Management of lower urinary tract symptoms due to BPH

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Until recently, a man presenting to his doctor with urinary symptoms was immediately labelled as having benign prostatic hyperplasia (BPH), with an assumption as to the aetiology of his symptoms. Subsequently, the term ‘lower urinary tract symptoms’ (LUTS) was introduced to dispel the perception that male urinary symptoms invariably arise from the prostate. The publication by the National Institute for Health and Clinical Excellence (NICE) in May 2010 of *The Management of Lower Urinary Tract Symptoms in Men* clinical guideline is a landmark in the recognition of the term ‘LUTS’ as the first national guideline to address this umbrella concept rather than focussing on BPH alone.¹ The guideline covers the management of a man presenting with LUTS from initial assessment, usually in a primary-care setting, all the way through to complex surgical management.

Given that there are now many excellent resources available for guidance (see Figure 1),² the aim of this review is to focus on tips and pitfalls in the management of LUTS, especially those nonsurgical aspects of the condition that can easily be managed by GPs.
BPH


diagram explaining the management of lower urinary tract symptoms (LUTS) for patients with overactive bladder (OAB) and chronic prostatic obstruction.

**GP:**
- History including symptoms assessment (IPSS)
- Examination and DRE
- Urinalysis/MSU
- PSA

**LUTS patient**

**bothersome LUTS?**

- No
determine nocturia?

- Yes

**prostatic obstruction?**

- No
do not proceed to risk factors for progression?

- Yes

**risk factors for progression?**

- No
- yes

- yes

- no

**urological referral**

- Yes

**nocturnal polyuria?**

- no

**overactive bladder**

- Lifestyle advice
  - 5-alpha reductase inhibitor, alpha-blocker or combination

- review at 6–12 weeks

**risk factors for progression?**

- No

- yes

**large prostate (>30cc) or high PSA (>1.4ng/ml)**

- Lifestyle advice
- 5-alpha reductase inhibitor

- review at 3–6 months

- no

**large prostate (>30cc) or high PSA (>1.4ng/ml)**

- Lifestyle advice

- 5-alpha reductase inhibitor

- Lifestyle advice

**PSA elevated for age**

- Yes

**DRE abnormal or of concern**

- Yes

**haematuria**

- Yes

**elevated urea/creatinine**

- Yes

**palpable bladder**

- Yes

**recurrent UTI**

- Yes

**abnormal cytology**

- Yes

**severe symptoms**

- Yes

**nocturnal polyuria**

- Yes

**urological referral**

**nocturnal polyuria?**

- Yes

**treat**

- urinary tract infection

- PSA elevated for age

- DRE abnormal or of concern

- haematuria

- elevated urea/creatinine

- palpable bladder

- recurrent UTI

- abnormal cytology

- severe symptoms

**significant lower urinary tract symptoms (LUTS)**

- yes

**risk factors for progression?**

- yes

- yes

- yes

**nocturnal polyuria?**

- yes

**treat**

- urinary tract infection

- PSA elevated for age

- DRE abnormal or of concern

- haematuria

- elevated urea/creatinine

- palpable bladder

- recurrent UTI

- abnormal cytology

- severe symptoms

**Figure 1.** British Association of Urological Surgeons (BAUS) guideline for the treatment of lower urinary tract symptoms; after reference 2

**LUTS = lower urinary tract symptoms**

**IPSS = International Prostate Symptom Score**
Common causes

The commonest urological conditions presenting with LUTS are BPH and overactive bladder (OAB) syndrome. These conditions have a high prevalence in the community, with studies estimating that over one-third of men aged 50 or over suffer from significant symptoms from BPH – this would equate to approximately 3.2 million men in the UK alone. There is no doubt, however, that there are a huge number of men with significant LUTS who are not receiving optimal treatment. This is for a variety of reasons, including failure to present to a healthcare professional (‘these symptoms are just a normal feature of ageing’), delayed presentation, misdiagnosis, incorrect choice of treatment, cessation of treatment due to side-effects, and not referring to secondary care for failed treatment at a primary-care level.

Assessment

GPs are now encouraged to make a full assessment of the patient presenting with LUTS through history taking, general and clinical examination and a number of simple investigations.

Many men with LUTS can be effectively managed in a primary-care setting. There has been a tendency to refer patients with LUTS for urological assessment, particularly due to fear of missing a patient with prostate cancer. The guideline makes it clear that, provided an adequate assessment is carried out, medical management can be safely instituted in a community setting without the need for immediate specialist involvement. It is only those patients with complex presentations or who fail to respond to initial therapy that should be referred for specialist urological assessment.

Care, however, is required to ensure that a diagnosis of prostate cancer or carcinoma-in-situ (CIS) of the bladder is not overlooked. For this reason a digital rectal examination (DRE), a prostate specific antigen (PSA) determination and dipstick with subsequent cystoscopy or cytological examination of the urine should be considered, as appropriate, in addition to the usual flowmetry and ultrasonic measurement of the postvoid residual (PVR) volume of urine.

Medical management

Recent advances in medical therapy have revolutionised the care of LUTS patients, with a dramatic reduction in the number of patients requiring surgical treatment. It has also transformed the specialty of urology from an exclusively surgical specialty to one in which a large number of patients can be successfully managed in the community.

Overactive bladder

Medical management of OAB is with anticholinergic drugs, expecting a fairly rapid improvement in symptoms. Side-effects from these drugs are relatively common and may lead to discontinuation of treatment – it is vital that GPs therefore warn patients of possible adverse effects, such as dry mouth and blurred vision, and encourage patients to re-attend should these occur. Different patients respond in different ways to anticholinergics, so if side-effects are experienced on one formulation, a trial with another is worthwhile.

Benign prostatic hyperplasia

Two drug groups form the mainstay of management of men with symptoms caused by BPH – alpha-blockers, eg tamsulosin, alfuzosin, doxazosin, etc, and 5-alpha-reductase inhibitors (5ARIs), eg finasteride or dutasteride (Avodart).

Alpha-blockers are generally regarded as the first-line medical therapy for LUTS suggestive of BPH. They work by relaxing the smooth muscle of the bladder neck and prostate (see Figure 3). All alpha-blockers are similarly effective in LUTS, but older, less ‘uroselective’ alpha-blockers such as doxazosin or terazosin have different side-effect profiles that may limit their use. Alpha-blockers have a rapid onset of action and are generally well tolerated. Tiredness, dizziness and postural hypotension may occur; moreover, they have not been shown to lower the risk of long-term progression of LUTS, eg deterioration in symptoms, acute urinary retention (AUR) or BPH-related surgery.

5ARIs decrease the size of the prostate through inhibition of the conversion of testosterone to its active metabolite dihydrotestosterone. They are most useful
in patients with significant risk factors for ‘progression’, e.g. large prostates on DRE (estimated >30g), a PSA >1.4ng per ml (a surrogate marker of prostate volume in the absence of prostate cancer), severe symptoms and in older men.\textsuperscript{4}

Combination therapy with an alpha-blocker and 5ARI is recommended for patients with both moderate to severe symptoms and significant risk factors for progression. Recent data from two four-year studies of combination therapy in men with significant risk factors has shown combination therapy to be more effective than either alpha-blocker or 5ARI monotherapy in controlling symptoms and reducing acute retention surgery.\textsuperscript{5,6}

Anticholinergic drugs also have a role in the management of men with BPH; for many years, however, clinicians have been cautious about prescribing this class of drugs in men considered to have BPH due to a perceived high risk of precipitating AUR. Studies have shown, however, that this risk is actually very low unless patients have severe voiding symptoms or high post-micturition residual volumes (>200ml).

Anticholinergics are particularly useful for the treatment of storage symptoms that have failed to respond to treatment with an alpha-blocker. These storage symptoms are far more troublesome than voiding symptoms due to the effect they have on a patient’s quality of life – thus improving voiding symptoms may lower the International Prostate Symptom Score (IPSS) and give an impression of success, but unless these symptoms of frequency, urgency and nocturia are addressed patients will experience little improvement in quality of life.

For patients identified with nocturnal polyuria on their frequency volume chart (defined as passing more than one-third of total daily urine output during the night), if simple measures such as evening fluid restriction fail the guideline recommends that first-line treatment is a loop diuretic, e.g. furosemide 40mg taken at 4pm. This aims to produce a diuresis during the evening, thus decreasing the number of nocturnal voids. Desmopressin (synthetic antidiuretic hormone) is a second-line therapy, but should be prescribed with caution and with careful monitoring of serum sodium in the early phase of therapy in patients over the age of 65 years to prevent the development of dilutional hyponatraemia.

Who and when to refer
By no means every patient with LUTS resulting from BPH needs to be referred to a urologist. Those with complications from BPH and those who fail to respond to medical therapy will, however, need specialist evaluation. The indications for referral include: AUR, haematuria, recurrent UTIs, bladder stones, elevated PSA indicating a risk of prostate cancer (usually >4.0ng per ml), positive urine cytology indicating a risk of transitional cell carcinoma (TCC) or CIS, and failure to respond adequately to medical therapy.

Surgical treatment options
Transurethral resection of the prostate (TURP) is still the dominant surgical treatment option, although newer techniques such as Holmium laser enucleation
of the prostate (HoLEP) are increasingly popular. This procedure has good results in the literature; however, there is a steep learning curve for surgeons with HoLEP and thus it should only be performed in centres specialising in the technique. 7,8

For smaller prostates an alternative surgical procedure is transurethral incision of the prostate (TUIP), and for very large prostates (>100g) an open prostatectomy may occasionally be required. Bleeding and urethral strictures are the main side-effects. Erectile dysfunction and urinary incontinence should be very rare after surgery for BPH. Newer laser techniques, such as green light laser (GLL), do not as yet have a sufficient evidence base to be recommended by NICE but are increasingly employed in the USA and elsewhere, especially since the introduction of the higher-powered device with a modified laser fibre.

Minimally invasive techniques such as microwave therapy (TUMT) or needle ablation (TUNA) are not recommended due to high failure and re-operation rates, which greatly decrease cost-effectiveness.

Conclusions

LUTS resulting from BPH are extremely common in men beyond middle age. 9 Traditionally, patients suffering from this disorder have been primarily referred to a urologist for specialist surgical care; however, this paradigm is now changing and more and more men are being managed in primary care by GPs with an interest in men’s health. The forthcoming shift of purchasing power to GPs is only likely to promote this trend.

While overall this is likely to be in the best interest of patients, GPs will need to be cautious to avoid overlooking a more serious and sinister diagnosis of prostate or bladder cancer. They will also need to be prompt in referring those men who are failing to respond to first-line medical therapy, as well as those who are developing complications of their BPH.

References


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Prescription review

Prescribing of drugs used to treat BPH continues to increase, growing by over 20 per cent since 2007 but with a similar fall in costs to £78.2 million in 2010. Alpha-blockers – which, with the exception of alfuzosin and tamsulosin, are also prescribed for hypertension – accounted for over 80 per cent of volume and cost of BPH drugs, whereas the two 5-alpha-reductase inhibitors accounted for less than 20 per cent.

Two drugs make up the bulk of prescribing for alpha-blockers. Doxazosin use has changed little but prescribing of tamsulosin has increased by 15–18 per cent per year in each of the last five years, though total spending on this drug is now less than half of the 2005 level.

Prescribing of dutasteride has also been rising at a rate of 15–17 per cent since 2006, faster than finasteride in the past two years (11 per cent). Following price cuts, spending on finasteride is now about one-quarter what it was in 2007 whereas cost growth has resumed for dutasteride, with spending in 2010 up 11 per cent on 2009.

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*includes all formulations, some of which are prescribed for other indications

Table 1. Number of prescriptions and costs for drugs used in BPH in England, 2010
BPH

Resources

Guideline

Groups and organisations
Bodytalk Online. www.bodytalk-online.com. Website with audio tapes that you can hear online. Doctor Hilary Jones explains a wide range of medical conditions, including prostate enlargement.

Men’s Health Matters. www.menshealthmatters.co.uk.


Men’s Health Forum. Tel: 020 7922 7908; www.menshealthforum.org.uk.

Prostate Action (formerly Prostate UK). Tel: 020 8788 7720. www.prostateaction.org.uk.

Prostate Help Association (PHA). www.prostatehelp.me.uk.

CPD: recommended treatment of BPH

Answer these questions online at Prescriber.co.uk and receive a certificate of completion for your CPD portfolio. Utilise the Learning into Practice form to record how your learning has contributed to your professional development.

1. One of these statements about men presenting with LUTS in primary care is false – which is it?
   a. Over one-third of men aged 50 or over suffer from significant symptoms from BPH
   b. Tests to rule out a diagnosis of prostate cancer include a digital rectal examination, a PSA determination and cystoscopy or cytological examination of the urine, as appropriate
   c. The reasons why men with significant LUTS may not receive optimal treatment include failure to present to a health professional
   d. Only patients with complex presentations should be referred for specialist urological assessment

2. Which one of these statements about the medical management of LUTS suggestive of OAB is false?
   a. Storage symptoms are far more troublesome than voiding symptoms
   b. Patients should be encouraged to reattend if they experience side-effects with an anticholinergic
   c. If side-effects occur with one anticholinergic, there is no point in trying a different one because the response will be the same
   d. A fairly rapid improvement in OAB symptoms should be expected with anticholinergic drug treatment

3. Which one of these statements about alpha-blockers is false?
   a. They are generally regarded as the first-line medical therapy for LUTS suggestive of BPH
   b. They are similarly effective in LUTS
   c. Older, less ‘uroselective’ alpha-blockers such as doxazosin or terazosin have side-effect profiles that may limit their use in LUTS
   d. They have a slow onset of action and are generally poorly tolerated

4. One of these statements about the treatment of LUTS suggestive of BPH is false - which is it?
   a. Combination therapy with an alpha-blocker and a SARI is recommended for patients with mild LUTS
   b. SARIs are considered most useful in patients with significant risk factors for progression
   c. Combination therapy is more effective than monotherapy with either an alpha-blocker or a SARI in controlling symptoms and reducing acute retention surgery over four years
   d. Risk factors for progression of BPH include a large prostate on DRE, a PSA >1.4ng per ml, severe symptoms and older age

5. Regarding other aspects of the treatment of LUTS suggestive of BPH, which one of these statements is false?
   a. The risk of precipitating AU R with anticholinergic drugs is very low in the absence of severe voiding symptoms or high post-micturition residual volumes
   b. Anticholinergics are not useful for treating storage symptoms that have failed to respond to an alpha-blocker
   c. Patients with nocturnal polyuria should be offered furosemide, to be taken at 4pm, if evening fluid restriction fails
   d. Treatment with desmopressin requires careful monitoring of serum sodium in the early phase of therapy in patients over the age of 65 years

6. Which of these statements about referral and surgery for patients with LUTS is false?
   a. Indications for referral include recurrent UTIs and haematuria
   b. Holmium laser enucleation of the prostate should only be performed in centres specialising in the technique
   c. An alternative surgical procedure for large prostates is transurethral incision of the prostate
   d. Minimally invasive techniques such as microwave therapy or needle ablation have high failure and reoperation rates