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Dr. Luke Fazio completed completed medical school at McGill University. He did his residency in urology at Western University and completed a fellowship in endourology and minimally invasive surgery through the University of Toronto at St. Michael's Hospital. He took an associate staff position at Queen's University before joining the Division of Urology at Humber River Hospital. His practice focuses on endourology as well as minimally-invasive and robotic surgery. For the last 4 years he has been the Division Head for urology at Humber River Hospital and the co-chair of the robotic surgery. He is also the medical director of urologic surgery at TCBH surgical centre in Toronto.

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MANAGEMENT OF BENIGN PROSTATIC HYPERPLASIA IN 2024

Background

Benign prostatic hyperplasia (BPH) is a condition involving the proliferation of smooth muscle and epithelial cells within the transition zone of the prostate. The process by which this takes place is not precisely known. It does require that testosterone and 5-alpha reductase convert it to dihydrotestosterone (DHT) which is the active androgen within the prostate. The growth of the prostate results from an imbalance between cell growth and cell death. Obstruction occurs via compression of the urethra by the resulting hyperplastic nodules, as well as increased smooth muscle tone and resistance within the enlarged gland. It is an almost universal process in men beginning in their 40's; it increases to a prevalence of 60% by age 60 and 80% by age 80.[1] This results in progressive bladder outlet obstruction (BOO) and lower urinary tract symptoms (LUTs). Patients can range from being asymptomatic to severely symptomatic. In the most extreme cases, it can result in complete urinary retention and renal dysfunction. The annual economic impact of BPH has been estimated at nearly $4 billion in the Unites States.[2]

Diagnosis

History

The initial management phase requires taking a history. Patients may experience a variety of symptoms which can be broadly divided into those that involve storage (e.g., frequency [urination eight or more times per day] and urgency [the inability to delay urination]) and emptying (slow flow; which may include trouble starting/maintaining a urine stream). The International Prostate Symptom Score (IPSS) is a validated questionnaire that is recommended in order to provide an objective measure of the severity of a patient's condition (**Figure 1**). Furthermore, it allows for a standardized method to monitor patients and gauge the success of any therapeutic interventions.

It is important to note that not all LUTS in men are due to BPH. Overactive bladder is a condition that results in storage symptoms. It can occur as a primary condition separate from BPH or it can be a secondary condition induced by BOO-caused by BPH. Interstitial cystitis (IC) and chronic prostatitis can be a source of LUTs and are associated with chronic pelvic pain. In the case of IC, patients often experience pelvic pain that is relieved by urination. Patients with prostatitis typically have perineal pain and may also have pain with ejaculation.

Urethral stricture should be considered in younger patients who have slow urinary flow, especially in the context of a history of urethral trauma or sexually transmitted infection. Distal ureteral stones may cause a combination of storage and emptying LUTs, including urinary retention in some circumstances. This would generally occur in the setting of typical renal colic. Isolated nocturia may be a sign of untreated sleep apnea and a sleep study should be considered in these patients.

Finally, behavioural factors can cause significant LUTs. The amount, type and timing of fluid intake can have

INTERNATIONAL PROSTATE SYMPTOM SCORE SHEET

Dr. Name: _____ **Address:** _____

Patient Name: _____ **Address:** _____

Date: _____

Age Group: 40-49 ☐ 50-59 ☐ 60-69 ☐ 70+ ☐

	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your score
1. INCOMPLETE EMPTYING Over the past month, how often have you had an occurrence of not emptying your bladder completely after you finished urinating	0	1	2	3	4	5	
2. FREQUENCY Over the post month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
3. INTERMITTENCY Over the past month, how often have you found you stopped and morted several trees when you urinated?	0	1	2	3	4	5	
4. URGENCY Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. WEAK STREAM Over the past month, how often have you had a very weak urinary stream?	0	1	2	3	4	5	
6. STRAINING Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
7. NOCTURIA Over the past month, how many times did you most typically get up to urinate from the time you went to bed of night until the same you got up in the morning?	0	1 **1** time	2 **2** times	3 **3** times	4 **4** times	5 **5** or more times	

Which of the above do you regard as most troublesome (1.7) _____

TOTAL PROSTATE SYMPTOM SCORE _____

	Delighted	Pleased	Mostly satisfied	About half the time	More than half the time	Almost always	Terrible
QUALITY OF LIFE DUE TO URINARY SYMPTOMS 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? (pick one).	0	1	2	3	4	5	6

Figure 1. IPSS (International Prostate Symptom Score Sheet).

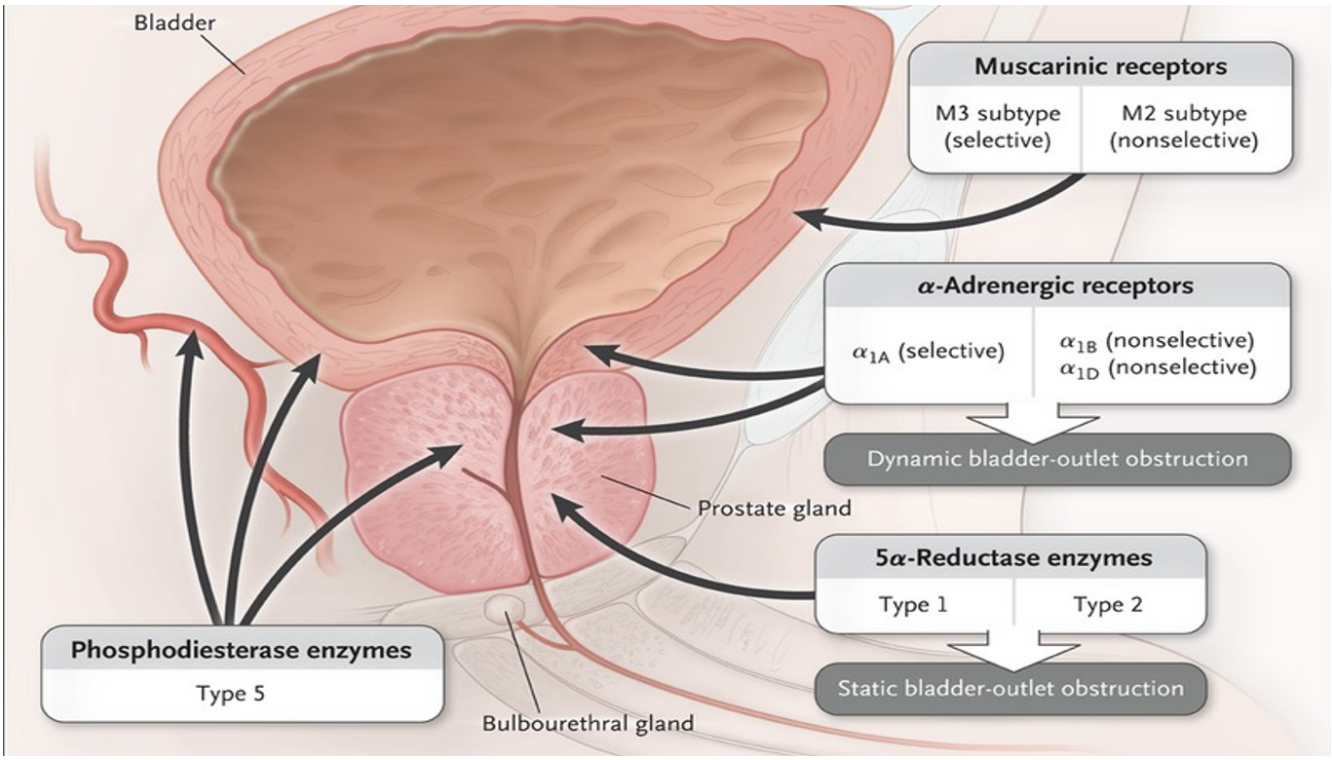

Figure 2. Classes of medication for the treatment of LUTs and site of action within the lower urinary tract; *adapted from Sarma AV, Wei JT. Benign prostatic hyperplasia and lower urinary tract symptoms. N Engl J Med. 2012;367:248-57.*

a significant effect on LUTs. Caffeine and alcohol act as diuretics and can exacerbate voiding symptoms. Furthermore, consumption of fluids in the evening and/or throughout the night can be a source of nocturia.

Physical Examination

It is recommended to perform a digital rectal exam (DRE) as part of the evaluation.[3] DRE provides useful information including an estimate of prostate size and detection of palpable irregularities. A tender prostate may be a sign of prostatitis.

Laboratory Tests

A urine analysis is important to rule out underlying conditions such as infection or hematuria. It is also recommended that a prostate-specific antigen (PSA) be performed in appropriate patients.[3] This includes men between the ages of 50-70 with at least 10 years of life expectancy or starting at age 45, and those who are at an increased risk of prostate cancer.[4] PSA screening decreases the risk of prostate cancer mortality in this patient population and can also provide a surrogate marker for prostate size. In 2012, the United States Preventive Services Task Force (USPSTF) recommended against using PSA to screen for prostate cancer and this was followed by a similar recommendation by the Canadian Task Force on Preventive Health Care. Since that time there has been an increase in the incidence of patients presenting with late-stage prostate cancer. This resulted in the USPSTF revising their statement and recognizing that there is a net benefit to PSA-based screening for prostate cancer.[5]

Serum creatinine and post-void residual measurement are optional tests that can help to rule out underlying renal dysfunction or significant urinary retention. Transrectal ultrasound is not recommended as a routine investigation but can be useful in cases where surgical intervention is being considered.[3]

Treatment

The treatment options for BPH can be divided into watchful waiting, medical therapy and surgery. The option selected depends on the degree of bother and, to a large degree, on patient preference. Therefore, there is no defined sequence required when treating BPH. Those with significant LUTs as defined by the IPSS may elect to proceed with watchful waiting. Patients who prefer to avoid long-term medical therapy may wish to proceed directly to surgery. It is important to provide patient counselling with respect to these options.

Watchful Waiting

Patients who are asymptomatic, have low bother from their symptoms or who wish to avoid medication and surgery can be observed. It is worthwhile to review reversible factors that could contribute to LUTs-caused by BPH such as the timing of fluid consumption, the use of decongestants and antihistamines, and the intake of caffeine and alcohol.

Pharmacotherapy

Various classes of medication are available for the treatment of LUTs related to BPH which act on various parts of the lower urinary tract **(Figure 2)**.

Alpha Blockers

Alpha blockers act by relaxing the smooth muscle at the bladder neck and within the prostate, and aid in improving urinary flow. Those used in the treatment of BPH include terazosin, doxazosin, tamsulosin, alfuzosin, and silodosin. This class of medication is the primary first-line option for pharmacologic management of BPH.[3] The most common side effects include dizziness, nasal congestion and retrograde ejaculation. Floppy iris syndrome can be seen with alpha blocker therapy and may be an issue for patients undergoing eye surgery. It is a condition involving loss of muscle tone in the iris and results in pupil constriction, despite pre-operative dilation. Increased awareness by ophthalmologists has resulted in effective management.[6]

Non-selective alpha blockers such as terazosin and doxazosin have demonstrated higher rates of hypotension and dizziness. The alpha-1A receptor subtype has greater expression at the bladder neck and prostate, and is involved in the contraction of these structures; it has minimal effect on blood pressure.[7] The selective alpha-blockers target the alpha-1A receptor and include tamsulosin, alfuzosin, and silodosin. This selectivity results in a greater effect on the lower urinary tract while minimizing the impact on blood pressure. It also results in a greater incidence of retrograde ejaculation which is highest with tamsulosin and silodosin. Retrograde ejaculation occurs less with alfuzosin so this may be a better option in patients where ejaculatory dysfunction is a greater concern.[1]

These five agents have similar clinical effectiveness so there is little benefit in switching to other alpha-blockers if a patient has not responded to one initially. However, it is reasonable to try a different alpha-blocker in the event a patient is having intolerable side effects with their current alpha-blocker.[8]

5-alpha Reductase Inhibitors (5-ARIs)

5-ARI's, including finasteride and dutasteride, act by inhibiting the conversion of testosterone to DHT. Finasteride inhibits the type 1 5-alpha reductase isoenzyme while dutasteride acts on type 1 and type 2 isoenzymes. DHT is the active androgen within the prostate and inhibition of its production results in a decrease in prostatic growth. Therefore, benefit is seen in larger prostates with a volume of 30 cc or greater and it is reasonable to consider 5-ARI monotherapy in such patients. This class of medication decreases the size of the prostate by approximately 25% after 6 months. As such, symptomatic improvement is not immediate, and patients should be counselled that it may take months for them to notice any change in symptoms. Unlike other BPH medications, 5-ARI's can alter the natural progression of the condition resulting in a lower risk of urinary retention and the need for surgical intervention.[9] Although dutasteride decreases DHT within the prostate to a greater degree, it does not appear to result in a significant decrease in clinical response when compared with finasteride.[10] Side effects of 5-ARI's include erectile dysfunction, decreased libido, ejaculatory disorders, and gynecomastia. Rarely, post-finasteride syndrome can occur, in which side effects persist despite medication cessation.[11]

It is important to note that as the size of the prostate decreases, it is expected that serum PSA levels will decrease. After 1 year of being on the medication it should be assumed that the true PSA is twice that which is being measured.[12] A lack of decrease in PSA or a rising PSA while on a 5-ARI represents a concern for underlying prostate cancer. A higher incidence of advanced prostate cancer has been described in patients taking 5-ARI but this may be secondary to the failure to account for the expected effects of this medication class on PSA results rather than being a causative factor.[1]

Combination therapy (alpha-blockers and 5-ARI's)
In general, given their side effect profile and onset of action, alpha-blockers are the first option for pharmacotherapy in symptomatic BPH. In patients with an incomplete response and an enlarged prostate (volume > 30 cc) adding a 5-ARI has been shown to improve symptom control more than with either medication alone. This was shown in two landmark studies for both finasteride (MTOPS trial) and dutasteride (CombAT trial).[13,14] After 9 months of combination therapy, stopping the alpha-blocker and continuing with 5-ARI monotherapy is tolerated in many patients.[15]

Phosphodiesterase-5 inhibitors

While Phosphodiesterase-5 inhibitors (PDE-5Is) are first-line treatment for erectile dysfunction they have also been shown to provide clinically significant benefit in improving LUTs secondary to BPH.[16] Because of the prolonged duration of action of tadalafil, it is the agent typically used at a dose of 5 mg/day. This is an option for patients being treated for BPH and erectile dysfunction concurrently.

Antimuscarinic and Beta-3 Agonist Medication

Urinary storage symptoms seen in the context of BPH can be challenging to treat. While there may be relief with medications targeting bladder outlet obstruction, it may also represent a component of underlying bladder overactivity. Therefore, medications targeting overactive bladder may be helpful either as monotherapy or in combination with alpha-blockers and/or 5-ARI. It is important to note that these medications may increase the risk of urinary retention, especially in those who already demonstrate incomplete bladder emptying.

Phytotherapy

There are a number of herbal medications marketed for BPH. However, they lack consistent formulation, predictable pharmacokinetics and regulatory oversight. Furthermore, in multiple clinical studies they have not demonstrated a benefit over placebo. Therefore, they are not recommended as standard treatment.[3]

Surgery

Surgery is considered in patients with symptoms such as urinary retention who do not respond to pharmacologic therapy. It is also indicated in those who experience intolerable side effects from medications or if there is a desire to avoid medication entirely.

The standard procedure is a transurethral resection of the prostate (TURP). This involves a transurethral endoscopic approach to the obstructive prostate tissue growing into the prostatic urethra and bladder neck. Risks of the procedure include infection, bleeding, urinary retention and rarely, incontinence. A high proportion of patients also experience retrograde ejaculation. Laser vaporization of the prostate involves a similar approach in which the obstructive prostate tissue is vaporized rather than resected. It has the benefit of causing less bleeding and is generally performed as an outpatient procedure.

With increasing prostate size, TURP and laser vaporization may be less efficacious and carry a higher risk of bleeding. For very large prostates (i.e., >100 cc) simple prostatectomy is an option. Traditionally, this involves an open surgical approach to the prostate in which the exterior capsule is opened, and the obstructive adenoma is excised from inside of it. More recently this has been achieved through laparoscopic and robotically-assisted approaches.

Laser enucleation of the prostate in which a transurethral endoscopic approach is taken offers an alternative to simple prostatectomy. A laser incision is carried out in the plane between the adenoma and prostatic capsule thereby enucleating the prostate from the inside. The enucleated adenoma is then placed in the bladder and subsequently removed by morcellation.

More recently, a number of minimally invasive, clinic-based procedures have gained popularity. They involve short periods of sedation or local anesthetic in some cases. They tend to cause minimal bleeding and less risk of sexual and ejaculatory dysfunction. These procedures include prostatic urethral lift (UroLift), water vapour energy ablation (Rezum), robotic water jet ablation (Aquablation), and a temporary implantable nitinol device (iTind).

Prostatic artery embolization is a procedure performed through interventional radiology. It can be an effective treatment for intractable hematuria. However, in terms of BPH treatment, it has demonstrated a lack of long-term durability.[3]

Conclusion

BPH is a common condition effecting millions of men globally. There are a number of treatment options available that can be tailored to an individual's symptoms and objectives.

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Financial Disclosures

None declared.

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