Management of Benign Prostatic Hyperplasia – South African Urological Association Guideline

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1. Introduction
Benign prostatic hyperplasia (BPH) is one of the most common conditions affecting older men. Strictly speaking, BPH is a histological diagnosis, and the term benign prostatic enlargement (BPE) is used when there is detectable enlargement of the prostate that is clinically not malignant. As a result of BPH, as many as 1 in 3 men over the age of 45 experience bothersome lower urinary tract symptoms (LUTS) that affect daily activities and sleep patterns. This symptom complex was previously referred to as prostatism. LUTS are divided into storage symptoms, including daytime frequency and nocturia, and voiding symptoms, including hesitancy, decreased flow rate and post-micturition dribbling. LUTS may also be due to other causes of bladder outflow obstruction (BOO), such as a urethral stricture, or conditions causing neurological dysfunction of the bladder detrusor muscle or sphincter mechanisms.

Hyperplastic changes in the prostate begin in the 3rd decade of life and by 60 years of age nearly half of all men have symptoms of BPH. These guidelines are specifically designed for clinical use by family practitioners to give an overview of the assessment and management options available for men with LUTS caused by BPH.

2. Diagnostic evaluation of men with LUTS

2.1 History
General medical history should include specific questions about the presence of any urinary symptoms and a family history of any cancers. Patients who request screening for BPH or prostate cancer should be assessed, but general screening of asymptomatic men is not recommended.

There are six focused questions related to specific LUTS that should be asked:
- Dysuria – ‘Do you have pain or burning on urination?’
- Nocturia – ‘How often do you wake at night to pass urine?’
- Hesitancy – ‘Do you have difficulty starting urination?’
- Urgency – ‘Do you ever have to rush to the toilet to urinate?’
- Incontinence – ‘Do you ever wet your pants?’
- Haematuria – ‘Have you ever seen blood in your urine?’

The use of a symptom scoring system such as the International Prostate Symptom Score (IPSS) (Table I) is useful to determine how much the patient is bothered by his symptoms, and it provides an essential baseline to evaluate the success of any treatment.

Keeping a voiding diary or frequency/volume chart is useful in interpreting the patient’s symptoms, particularly if nocturia is a dominant symptom.

2.2 Examination

General examination, including a focused neurological assessment.

Specific examination of the abdomen, genitalia and a digital rectal examination (DRE) are mandatory in the assessment of men with LUTS and none of these should be omitted.

2.3 Recommended investigations

1. Dipstick urinalysis testing. Patients with haematuria should be referred for further evaluation.
2. Prostate-specific antigen (PSA).

Age-adjusted PSA normal values used:
- < 50 years old: PSA < 2.5 ng/ml
- 51 - 65 years: PSA < 4.0 ng/ml
- > 65 years: PSA < 6.5 ng/ml.

PSA velocity: If > 20% increase in PSA in 1 year – refer.
3. Serum creatinine.

2.4 Optional investigations

These are usually performed by a urologist on the basis of specific clinical indications.
- Urinary flow rate recording
- Post-void residual urine measurement

Note: Haematuria of any degree should NOT generally be ascribed to BPH and needs further investigation.
GUIDELINE

3. Treatment recommendations

If any of the following is found on initial evaluation of LUTS, patients should be referred for specialist opinion:

- Suspicious DRE
- Recurrent urinary tract infection
- Haematuria
- Palpable bladder

- Ultrasound of upper tracts and/or prostate
- Urine cytology
- Pressure/flow urodynamic studies
- Urethro-cystoscopy

- Abnormal PSA
- Neurological disease
- Pain – suprapubic, perineal, or low lumbar pain.

3.1 Watchful waiting/reassurance

This is the preferred management strategy for patients with mild LUTS. Patients are monitored by their doctor but receive no medical or surgical therapy. Patients considered for this management must have low impact of their symptoms on their quality of life (IPSS score < 7) and must have no objective evidence of BPH complications (infection, stones, haematuria, renal failure or chronic retention).

Patients should be informed about lifestyle adaptations including selected restriction of fluid intake, decreasing...
cafeine and alcohol intake, and behavioural modifications such as double voiding, lengthening the voiding intervals and avoiding constipation.

Patients should also be reassured about the absence of prostate cancer, and that progression of LUTS or the development of complications due to BPH is not inevitable. They should be followed up at yearly intervals.

3.2 Medical treatment
Medical therapies for LUTS due to BPH, while not as efficacious as surgical therapies, still provide adequate symptom relief in many patients and are associated with fewer adverse events. Patients selected for medical treatment include those with mild to moderate symptoms (IPSS score 7 - 19) who are bothered by these symptoms, and those with severe symptoms (IPSS score > 19). Ideally, patients should have a urinary flow rate measurement before commencing medical treatment, because virtually all clinical trials showing efficacy of medical treatment were performed in men with a peak flow rate between 5 and 15 ml/sec. Men with severe LUTS and a peak flow rate above 15 ml/sec are less likely to have BOO, and ideally require pressure-flow studies to prove the existence of outflow obstruction before treatment is given.

Before commencing medical treatment, first attend to any modifiable factors: concomitant drugs, regulating fluid intake, lifestyle and dietary modifications.

3.2.1 Alpha-adrenergic receptor antagonists (alpha-blockade)
Alpha-blockers act by inhibiting alpha-1-adrenergic mediated contraction of prostatic smooth muscle, thus relieving bladder outlet obstruction. One-third of men do not show significant symptom reduction and there is no point in continuing the use of the drugs beyond 1 month if the patient does not respond. The most advantageous subtype selectivity profile of these drugs has not been established.

Alfuzosin, doxazosin, tamsulosin and terazosin are all appropriate treatments for LUTS secondary to BPH, and have similar clinical effectiveness. There are slight differences in the adverse effect profiles of these agents. The main adverse events associated with this class of drugs are orthostatic hypotension, dizziness, tiredness, nasal congestion and ejaculatory problems.

Alfuzosin and tamsulosin are more uro-selective alpha-1-blockers than doxazosin and terazosin. Tamsulosin is more likely to cause ejaculatory dysfunction (5%) than the other alpha-blockers. This is reversible on discontinuation of the drug. These two drugs have been shown to be safe when used in combination with PDE-5 (phospho-diesterase-5) inhibitors which are used for the treatment of erectile dysfunction (ED).

Doxazosin and terazosin are available in different dose strengths and efficacy is dose-dependent. Doxazosin should be used with caution in men with hypertension and cardiac risk factors as there is a higher incidence of reported congestive heart failure in this group. These two drugs have not been shown to be safe when used in conjunction with PDE-5 inhibitors.

Prazosin and phenoxybenzamine are NOT recommended in the treatment of LUTS secondary to BPH.

Alpha-blockers are not appropriate single-agent therapy for hypertension; patients with LUTS and hypertension should therefore also be treated with more appropriate agents for management of their hypertension.

3.2.2 5-alpha-reductase inhibitors
The 5-alpha-reductase inhibitors finasteride and dutasteride are appropriate treatments for patients with LUTS associated with prostatic enlargement secondary to BPH. They reduce prostate volume and improve symptom scores and flow rates. They are not indicated in men with normal-sized prostates and are more effective in patients with prostate volumes > 30 ml and/or PSA readings > 1.5 ng/ml. They are less effective than alpha-blockers in relieving LUTS, and their maximum effect is only seen after 6 months of therapy. Patients with LUTS that are not bothersome can be offered these drugs to prevent the progression of BPH and the development of complications such as urinary retention. They are also effective for the treatment of haematuria due to BPH.

Side-effects of the drugs are minimal and mainly related to sexual function (decreased libido in 6% and ED in 8%). These do not increase with time. Serum PSA levels are lowered by these drugs to 50% of baseline value, but the progressive increase in PSA caused by prostate cancer is not suppressed, so the detection of prostate cancer by serial PSA monitoring is not compromised, despite the lowered actual PSA values.

3.2.3 Combination therapy
The combination of an alpha-adrenergic receptor blocker and a 5-alpha-reductase inhibitor is an appropriate and effective therapy for patients with LUTS associated with BPE. Combination therapy lowers the incidence of urinary retention and the rate of surgical intervention in these patients. Discontinuation of the alpha-blocker after 6 - 12 months of treatment results in little or no worsening of symptoms. Potential benefits should be weighed against the increased cost of combination therapy to the patient.

3.2.4 Phytotherapeutic agents
While popular in many parts of the world, there is no objective evidence to demonstrate the efficacy, mode of action or biological effect of these agents and their use cannot be recommended.
3.2.5 Medications to avoid or use with caution in patients with BPH

- **Testosterone** – metabolised to dihydrotestosterone (DHT), known to cause prostate enlargement and growth.
- **Alpha-adrenergic agonists** – cause bladder neck contraction and may compromise bladder emptying. These include pseudo-ephedrine, ephedrine, and phenylephrine.
- **Anticholinergic agents** – may decrease detrusor contractility resulting in acute urinary retention. These include antispasmodics and anti-parkinsonian agents (e.g. benztropine, trihexyphenidyl) as well as those commonly used for treatment of overactive bladder symptoms: oxybutynin, tolterodine, darifenacin, solifenacin, trospium and propiverine.
- **Drugs with significant anticholinergic side-effects** – may decrease detrusor contractility, resulting in acute retention. These include antihistamines, tricyclic antidepressants and phenothiazines.
- **Diuretics** – polyuria, secondary to high-dose therapy, may present as urinary frequency and nocturia.

3.3 Minimally invasive therapies (MIT)

In the South African context MIT are not widely available due to cost restrictions and availability. However, they have defined roles and are used internationally. These therapies lend themselves to outpatient procedures under conscious sedation or local anaesthesia, and are suitable for high-risk patients unfit for anaesthetic, patients on continuous anticoagulation therapy and patients wishing to retain ejaculatory function. These therapies include:

- Transurethral microwave thermotherapy (TUMT)
- Transurethral needle ablation (TUNA)
- Intra-prostatic stents
- Laser vapourisation.

3.4 Emerging/experimental therapy

- Botulinum toxin (Botox) intraprostatic injections
- Absolute ethanol intraprostatic injections
- High-intensity focused ultrasound (HIFU)
- Plasmakinetic tissue management system
- Water-induced thermotherapy (WIT).

3.5 NOT RECOMMENDED

- Balloon dilatation of prostate
- Urethral dilatation.

3.6 Surgical treatment

Surgical intervention is an appropriate treatment for men with moderate to severe LUTS and recommended for those who develop complications of BPH such as:

- Acute urinary retention refractory to alpha-blockade
- Recurrent urinary retention
- Chronic urinary retention with a palpable bladder (without discomfort)
- Recurrent urinary tract infections
- Bladder stones
- Upper tract dilatation
- Renal insufficiency
- Recurrent macroscopic haematuria.

Optional surgical indications include:
- Bladder diverticulum
- Large post-void residual volume.

The following surgical treatment modalities can be recommended:

- Transurethral resection of the prostate (TURP) – suitable for prostates > 20 - 30 cm³ volume
- Transurethral incision of the prostate (TUIP) – suitable for prostate volume < 20 - 30 cm³
- Transurethral vapourisation of the prostate (TUVP) – comparable to TURP
- Open prostatectomy (retropubic/transvesical prostatectomy) – large prostates > 50 - 100 cm³
- Holmium laser enucleation of the prostate (HOLEP).

All the recommended surgical modalities are more or less equivalent with regard to outcome and efficacy. Retrograde ejaculation is less common after TUIP, whereas blood loss is greater with open prostatectomy.

4. Statements

This Guideline has the approval of the South African Urological Association.

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5. Reading

INITIAL MANAGEMENT OF LUTS IN MEN

**Recommended Tests:**
- Relevant medical history
- Assessment of LUTS symptom severity and bother (IPSS score)
- Physical examination including DRE
- Urinalysis
- Serum PSA
- Frequency-volume chart

**Complicated LUTS:**
- Suspicious DRE
- Haematuria
- Abnormal PSA
- Pain
- Infection
- Palpable bladder
- Neurological disease

**LUTS causing little or no bother**
- Reassurance and follow-up

**Bothersome LUTS**

**Standard Treatment**
- Alter modifiable factors
  - Drugs
  - Fluid & food intake
- Lifestyle advice
- Bladder training

**Drug Treatment**

**Failure**

**Success in relieving bothersome LUTS:**
- Continue treatment

**Refer for specialised management**