Management of lower urinary tract symptoms in BPH

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Recent advances in drug treatment have revolutionised the management of patients with lower urinary tract symptoms due to benign prostatic hyperplasia. Our Drug review discusses current approaches to management followed by further sources of information and an analysis of prescription data.

Until recently, a man presenting to his doctor with urinary symptoms was almost invariably 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 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.

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, including a recent guideline from the European Association of Urology, the aim of this review is to focus on tips and pitfalls in the management of LUTS, especially those non-surgical aspects of the condition that can easily be managed by GPs.

Common causes

The commonest urological conditions underlying a presentation 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 and bothersome 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, dismissal of symptoms at initial assessment,
LUTS = lower urinary tract symptoms  
IPSS = International Prostate Symptom Score

Figure 1. Recommended management of lower urinary tract symptoms; after reference 3
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 NICE 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 (see Figure 2).

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 dis-continuation 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). In addition, anticholinergic agents may have a role when urgency and urge incontinence are the main presenting symptoms, and the phosphodiesterase type-5 (PDE5) inhibitor tadalafil (Cialis) is now also indicated for the treatment of BPH.

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 dihydrotosterone. They are most useful in patients with significant risk factors for ‘progression’, eg 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.

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

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 postmicturition 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 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.

Mirabegron (Betmiga) is now recommended by NICE when anticholinergics are ineffective or have unacceptable side-effects.

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), the guideline recommends that first-line treatment is a loop diuretic, eg furosemide 40mg taken at 4pm, if simple measures such as evening fluid restriction fail. 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.
**PD5 inhibitors** The prevalence of bothersome LUTS/BPH increases with age, and epidemiological and pathophysiological links between LUTS/BPH and erectile dysfunction (ED) have been demonstrated. As mentioned above, medical therapy for LUTS/BPH currently consists of alpha-blockers, 5ARIs or combination therapy. Although efficacious, these therapies have the potential for side-effects relating to sexual dysfunction.

Tadalafil is a PD5 inhibitor widely approved for the treatment of ED, and several placebo-controlled studies in men with LUTS/BPH have also demonstrated improvements in IPSS. Tadalafil was recently approved for the treatment of signs and symptoms of BPH in adult males.

Although the mechanisms for improvement in LUTS with PD5 inhibition have yet to be fully clarified, proposed contributors include inhibition of PD5 isoenzymes present in the bladder, prostate, urethra and supporting vasculature, and consequent increases in intracellular nitric oxide–cyclic guanosine monophosphate concentration, relaxation of the smooth muscle cells in these structures, improved blood perfusion and reduced afferent signalling from the urogenital tract.

**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.

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. ED 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. 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 current 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


Resources

Guidelines


Prescriber articles


Prescription review

GP prescribing of drugs to treat urinary retention in men has been increasing for several years. This category appears to be dominated by the alpha-blockers, though most are also prescribed for hypertension (alfuzosin and tamsulosin are the exceptions).

Prescribing of tamsulosin in 2012 was 14 per cent higher than in 2011 and spending was increased by 18 per cent, whereas the use of alfuzosin fell slightly.

Over the same year, the volume of dutasteride prescribing decreased slightly but costs increased by 16 per cent. By contrast, the use of finasteride is growing (and was 14 per cent higher than in 2011). Almost all finasteride is prescribed generically and it is now substantially cheaper than in 2009, when spending exceeded £11 million for 27 per cent fewer scrips.

Prescribing of the combination of dutasteride and tamsulosin (Combotart) has increased from only 9000 scrips in 2010 and almost doubled over the past year, with a corresponding increase in cost.

European Association of Urology, 2012.

Declaration of interests

Professor Kirby has lectured at symposia for Astellas, Janssen, GlaxoSmithKline and Pfizer.

Roger Kirby is professor of urology and director of The Prostate Centre, London

Table 1. Number and cost of prescriptions for drugs used to treat BPH in England, 2012

<table>
<thead>
<tr>
<th>Stratum</th>
<th>No. scrips (000s)</th>
<th>NIC (£000s)</th>
<th>NIC per scrip (£)</th>
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<tr>
<td>Alpha blockers</td>
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<td>alfuzosin</td>
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