Management of male LUTS in general practice

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The initial management of lower urinary tract symptoms in men is usually carried out in primary care. The authors explain that the primary goal of treatment is to improve bothersome symptoms; more recently, however, treatment has also focused on the alteration of disease progression and the prevention of complications.

Although now well supported by the NICE guideline,1 the management of men with lower urinary tract symptoms (LUTS) still requires a certain background level of knowledge and experience to achieve appropriate investigation and treatment for these patients. It is encouraging, however, to see that a survey conducted one year after the launch of the guideline showed that nearly half (46 per cent) of GPs surveyed were following NICE advice on the management of LUTS in men. Of those GPs who said they were implementing the guideline, 80 per cent reported that they had also seen a reduction in referral costs.2

Guidelines are important to provide a basis for education and to guide best practice and, where appropriate, summarise consensus. They also, to some extent, regulate practice and may cut costs. Finally, if there are problems, they may well provide a basis for medicolegal assessment.

Evolving terminology

Although the terminology of LUTS has become established in urology, it is still common to see GP letters referring to benign prostatic hyperplasia (BPH) as though it was a clinical syndrome rather than a pathological diagnosis. Occasionally referral letters even mention prostatism – a term that should have disappeared years ago.

The progression in terminology, over the past 30 years, from ‘prostatism’ to ‘LUTS’ was effectively hijacked by the term ‘BPH’ for most of those years. The advantage of referring to LUTS is that it distances male lower urinary symptoms from any suggested site of symptom origin, such as the prostate, and no longer makes it gender specific. This is important because both men and women may have remarkably similar LUTS.

While it is easy now to be disparaging about the use of the old term ‘prostatism’, it did make us consider the interplay between prostatic disease, prostate

Figure 1. The overlapping relationship between lower urinary tract symptoms (LUTS), bladder outlet obstruction and benign prostate enlargement, as well as non-urological causes of LUTS

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Go to the Trends website to view Mark Speakman’s video on ‘Management of male LUTS in general practice’ from the 5th National Better Health for Men Conference: www.trendsinurology/videos
enlargement and symptoms. We now recognise that at a prostatic level there is an important interplay between LUTS, benign prostatic enlargement (BPE) and bladder outlet obstruction (BOO). There is a complex overlap between these conditions. In addition, there are important effects from the urethra, the bladder and both peripheral and central nervous system influences, as well as non-urological causes of LUTS. These non-urological causes include renal, endocrine, neurological and cardiac causes that can also influence these symptoms (Figure 1).

Benign prostatic hyperplasia is first and foremost a histological diagnosis reached essentially from biopsy material after pathological analysis showing evidence of cellular and stromal proliferation of the prostate. In BPH we essentially have a large increase in the number of benign prostate cells. The term benign prostatic hypertrophy is wrong. The bladder or cardiac muscle cells become hypertrophic, describing larger cells, while the prostate has many ‘carbon copies’ of the original cells (hyperplasia).

Benign prostatic enlargement, an enlarged prostate, is what we identify on digital rectal examination (DRE) and quantify by transrectal ultrasound. It is now recognised that knowledge of prostate size may influence both treatment selection and long-term treatment outcome because of the potential to influence disease progression; assessment of size is therefore important.

Bladder outlet obstruction can be inferred from a poor flow rate, but can be properly diagnosed only with formal urodynamic testing showing a high bladder pressure associated with a low flow rate. Poor flow rate alone could be a result of poor bladder (detrusor) contractility.

INITIAL MANAGEMENT OF MALE LUTS

In the UK the majority of first-line management of male LUTS is carried out in primary care, and this is entirely appropriate. Men present to their GPs with LUTS for a variety of reasons. These include fear that they have prostate cancer, concern that certain symptoms are getting worse or because they have read some publicity, perhaps in the toilet in the motorway service station, telling them that they should go to their GP.

In reality, the commonest reason they present is that their partner has told them to go, whether this is their mother, wife/partner or daughter. Discussing their symptoms, plans for investigation and treatment with their partner clearly makes sense and including them when the patient presents or is reviewed is beneficial to both. An important part of the consultation is to identify the primary reason for them being there, which may be their most bothersome symptom, and also to set realistic goals for their management.

The NICE male LUTS guideline should reassure GPs that most men (perhaps 70 per cent) with LUTS can be safely assessed and treated in the community and without the need for costly hospital referrals.1 The guideline is clear that once the worrisome symptoms or signs or ‘red flags’ have been excluded, only limited investigation is required before offering first-line therapy (Box 1).

The primary goal of treatment is to improve bothersome LUTS; more recently, however, treatment has also focused on the alteration of disease progression and the prevention of complications secondary to LUTS.

First-line investigations (Box 2) should include a general medical history, including assessment of any associated comorbidities. As part of this it is important to review drug medication, including any over-the-counter medicines, to identify drugs that may be contributing to the problem. Physical examination should be directed by symptoms and other medical conditions, but should always include an examination of the abdomen and external genitalia, and a DRE.

A urinary frequency-volume chart is of great value in both quantifying and identifying underlying causes of LUTS and should be included wherever possible, but particularly in patients with significant nocturia.4

A symptom score such as the International Prostate Symptom Score (IPSS) is not a diagnostic test, but is of value in quantifying the level of a patient’s symptoms and can be valuable in measuring change in the condition after treatment or over a period of time off treatment.

BOX 1. Indications for specialist referral in men with lower urinary tract symptoms (LUTS)

- Recurrent or persistent urinary tract infection
- Urinary retention
- Urinary incontinence, particularly at night
- LUTS associated with haematuria
- Renal impairment that is suspected to be secondary to LUT dysfunction
- Suspected urological cancer

BOX 2. Initial investigation of male lower urinary tract symptoms

- General medical history, including drug history
- Focused physical examination, including genital examination
- Digital rectal examination
- Urine dipstick testing, including glucose, blood, leucocytes, nitrites, protein
- Frequency-volume chart (voiding diary)

In selected patients:
- Renal function, including creatinine and estimated glomerular filtration rate
- Post-void residual urine and flow tests
A urine dipstick test to detect blood, glucose, protein, leucocytes and nitrites should be carried out.

Flow rate testing and post-void bladder scanning is not required in patients with uncomplicated LUTS undergoing first-line management. Perform a serum creatinine test (plus estimated glomerular filtration rate) only if you suspect renal impairment.1

If size matters – as it appears to do – a prostate-specific antigen (PSA) test as a proxy for volume may be useful in the management of benign prostatic disease. Although a provocative suggestion, a single PSA test may be of greater value in managing benign prostate disease than in managing and diagnosing malignant prostate disease, where sequential testing is likely to be more important.

Increasing age is the main risk factor for the development of LUTS. Modifiable risk factors for LUTS may include lack of physical activity, obesity, hyperlipidaemia, smoking, excess alcohol consumption, hypertension and diabetes. Genuinely improving overall fitness therefore can have beneficial effects on LUTS.

TREATMENT OF LUTS

If a patient’s LUTS are not bothersome, give reassurance and offer advice on lifestyle interventions (eg adjustment of fluid intake, avoiding caffeinated drinks, artificial sweeteners, alcohol), appropriate exercises such as bladder training and pelvic floor exercises where appropriate and consideration of containment devices such as pads and catheters in a small percentage of men. Providing information on the nature and high prevalence of their condition may also help. Offer patients a chance to be seen again if their symptoms change or become more bothersome.

For men with mild or moderate bothersome LUTS, discuss lifestyle advice without immediate treatment or active intervention if preferred by the patient. In both these groups a baseline assessment of their LUTS with a validated symptom score such as the IPSS is useful to measure change over time or change after treatment.

Before offering PSA testing, explain that while it is a useful test, there can be both false positives and false negatives. It can be helpful in men who are concerned about cancer, particularly if they have been tested in the past (although this cannot completely remove this worry). It is certainly advised in men with an abnormal DRE, but can also be helpful in men with LUTS that are suggestive of BOO secondary to BPE.

Medical treatment should be offered to men with bothersome LUTS when conservative treatment has failed or would be inadequate alone. There are essentially four pharmacological treatment pathways that can help men with LUTS: alpha-adrenergic blockers, 5-alpha reductase inhibitors, anticholinergic drugs and vasopressin analogues. These can all be used in combination; however, patients’ comorbidities should be considered before starting any of these medications.

**Alpha-blockers**

Alpha-blockers are rapidly acting and are the usual first line of treatment in bothersome LUTS. Typically patients will see beneficial effects within the first few days of treatment and it is reasonable to review their effects after six weeks’ treatment. Possible side-effects include postural hypotension and retrograde ejaculation, but most patients can take alpha-blockers long-term with little problem. They can also be used as intermittent treatment in men with fluctuating symptoms. Examples of commonly used drugs include alfuzosin (Xatral XL, 10mg once daily), doxazosin (Cardura XL 4mg or generic, requires dose titration) and tamsulosin (Flomaxtra XL 0.4mg or generic, once daily).

It has been identified recently that men who undergo cataract surgery need to inform their ophthalmologist if they are taking alpha-blockers, and this appears particularly important if they are taking tamsulosin. A condition called intraoperative floppy iris syndrome has been described and it is usually suggested that men stop alpha-blockers one month before cataract surgery.

**5-alpha reductase inhibitors**

5-alpha reductase inhibitors work less quickly than alpha-blockers and typically require three to six months to achieve their full effect. Dutasteride (Avodart 0.5mg once daily) and finasteride (generic 5mg once daily) should be considered in men with bothersome LUTS and significant prostate enlargement (prostate volume >30cc or a PSA >1.4ng/ml) and in men with more than two risk factors for disease progression. These drugs will achieve a reduction in prostate size of 20–25 per cent and a drop in PSA level of approximately 50–60 per cent. The benefits in addition to symptom improvement include a reduction in risk of urinary retention and reduced need for prostactic surgery, and also a reduced risk of long-term prostate cancer. Treatment needs to be long-term, however, and patients should be warned about a 5–10 per cent risk of erectile or ejaculatory dysfunction.

**Anticholinergic drugs**

Anticholinergic drugs decrease the parasympathetic influence on the bladder and help reduce the storage symptoms suggestive of the overactive bladder, namely urgency with or without incontinence usually associated with daytime frequency and nocturia. Examples include fesoterodine (Toviaz 4–8mg once daily), oxybutynin (various 2.5–5mg three times daily or Lyrinel XL 5–20mg once daily), solifenacin (Vesicare 5–10mg once daily), tolterodine (Detrol 0.4mg or generic, once daily), trospium (Mytelase 100mg once daily) and darifenacin (Emsam 10mg once daily).

Find the International Prostate Symptom Score (IPSS) and a frequency-volume chart on the Trends website: www.trendsinurology/usefultools

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Once daily) and tolterodine (Detrusitol XL 4mg once daily).

Traditionally there has been a reluctance to treat men with this class of drug for fear of retention. However, in men with post-void residual volumes below 200ml, it appears safe to use them and men can get considerable benefit. Most urologists will still use these as second-line therapy, treating first with an alpha-blocker and later adding in an anticholinergic drug at six-week review if the storage symptoms are still bothersome.

Nocturia
Nocturia is a bothersome LUT symptom. This is particularly so if the number of times up at night is greater than two or if there are less than three to four hours of undisturbed sleep. Although this may relate to high evening fluid intake, it is commonly associated with pathological conditions. The general medical history and examination will indicate causes such as heart failure and peripheral oedema.

The frequency-volume chart helps considerably in identifying likely causes. If the overnight volume of urine, including the first void of the morning, is greater than 33 per cent of the total 24-hour output, this is diagnostic of nocturnal polyuria rather than more simple nocturnal frequency. Simple measures such as lying on the bed for one hour after lunch will sometimes reduce peripheral oedema and reduce nocturnal urine production. The use of a loop diuretic such as furosemide in the late afternoon can also produce a useful diuresis, reducing the need for excess nocturnal production.

Vasopressin analogues such as desmopressin are used for children with nocturnal enuresis, which has the same basic pathophysiology of excess nocturnal urine production. They can be used successfully in older men but require careful consideration and monitoring. Desmopressin can cause fluid retention overnight and therefore must be used with caution in men with hypertension. Serum sodium levels need to be checked before treatment and three days after the start of treatment and after a further month, because of the potential for hyponatraemia. Many urologists will withdraw the treatment for one month in every six. Refer to the British National Formulary for detailed prescription information and cautions.

Recently epidemiological research has shown a strong link between inflammation and nocturia, and there are some data indicating that anti-inflammatory agents may reduce nocturia. In men who are not sensitive to non-steroidal anti-inflammatory drugs, a low dose of an anti-inflammatory such as ibuprofen 200mg at night may reduce nocturia.

Phosphodiesterase inhibitors
Phosphodiesterase inhibitors such as sildenafil (Viagra), tadalafil (Cialis) and vardenafil (Levitra) all have a modest beneficial effect on LUTS, and there is a strong correlation between increasing LUTS and male erectile dysfunction. Their use in men with LUTS associated with erectile dysfunction is entirely appropriate, with or without a concomitant increase in symptoms.

BOX 3. Risk factors for LUTS progression

- Age ≥70 years
- International Prostate Symptom Score ≥7
- $Q_{\text{max}}$ ≤12ml/s
- Prostate volume ≥30cc
- PSA ≥1.4ng/ml
- Failure to respond to alpha-blockers
Combination therapy
Many patients will improve significantly with monotherapy of any of these drugs, while others will benefit from the combination of two or more. The commonest combination is an alpha-blocker to achieve rapid symptom relief together with a 5-alpha reductase inhibitor to reduce disease progression and the need for surgery. The second commonest combination is the addition of an anticholinergic drug to an alpha-blocker for patients with irritative storage symptoms. Currently there is a combination pill with dutasteride and tamsulosin (Combodart, one capsule daily) together and combination pills with alpha-blocker and anticholinergic are in clinical trials.

Overview of treatment regimens
The most useful way to approach the treatment of male LUTS is to consider the patient’s most bothersome symptoms and to evaluate to which category they belong (Figure 2), as this will guide you in the direction of the most beneficial initial treatment(s).

DISEASE PROGRESSION
Men with larger prostates are at higher risk of bothersome and progressive LUTS, which impact considerably on quality of life. While the correlation between size and symptoms is far from perfect, an assessment of prostate size is therefore an important consideration in the evaluation of men with LUTS. Men with larger prostates run a significantly increased risk of acute urinary retention and are more likely to progress to surgery. Risk appears to increase at a prostate size >30cc (about the size of a golf ball), which correlates with a PSA around 1.4–1.5ng/ml (Box 3).

PATIENT INFORMATION
Finally, and probably most importantly to the patient, make sure that men with LUTS have access to care and services that can help them develop coping mechanisms for their relevant physical, emotional, psychological, sexual and social issues. A number of support groups provide advice and relevant information (Box 4).

Declaration of interests
Mark Speakman has received honoraria for lectures, research grants and has sat on advisory boards for Abbott, Astellas, GenProbe, GSK, Lilly and Pfizer.

REFERENCES