of the topic, the American Urological Association's 2021 clinical BPH guidelines reported that impact of the combination of low-dose daily tadalafil with finasteride offers little or no advantages in symptom improvement over finasteride alone

in the short term [58]. Not surprisingly, the combination of low-dose daily tadalafil with finasteride increases erectile response over finasteride alone.

HERBAL REMEDIES

Nonconventional approaches to the management of lower urinary tract symptoms (LUTS)/benign prostatic hyperplasia (BPH) are of interest to many patients, and the use of plant/herb-based remedies for LUTS/BPH is common. Of particular appeal are the dietary supplements, which include extracts of the saw palmetto plant (*Serenoa repens*) and stinging nettle (*Urtica dioica*). A 2008 survey found that phytotherapy was the second most commonly utilized remedy behind only the alpha-adrenergic blocker monotherapy across Europe; these agents were typically used by patients with the lowest International Prostate Symptom Score (IPSS) [59]. As the production and sale of these agents are not subject to the stringent requirements of the US Food and Drug Administration (FDA)'s drug approval process, the manufacturing of these agents is not standardized, and the efficacy and safety of most herbal products that are sold over the counter have not been rigorously tested. Although 5-alpha reductase inhibition, antiinflammatory effects, and growth factor alteration have been postulated as potential mechanisms, proof of mechanism studies have been generally lacking.

Saw palmetto — Saw palmetto, derived from berries of the *S. repens* (dwarf palm plant), has commonly been utilized as a phytotherapeutic for BPH. This is discussed in detail elsewhere. (See "Clinical use of saw palmetto", section on 'Benign prostatic hypertrophy'.)

Hypoxis rooperi — South African star grass (*Hypoxis rooperi*) contains a beta-sitosterol which is believed to be its active ingredient. A meta-analysis noted that while studies of beta-sitosterol have reported improvements in urine flow rates and symptom scores, the problems of study design in these studies precluded strong inferences. Therefore, the long-term efficacy and safety of this product remain unclear [60]. Similar to case with saw palmetto, the American Urological Association guidelines in 2011 recommended against these agents.

Pygeum africanum — African plum (*Pygeum africanum*) is believed by some to exert an antiinflammatory effect by an inhibitory effect on neutrophils as well as on basic fibroblastic growth factor- and epidermal growth factor-induced prostatic fibroblast proliferation. Proof of this postulated potential mechanism is lacking. There has been a paucity of randomized placebo-controlled trials and the efficacy of *P. africanum* remains uncertain.

REFERRAL FOR SURGICAL MANAGEMENT

In general, patients should be trialed on medical management before proceeding to surgical intervention. If patients have not responded to medical management, they should be considered for surgical therapy to relieve obstruction and improve symptoms and overall quality of life. However, many men with lower urinary tract symptoms (LUTS)/benign prostatic hyperplasia (BPH) will not experience a significant degree of bother from their symptoms, and these individuals may elect a period of active surveillance. The clinician should reassure the patient that a period of active surveillance is unlikely to result in any serious or irreversible damage to the urinary tract. (See "Surgical treatment of benign prostatic hyperplasia (BPH)".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Benign prostatic hyperplasia".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Benign prostatic hyperplasia (enlarged prostate) (The Basics)")
- Beyond the Basics topics (see "Patient education: Benign prostatic hyperplasia (BPH) (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Lifestyle modifications for all patients** – It is suggested that all men with lower urinary tract symptoms (LUTS)/BPH be instructed in lifestyle interventions. These should be tailored to symptoms but may 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. (See 'Lifestyle modifications' above.)

- **Medical management for symptom relief** – Men with LUTS/BPH can be treated with one or more classes of medications and, in general, should try medical treatment prior to considering surgical interventions. For most patients, we initiate monotherapy with an alpha-1 adrenergic antagonist for initial treatment (table 1) (see 'Alpha-adrenergic receptor blockers for most patients' above). Alternative monotherapy agents may be used in certain settings (table 2). These include:

  - In men who have concomitant erectile dysfunction, phosphodiesterase type 5 (PDE5) inhibitors are a reasonable alternative to alpha-1 adrenergic antagonists for initial medical therapy. (See 'Phosphodiesterase type 5 inhibitors' above and "Treatment of male sexual dysfunction", section on 'Erectile dysfunction'.)

  - In men with low post-void residual urine volumes and irritative symptoms, anticholinergics or beta-3 agonists are a reasonable alternative to alpha-1 adrenergic antagonists for initial medical therapy. (See 'Patients with overactive bladder symptoms' above.)

- **Therapy to prevent progression** – In men with demonstrated benign prostatic enlargement (BPE), treatment with 5-alpha reductase inhibitors (5ARIs) to prevent disease progression is a reasonable option. Treatment for 6 to 12 months is generally needed before prostate size is sufficiently reduced to improve symptoms. Finasteride and dutasteride appear to have similar efficacy and side effect profiles. (See '5-alpha reductase inhibitors' above.)

- **Combination therapy for some patients**

  - For patients with low post-void residual urine volumes and irritative symptoms (eg, frequency, urgency) that persist during monotherapy with an alpha-1 adrenergic antagonist or anticholinergic agents, we use combination treatment with alpha-1 adrenergic antagonists and anticholinergic agents or beta-3 agonists. (See 'Combination therapy' above.)

  - We use combination therapy with an alpha-adrenergic blocker and a steroid 5ARI in men who have demonstrated prostate enlargement and moderate to severe symptoms

of BPH. (See 'Combination of alpha-adrenergic blockers and steroid 5-alpha reductase inhibitors' above.)

- **When to refer to urology** – Referral to a urologist is appropriate for patients with the complications of renal insufficiency, refractory urinary retention, recurrent urinary tract infections, recurrent bladder stones or gross hematuria, rising post-void residual urine volume, or bilateral hydronephrosis with renal function impairment. In addition, patients with persistent bothersome symptoms after basic management, or those who present with severe symptoms, should be referred to a urologist for possible surgical therapy. (See 'When to refer to a urologist' above and "Surgical treatment of benign prostatic hyperplasia (BPH)".)

- **No role for herbal remedies** – Data concerning efficacy and safety of herbal therapies for BPH are concerning. Until additional studies are available, we do not use these agents for the treatment of BPH. (See 'Herbal remedies' above.)

- **Surgical management** – If patients have not responded to medical management, they should be considered for surgical therapy to relieve obstruction and improve symptoms and overall quality of life. (See 'Referral for surgical management' above.)

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GRAPHICS

Alpha-1-receptor antagonists used to treat lower urinary tract symptoms due to benign prostatic hyperplasia (BPH)

Medication	Dose*		Administration
Alfuzosin (Uroxatral, Xatral)	Initial and maintenance	10 mg	Once daily immediately following a meal at the same time each day
Silodosin (Rapaflo)	Initial and maintenance	8 mg	Once daily with a meal at the same time each day
Tamsulosin (Flomax)	Initial and maintenance	0.4 mg	Once daily approximately 30 minutes after a meal at the same time each day; 0.8 mg dose may be administered as 0.4 mg twice daily
	If inadequate response after 2 to 4 weeks	0.8 mg	
Tamsulosin extended-release (Flomax CR) (NOTE: formulation available in some countries other than the United States)	Initial and maintenance	0.4 mg	Once daily with a meal at the same time each day; maximum dose 0.4 mg once daily
Conventional agents: Titration recommended to reduce orthostatic effects Dose is advanced as shown if patient remains symptomatic and is tolerating current dose			
Doxazosin immediate-release (Cardura)	Days 1 to 3	1 mg	Once daily at bedtime
	Days 4 to 14	2 mg	
	Weeks 2 to 6	4 mg	
	Week 7 and thereafter	8 mg	
Doxazosin extended-release (Cardura XL)	Days 1 to 21	4 mg	Once daily with morning meal
	Week 4 and thereafter	8 mg	
Terazosin (Hytrin)	**Standard titration (appropriate for most patients)**		
	Days 1 to 3	1 mg	Once daily at bedtime
	Days 4 to 14	2 mg	
	Weeks 2 to 6	5 mg	

	Week 7 and thereafter	10 mg	
	If inadequate response after 4 to 6 weeks of 10 mg/day	20 mg	
	Rapid titration (for selected patients)		
	Days 1 to 3	1 mg	Once daily at bedtime
	Days 4 to 14	2 mg	
	Weeks 2 to 3	5 mg	
	Week 4 and thereafter	10 mg	
	If inadequate response after 4 to 6 weeks of 10 mg/day	20 mg	

- Dosing recommendations are for oral administration in adult patients with normal organ function. Titration schedules are examples; other regimens may be appropriate. For recommendations on clinical use and individualizing drug selection, refer to the clinical topic review of BPH and individual drug information topics.
- Alpha-1-receptor antagonists may have additive hypotensive effects with phosphodiesterase-5 inhibitors (eg, sildenafil) and other agents that lower blood pressure. For specific drug interactions, refer to the Lexicomp drug interactions database included within UpToDate.
- Dosing recommendations for other agents used to treat lower urinary tract symptoms due to BPH is available in a separate table within UpToDate.

* If therapy is interrupted for 3 or more days, reinitiate at lowest dose and re-titrate according to schedule.

Data from:

1. *Lee M. Management of benign prostatic hyperplasia. In: Pharmacotherapy, 7th ed, Dipiro JT, Talbert RL, Yee GC, et al (Eds), McGraw-Hill Medical 2008.*
2. *Lexicomp Online. Copyright © 1978-2022 Lexicomp, Inc. All Rights Reserved.*
3. *AUA Practice Guidelines Committee. AUA guideline on management of benign prostatic hyperplasia (2003). Chapter 1: Diagnosis and treatment recommendations. J Urol 2003; 170:530.*