Benign prostatic hyperplasia: solutions to an ageing problem

Charlotte L Foley, Simon RJ Bott, Manit Arya, Roger S Kirby

As the population ages, the demand for treatment of the symptoms of benign prostatic hyperplasia has never been higher. Equally the choice of treatments has never been greater. This review considers the medical and surgical options.

Miss Charlotte L Foley, Mr Simon RJ Bott, and **Mr Manit Arya** are Clinical Research Fellows, Institute of Nephrology and Urology, University College London, London W1W 7EJ and **Professor Roger S Kirby** is Professor of Urology, St George's Hospital Medical School, London

Correspondence to: Miss CL Foley

With increasing awareness of health issues among Western males, the morbidity caused by benign prostatic hyperplasia (BPH) is no longer accepted as 'just part of growing old'. Men are increasingly asking doctors to treat their urinary symptoms. At the same time the treatment choices have never been wider. This review gives an overview of the clinical manifestations of BPH, and the medical and surgical treatments available.

PATHOLOGY

BPH is benign proliferation and enlargement of prostate epithelium and stroma. This occurs primarily in the prostate transitional zone which, being adjacent to the urethra, causes obstruction of urinary flow (*Figure 1*). BPH has been defined by the characteristic clinical picture, the urodynamic findings, histologically or as a combination of these. Histologically, BPH occurs in >50% of 60-year-old men but enlargement develops later – only 30% of 60-year-olds have enlarged prostates. Lower urinary tract symptoms (LUTS) occur in 25–40% of 60-year-olds, although these may arise from other pathologies too.

The aetiology of BPH is unclear. No risk factors other than age have been reliably identified, although testosterone is known to be essential for its development.

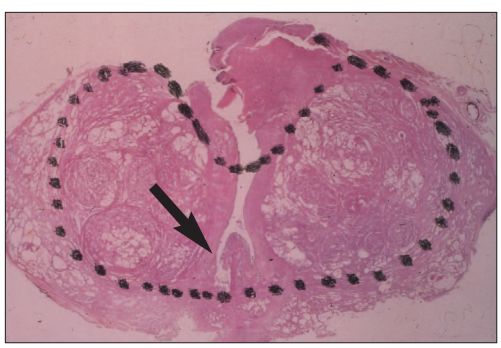

Figure 1. Histological cross section of a prostate with the greatly enlarged, hyperplastic transitional core delineated. Note the compressed urethra (arrow).

CLINICAL PRESENTATION

The typical symptoms accompanying BPH may be obstructive (as a result of prostatic urethra compression) or irritative (from increased bladder detrusor muscle instability, *Table 1*). In general, obstructive symptoms respond better to treatment. Complications arising from BPH (*Table 2; Figure 2*) may cause additional symptoms.

Symptom severity can be assessed using the International Prostate Symptom Score (IPSS), also known as the American Urologists

TABLE 1. Symptoms of BPH

Obstructive symptoms	Hesitancy
	Weak urinary stream
	Intermittent stream
	Prolonged voiding time
	Straining to void
	Incomplete emptying
Irritative/storage symptoms	Nocturia
	Frequency
	Urgency

BPH = benign prostatic hyperplasia

TABLE 2. Complications of BPH

Urinary tract infection
Bladder calculi
AUR with or without acute renal failure
Chronic urinary retention with or without overflow incontinence
Chronic renal failure
Haematuria
Bladder diverticulae

AUR = acute urinary retention; BPH = benign prostatic hyperplasia

Association symptom index (*Table 3*) (Barry et al, 1992). This grades the answers to seven questions from 0–5. Those with 0–7 points have mild symptoms, 8–19 points suggests moderate symptoms and 20–35 severe symptoms.

INVESTIGATIONS

Investigation must confirm the diagnosis, assess the severity of BPH and exclude other diagnoses (*Table 4*). A digital rectal examination of the prostate is obligatory to assess size and exclude palpable prostate cancer. Investigations should include measurement of serum creatinine and glucose levels, and urine culture. A urinary flow rate and post-void residual urine volume is an objective indicator of bladder outflow obstruction, although patients must pass >150 ml of urine and void 'typically' for reliable results. Transrectal ultrasound can objectively calculate prostate volume and urodynamics is useful where symptoms persist or recur after surgery, or the diagnosis is equivocal. Measurement of serum prostate specific antigen (PSA) in patients with LUTS is controversial and should be offered with appropriate counselling if diagnosing prostate cancer would change management.

TREATMENT

The treatment of BPH is highly individualized and depends on the extent of symptoms and complications. Watchful waiting involves careful follow-up and is recommended for most patients with mild symptoms (IPSS score 0–7). Barry et al (1997) followed 60 men with mild symptoms for 4 years: 63% required no treatment, 27% commenced medical therapy and 10% required surgery. In contrast, of 66 men with severe symptoms, at 4 years, 33% were untreated, 27% needed medical therapy and 39% underwent surgery. The risk factors for acute urinary retention (AUR) are LUTS, an enlarged prostate (>30 g), peak urinary flow rates <12 ml/sec and older age (Jacobsen et al, 1997). Treatment lowers the incidence of AUR so should be considered in those at significant risk.

MEDICAL MANAGEMENT

Two classes of drugs are used in the management of BPH:

Alpha-blockers

These relax prostate and bladder neck smooth muscle by blocking alpha1a-adrenoceptors, thus inhibiting sympathetic tone. The alpha-blocker family is shown in *Table 5*.

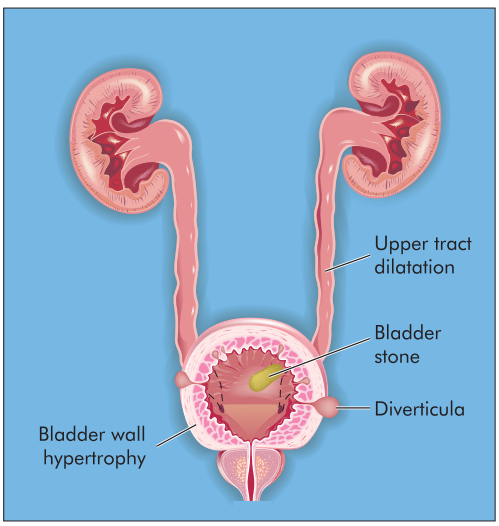

Figure 2. Secondary effects of bladder outflow obstruction caused by benign prostatic hyperplasia.

TABLE 3.
American Urologists Association (AUA) symptom index

Questions to be answered	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
	Circle one number on each line					
1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2. Over the past month, how often have you had to urinate again less than 2 hours after you finished urinating?	0	1	2	3	4	5
3. Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5
4. Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5
6. Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
7. Over the past month, how many times did you most typically get up to urinate from the times you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5
Sum of 7 circled numbers (AUA symptom score):.....						

From Barry et al (1992)

All alpha-blockers are specific to alpha-1 receptors, but only tamsulosin is selective for the alpha-1a receptors found specifically in the bladder. All improve BPH-related symptoms and urinary flow rates similarly. Non-selective alpha-blockers can be additionally used to also lower blood pressure in hypertensive patients, although they do not affect blood pressure in normotensive subjects (Kirby, 1995).

Alpha-blockers achieve optimal flow rates with one dose, symptom improvement after a week and full therapeutic benefit after 3 months with efficacy lasting at least 3–4 years. Roehrborn et al (1996) showed that, over 1 year, alpha-blockers achieve a significant (P<0.001) average decrease of 7.6 IPSS points compared to 3.7 with placebo. Alfuzosin has been shown to reduce post-void residual urine volumes, and in a 6-month trial decreased the incidence of AUR from 2.4% with placebo to 0.4% with alfuzosin (Hartung, 2001). A small trial by McNeill et al (1999) showed that sustained-release alfuzosin taken for 48 hours before catheter removal increased the chances of voiding after AUR from 5% to 29%.

TABLE 4.
Differential diagnosis of lower urinary tract symptoms

Malignancy	Prostate cancer
	Bladder cancer, especially carcinoma-in-situ
Infection	Bacterial
	Tuberculosis/bilharzia
Neurological	Parkinson's disease
	Cerebrovascular event
	Multiple sclerosis
	Bladder neck dyssynergia
Inflammation	Bladder stone
	Interstitial cystitis
Mechanical	Urethral stricture
	Severe phimosis
Drug induced	Antidepressants
	Anticholinergics
	Diuretics

TABLE 5.
Types of alpha blockers

Alpha-1 blockers	Duration of action	Incidence of side effects	Side effects
Prazosin	Short	High	Require dose titration Dizziness Headache Gastrointestinal disturbance First dose hypotension Antihypertensive properties
Indoramin	Short	Moderate	
Alfuzosin	Short	Moderate	
Doxazosin	Long	Moderate	
Terazosin	Long	Moderate	
Alfuzosin sustained release/XL	Long	Moderate	
Tamsulosin	Long	Low	Retrograde ejaculation

TABLE 6.
Overview of drug actions

Alpha-blockers	Improve symptoms, flow rates and quality of life in men with BPH
	Reduce post-void residual urine volumes and decrease incidence of AUR
	Increase success of trial without catheter
	Some have antihypertensive effects
5-alpha-reductase inhibitors	Improve symptoms, flow rates and quality of life in men with BPH
	Decreases incidence of AUR and progression to surgery
	Decreases BPH-associated haematuria

AUR = acute urinary retention; BPH = benign prostatic hyperplasia

5-alpha-reductase inhibitors

These block the enzyme that converts testosterone to the more potent dihydrotestosterone, causing 20% reduction in prostate volume. The only currently available 5-alpha-reductase inhibitor is finasteride. This reaches full therapeutic potential over 3–6 months. Finasteride only has significant benefits in men with prostates >40 g; above this, benefits improve as prostate size increases (Boyle et al, 1996). The PLESS study (Proscar Long-Term Efficacy and Safety Study) followed 3040 North American men taking finasteride for 4 years and found a 1.6-point reduction in symptom score, flow rate increases of 1–2 ml/sec, 58% decrease in AUR and 50% decrease in progression to surgery (McConnell et al, 1998). Finasteride is well tolerated, and has long-term efficacy, but 3% experience reversible impotence, decreased libido or reduced ejaculatory volume. It also approximately halves serum PSA levels. In theory this could complicate prostate cancer detection, but in the PLESS study, prostate cancer detection rates did not differ between treated and placebo groups. Finasteride is also effective against BPH-associated haematuria (Foley et al, 2000).

In two trials evaluating combined treatment, no additional benefit was seen with finasteride plus an alpha-blocker compared to alpha-blockers alone (Lepor et al, 1996; Debruyne et al, 1998).

Table 6 summarizes the actions of these two classes of drug. Ideally, medically treated patients should be reassessed 6-monthly.

PHYTOTHERAPY

Over-the-counter plant extracts are widely used on the continent and in North America as first-line treatment for symptomatic BPH. In the UK,

increasing awareness of alternative therapies has promoted interest in these compounds (*Table 7*).

While some of these compounds (saw palmetto, beta-sitosterol and African plum) have improved symptoms in small placebo-controlled trials, little is know of their effects, long-term efficacy or safety. The proportion of active ingredients may vary between different batches of plant extracts. Phytotherapy does seem to have (real or placebo-induced) benefits, without troubling side effects. However, more trials and purer preparations are needed before they can be recommended over well-established drug therapies.

SURGICAL MANAGEMENT

Transurethral resection of the prostate (TURP) remains the gold standard treatment for BPH for improvement in symptoms, flow rate and quality of life, against which newer surgical approaches must prove themselves (*Figure 3*). TURP is the second most commonly performed operation in North America, although medical therapies have resulted in 60% fewer TURPs being performed compared to 10 years ago (Borth et al, 2001). Surgery is still recommended as first-line treatment for patients with obstructive renal failure, bladder stones, recurrent urinary tract infection, refractory AUR, high residual urine volumes, recurrent haematuria or failed medical therapy.

TURP represents 95% of operations undertaken for BPH. There are several alternative operations: open, endoscopic or 'minimally invasive' procedures (*Table 8*, Madersbacher and Marberger, 1999; De la Rosette et al, 2001; Yang et al, 2001) (*Figure 4*).

Figure 3. Cystoscopic appearance of obstructing lobes of the prostate, before transurethral resection of the prostate.

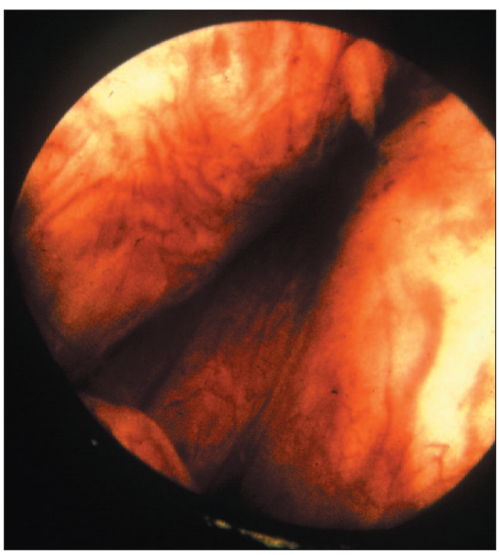

TABLE 7.
Commonly used phytotherapeutic compounds for BPH

Liposterolic extract of Saw palmetto berries (*Serenoa repens*)
African plum tree bark extract (*Pygeum africanum*)
Beta-sitosterol containing plants, e.g. South African star grass root (*Hypoxis rooperi*)
Purple cone flower root (*Echinacea purpurea*)
Stinging nettle root (*Urtica dioica*)
Pumpkin seeds (*Cucurbita pepo*)
Rye grass pollen extract (*Secale cereale*)

BPH = benign prostatic hyperplasia

CONCLUSIONS

BPH affects the quality of life of patients and their partners, and with increasing longevity, it is affecting more and more individuals. Having excluded other pathology, drugs are safe first-line therapies, although TURP remains the gold standard treatment with some risks. Given the many options available, a life untroubled by BPH symptoms is a realistic goal for most men. HM

Conflict of interest: none.

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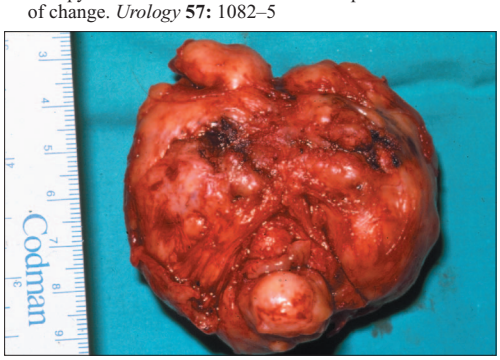

Figure 4. An excised prostate showing nodular benign prostatic hypertrophy.

KEY POINTS

- Benign prostatic hyperplasia is common, and can have a significant impact on quality of life.
- Those with mild symptoms may not need treatment but should be regularly reassessed.
- Medical treatments include alpha-blockers, which achieve rapid and durable benefits by relaxing prostate and bladder neck smooth muscle.
- Finasteride reduces prostate volume by 20%, having full effect after 3–6 months.
- Alpha-blockers and finasteride have similar effects but different side effects.
- Some patients require surgery. The gold standard surgical treatment is transurethral resection of the prostate which has better outcomes than medical therapy but increased risks.
- Some newer surgical techniques show promise, but longer-term data are needed.

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TABLE 8.
Different surgical procedures for benign prostatic hyperplasia

Procedure		Indications	Decrease in symptom score	Increase in Qmax	Outcomes and complications
Open procedures	Open prostatectomy (prostate adenoma shelled out of its surgical capsule through a lower abdominal incision)	Optimum first-line treatment for prostates >100 g and with co-existing bladder pathology, e.g. stones/diverticulae	79%	175%	Mortality 0.8%; transfusion 4.6%; total incontinence 0.5%; RE 80%; impotence 15%
Endoscopic procedures	TURP (endoscopic resection of the periurethral prostate using a diathermy loop)	Gold standard for medium size prostates. Unsurpassed long-term results. Best in those with severe symptoms	85%	125%	Mortality 0.8%; transfusion 1%; RE 70%; impotence 13%; incontinence 1.0%; re-do 2% per year
	Transurethral incision of prostate/ bladder neck incision (up to 2 cuts made. No tissue resected)	Best used for small prostates with a high bladder neck where patient wishes to retain ejaculation	73%	100%	Time with catheter less than TURP; Incontinence 0.1%; RE 39%; impotence 4.6%
Minimally invasive procedures	Transurethral microwave thermotherapy (delivered from a urethral device, with rectal probe watching temperature)	Possible alternative to surgery, especially if anaesthetic risks. Well tolerated under local anaesthesia	78%	35%	Catheter kept for 2 weeks; Impotence 5%; RE 11–44%; re-do rates 10% at 1 year
	Transurethral electro-vaporization of the prostate (diathermized rollers cause heat vaporization and coagulation together)	Comparable results to TURP. Efficacy decreases with prostates larger than 50 g	75%	155%	Slower than TURP; reduced bleeding; irritative symptoms for 4–6 weeks; RE 85%; Impotence 0–15%
	Transurethral needle ablation (radio-frequency needles deployed from catheter tip cause coagulative necrosis)	Not recommended because of high failure rates.	50–70%	50–60%	Minimal bleeding. Possible outpatient procedure under local and/or intravenous sedation. Catheter for 1–3 days
	High intensity focused ultrasound (delivered per rectum, heating causes necrosis and later tissue resorption)	Not recommended	50–60%	40–50%	Minimal bleeding; postoperative retention for 3–6 days; re-do rate 10%/year
	Holmium laser resection of the prostate (prostate enucleated with a cutting laser, tissue morselated then removed)	Promising technique with outcomes matching TURP. First reported 1995; long-term data awaited.	65%	125%	Catheter time and hospital stay <1 day. Dysuria 10%; RE 75–80%; impotence 0%
	Visual laser ablation of the prostate (various side-firing lasers vaporise or coagulate tissue which resorbs later)	Not recommended as first-line treatment. Maybe for high-risk patient groups, e.g. unfit for TURP/ anti-coagulated	60%	70%	Benefits after 3–4 weeks; catheter for 1–2 weeks and severe dysuria; RE 22%; 2% re-do rate per year
	Interstitial laser coagulation (laser fibres inserted into the prostate cause coagulative necrosis while sparing mucosa)		55%	65%	Use local anaesthetic and/or intravenous sedation; irritative symptoms 5–15%; catheter 1–2 weeks; re-do 3–15% at 1 year
	Balloon dilatation of the prostate	Results least poor for small prostates. Short-lived benefits. Rarely used today	40%	20%	Re-do rates 44% at 1 year
	Intra-prostatic expandable metal stents	For unfit patients with limited life expectancy Rarely used.			Stents encrust or migrate yet are difficult to remove

RE = retrograde ejaculation; TURP = transurethral resection of the prostate