GP POCKETGUIDE

Overactive bladder

Written by Natalia Price and Simon Jackson

Reviewed by Sally Hope, Michael Kirby and Adrian Wagg

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Vesicare® is indicated for treatment of all the symptoms of overactive bladder.
Prescribing information is available on the inside back cover.

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Introduction

There have been huge changes in the management of urinary incontinence over the last decade. These have been driven both by increased awareness of the condition and by new developments in this field. The prevalence of overactive bladder (OAB) in the UK is about 11.8 per cent of adults.[1] This short guide aims to give a concise update on its diagnosis and management for the primary healthcare team.

What is an overactive bladder?

OAB is a condition defined by urinary urgency, with or without urge incontinence, usually with frequency and associated with nocturia. It is used to imply possible underlying detrusor overactivity (DO). However, DO is a purely urodynamic observation characterised by involuntary detrusor contractions during the filling phase, which may be spontaneous or provoked.[2]

What is the impact of OAB?

- OAB is a common condition affecting almost one in eight women and one in nine men in the UK.[1]
- The incidence of OAB increases with age and the experience of disease in later life appears to be more severe.[3]
- Quality of life can be significantly impaired by OAB, due to the unpredictability of incontinence episodes and large volume of leakage, leading to limitation of daily activities and sleep disturbance.
- In 2000 it was estimated that in the UK at least £423 million is spent on managing and treating incontinence and related symptoms every year.[4]

How do you diagnose OAB?

It frequently takes courage for people to seek help for incontinence. Such problems are often only mentioned at the end of a consultation about a different matter.

- Symptoms of OAB include urinary frequency, urgency, urge incontinence, nocturia and nocturnal enuresis, either singly or in combination.
- Provocative factors often trigger OAB (such as cold weather, putting the key in the front door, hearing the sound of running water or emotional stress).

- Bladder contractions and subsequent incontinence may also be provoked by rises in intra-abdominal pressure (for example, coughing and sneezing), leading to complaints of stress incontinence, which can be misleading.
- There may be a mixture of stress and urge incontinence symptoms that are difficult to clarify.
- Women with purely sphincter incompetence (stress incontinence) may report urgency.

Diagnosis can be assisted with the use of:

- A frequency/volume chart (urinary diary). This is a simple and practical method of obtaining objective quantification of fluid intake, functional bladder capacity and voiding behaviour. Frequency and times of voiding, voided volumes and leakage episodes (day and night) are all recorded for at least 24 hours and typically three days.
- A diagnostic aid (see Figure 1) such as that developed by the Primary Care in Overactive Bladder Group.
- Disease-specific questionnaires.[5–7]

Differential diagnosis/secondary causes

Other conditions must be excluded before diagnosis of OAB:

- UTI.
- Bladder outflow obstruction; uncommon in women unless there is history of pelvic/incontinence surgery. In men this is often due to benign prostatic hyperplasia.
- Bladder stones or tumours.
- Severe chronic constipation can cause a physical outflow obstruction.
- Psychological and metabolic causes of polydipsia and polyuria, such as diabetes mellitus, diabetes insipidus, excessive fluid consumption or hypercalcaemia.
- Neurological abnormalities (spinal cord injuries, spina bifida, MS or upper motor neurone disease).
- Cognitive impairment and disability.
- Drugs/medications.

Investigations

Urinalysis

Reagent strip testing of urine for leucocyte esterase, nitrates, protein, blood and glucose is a sensitive and cheap screening test.

FIGURE 1

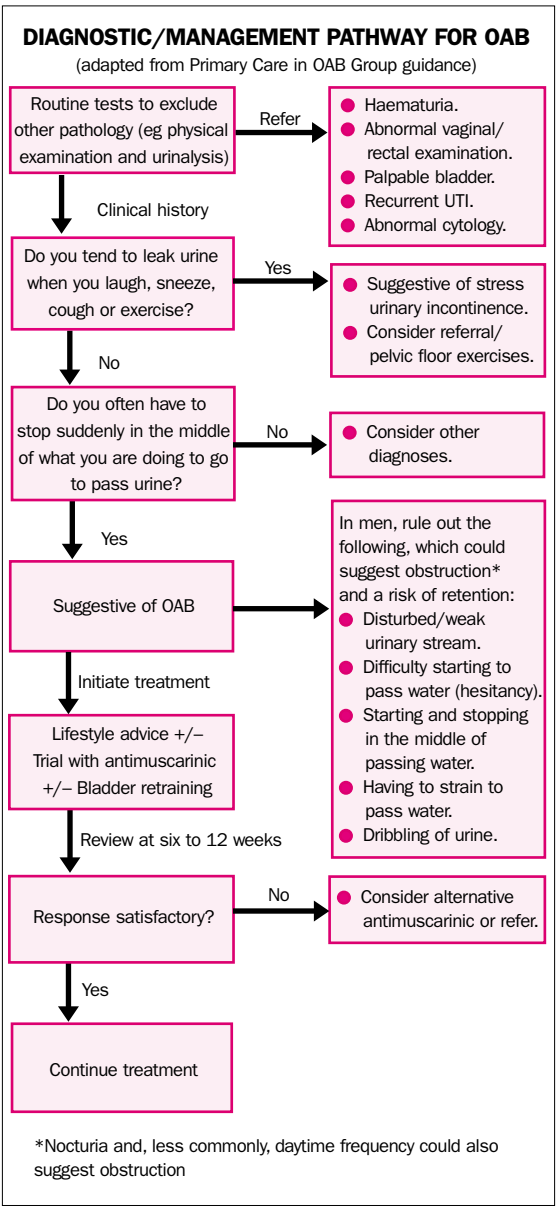
DIAGNOSTIC/MANAGEMENT PATHWAY FOR OAB
(adapted from Primary Care in OAB Group guidance)
Routine tests to exclude other pathology (eg physical examination and urinalysis)
Refer
Haematuria.
Abnormal vaginal/ rectal examination.
Palpable bladder.
Recurrent UTI.
Abnormal cytology.
Clinical history
Do you tend to leak urine when you laugh, sneeze, cough or exercise?
Yes
Suggestive of stress urinary incontinence.
Consider referral/ pelvic floor exercises.
No
Do you often have to stop suddenly in the middle of what you are doing to go to pass urine?
No
Consider other diagnoses.
Yes
Suggestive of OAB
In men, rule out the following, which could suggest obstruction* and a risk of retention:
Disturbed/weak urinary stream.
Difficulty starting to pass water (hesitancy).
Starting and stopping in the middle of passing water.
Having to strain to pass water.
Dribbling of urine.
Initiate treatment
Lifestyle advice +/– Trial with antimuscarinic +/– Bladder retraining
Review at six to 12 weeks
Response satisfactory?
No
Consider alternative antimuscarinic or refer.
Yes
Continue treatment
*Nocturia and, less commonly, daytime frequency could also suggest obstruction

TABLE 1

EXAMINATION OF PATIENTS WITH SUSPECTED OAB

- Exclude an abdominal or pelvic mass (including pregnancy).
- Exclude a full bladder (obstruction/retention).
- Exclude constipation.
- Check for prolapse.
- Check for postmenopausal atrophy.
- Determine pelvic floor strength.
- Conduct a neurological examination, if indicated.
- Exclude a urinary tract infection/haematuria with a urinalysis dipstick and send for MSU, if indicated.

Urine culture

Urine microscopy and culture is reserved for those with a positive screening test result. Exclusion of infection is mandatory, as symptoms overlap with those of UTI.

Residual check

A post-void residual check should be carried out (either by ultrasound scan or by catheterisation) if there are symptoms suggestive of incomplete bladder emptying.

Urinary diary

Typical features of OAB are an increase in diurnal urinary frequency associated with urgency incontinence. Nocturia is one of the salient features of OAB.

Urodynamic investigations

These include uroflowmetry, post-void residual measurement and cystometry. It is important that any clinician referring a person for such tests has an understanding of what the tests entail and the indications for them.

Aims of treatment

The ideal is to help the patient to become symptom-free, although this may not always be possible. Our aim should be to give the patient more control and improve their quality of life. A realistic goal needs to be discussed and agreed

TABLE 2

CLINICAL INDICATIONS FOR URODYNAMIC ASSESSMENT

- Complex mixed urinary symptoms (urge incontinence and stress incontinence).
- Symptoms suggestive of detrusor overactivity unresponsive to pharmacotherapy.
- Voiding dysfunction with incomplete bladder emptying.
- Neuropathic bladder disorder (videourodynamics preferred).

with the patient during the consultation and might include:

- Being able to undertake their normal daily routine (such as shopping, meetings, travel and so on).
- Reducing the number of incontinence episodes.
- Regaining the confidence to socialise.

Lifestyle changes and behavioural therapy

It is wise to start with the simplest of conservative therapies and progress through to treatments that are more radical, if necessary.

Reducing fluid intake, if the urinary diary suggests this is excessive, and cutting caffeinated products out of the diet may have a beneficial effect. Simple advice such as this may be all that is required to cure frequency and urgency. Various drugs, such as diuretics and antipsychotics, may predispose patients to incontinence and should be reviewed.

Bladder training lasting for a minimum of six weeks should be offered as the first-line treatment to women with OAB and with or without urinary incontinence.[8] This can be in combination with antimuscarinic therapy. The three main components of bladder training are patient education, timed voiding with systematic delay in voiding and positive reinforcement. The patients should be asked to resist the sensation of urgency and void according to a timetable.

A self-completed urinary diary should be used to monitor the times of voids. Continence rates of up to 90 per cent have been reported but the corresponding cure rates could be considerably lower than this.

TABLE 3

ANTIMUSCARINIC DRUGS AND THEIR DOSAGES

Drug	Route of delivery	Adult dosage	Cost per 28 days*
Oxybutynin	Oral	(a) 2.5mg–5mg, two to four times/day (b) 5mg to 20mg once daily (sustained release)	£7.24–£21.78 £10.71–£42.84
Oxybutynin	Trans-dermal patch	One patch, twice/week (3.9mg/24hours)	£27.20
Propiverine hydrochloride	Oral only	(a) 15mg, two to four times/day (b) 30mg once daily (sustained release)	£24.45–£48.90 £24.45
Solifenacin succinate	Oral only	5mg–10mg once daily	£25.78–£33.52
Tolterodine tartrate	Oral only	(a) 2mg, twice daily (b) 4mg, once daily (sustained release)	£30.56 £29.03
Trospium chloride	Oral only	20mg, twice daily	£24.27
Darifenacin	Oral only	7.5mg or 15mg once daily (sustained release)	£26.13
Fesoterodine fumarate	Oral only	4mg–8mg once daily (sustained release)	£29.03

*Approximate NHS cost. Source: *MIMS* December 2008

Pharmacotherapy

Antimuscarinics

Pharmacological suppression of DO with antimuscarinics is the most widely used treatment for this condition. These

drugs are well-tolerated and, therefore, it would seem reasonable practice to begin empirical treatment. If symptoms are not improved after one or two months of antimuscarinics, the patient should be referred to a specialist clinic.

For treatment of lower urinary tract symptoms in men, an alpha adrenergic antagonist is traditionally started before an antimuscarinic despite little evidence of the risk of precipitating retention.

There are a number of treatments available (see Table 3). Antimuscarinic drugs block receptors that mediate detrusor smooth-muscle contraction and have a direct, relaxing effect on the detrusor muscle.

Oxybutynin, propiverine, tolterodine and trospium chloride have been used for many years to treat OAB symptoms. Sustained release oxybutynin transdermal patches, which release 3.9mg every 24 hours, are also effective and have a lower incidence of typical antimuscarinic side-effects but an approximate 15 per cent likelihood of local skin irritation.[9,10]

Darifenacin, fesoterodine and solifenacin are newer bladder-selective preparations. They are useful additions to existing drugs and may have a lower incidence of adverse effects.

Darifenacin is a selective M_3 receptor antagonist available in 7.5mg or 15mg once-daily sustained-release form, shown to be effective in treating OAB.[11]

Fesoterodine is a nonselective oral antimuscarinic agent that exerts its pharmacological effects as a competitive muscarinic receptor antagonist. Fesoterodine acts as a prodrug; it is rapidly hydrolysed to the active metabolite, 5-hydroxymethyl tolterodine. Fesoterodine 4mg and 8mg demonstrated significant improvements in most OAB symptoms.[12,13]

Solifenacin is a long-acting muscarinic antagonist. At 5mg

TABLE 4

CONTRAINDICATIONS OF ANTICHOLINERGICS

- Acute (narrow angle) glaucoma.
- Myasthenia gravis.
- Urinary retention or outflow obstruction.
- Severe ulcerative colitis.
- GI obstruction.

and 10mg daily dosing it reduces the frequency of daily voids and number of urge and incontinence episodes.[14,15] In one study, two thirds of the effect obtained after 12 weeks was evident after four weeks.[14]

Patients should be advised on the possibility of side-effects before starting treatment. The dosage may need to be titrated against clinical efficacy and adverse effects profile.

Adverse effects of antimuscarinics may include:

- Dry mouth (in up to 30 per cent of cases).
- Constipation.
- Blurred vision.
- Nausea, dyspepsia and flatulence.
- Palpitations and arrhythmia.
- Dizziness, insomnia.
- Skin reactions.

The tolerability of antimuscarinics

Many patients do not like the side-effects of antimuscarinic drugs. However, by starting at a low dose and working up over about a month, they can often adjust to these side-effects. Sustained-release preparations are generally better tolerated than immediate-release preparations. A Cochrane systematic review of efficacy and tolerability did not find a statistical difference between sustained-release and immediate-release tolterodine preparations for cure or improvement. However, the side-effect profile of the former was better, with fewer patients treated with sustained release preparations complaining of dry mouth.[16]

The oxybutynin transdermal patch is thought to have a lower incidence of side-effects due to its continuous low-dose percutaneous delivery, which avoids the first pass GI and hepatic metabolism that occurs with oral tablets.[17]

Studies have shown that darifenacin and solifenacin are well-tolerated and effective, with favourable adverse effect profiles.[11,14]

Desmopressin

Desmopressin is a long-acting synthetic analogue of vasopressin. It is available as a nasal spray and, more recently, as a tablet. The use of desmopressin may be considered specifically to reduce nocturnal polyuria in patients with OAB who

find it a troublesome symptom. It has been shown to be well-tolerated for long-term use. However, its main side-effects, hyponatraemia and fluid retention, must be considered, especially prior to use in elderly patients. Serum sodium should be measured within three days of treatment.[8]

The role of oestrogens

Many women develop urinary storage symptoms after the menopause. Treatment with estriol cream or estradiol pessaries or rings in post-menopausal women improves symptoms of urogenital atrophy such as vaginal dryness and irritation. In one study, vaginal oestrogen administration was found to be superior to placebo, after 12 months of treatment, when considering symptoms including urinary frequency and urinary incontinence.[18]

Complementary therapy

Women who do not find conventional treatment acceptable often explore the use of complementary therapies for urinary incontinence and as adjuncts to standard treatments.

There is some evidence, albeit of poor quality, which shows that acupuncture may reduce nocturia and both stress and urge incontinence in the short term (up to four weeks) but it is unclear whether any particular area of acupuncture treatment is more effective than another. There is also limited evidence that hypnotherapy for women with urinary incontinence secondary to DO may offer some benefit over the short term (up to six months).[19] However, there is no evidence that herbal medicines work for urinary incontinence or OAB, apart from the usual non-drug effect.

No recommendations on complementary therapies were made by NICE for the treatment of urinary incontinence or OAB.[8]

New developments

New treatments such as neuromodulation, sacral nerve stimulation and intravesical botulinum toxin A (BTX) injections are promising developments for the management of OAB.

BTX has the potential to revolutionise the management of OAB and refractory DO. It blocks neuromuscular

transmission, causing the affected muscle to become weak. There is preliminary evidence of BTX injections showing efficacy in inhibiting symptoms of OAB.[20] The toxin is injected cystoscopically under local or general anaesthesia into detrusor muscle in 10 to 30 different locations. Efficacy is short-lived and injections require repetition every six to 12 months. Additional studies to determine ideal doses are urgently needed.

Neuromodulation and sacral nerve stimulation involves electrical stimulation of a peripheral nerve or the spinal cord and is thought to improve the ability to suppress detrusor contractions. It is being used increasingly in cases of refractory DO. The various techniques for neuromodulation include removable and implantable electrodes. Overall, neuromodulation has a clinical success rate of approximately 30–50 per cent.[21]

Sacral nerve stimulation provides continuous stimulation of the S_3 nerve root via an implanted electrical pulse generator. It provides effective relief from frequency–urgency symptoms in the difficult-to-treat group of patients who have exhausted conservative management options. Women should be offered sacral nerve stimulation on the basis of their response to preliminary percutaneous nerve evaluation. It is, however, a very expensive treatment, as the implant alone costs approximately £10,000. Insertion of the implant is an invasive procedure and lifelong follow-up is required.[22]

Surgical management

Surgery is reserved for those with debilitating symptoms and who have failed to derive benefit from medical and behavioural therapy. Procedures, such as bladder distention, detrusor myomectomy and augmentation cystoplasty have limited efficacy and high rates of complication. Permanent urinary diversion is occasionally indicated in women with intractable incontinence.

Resources

Bladder and Bowel Foundation:
www.bladderandbowelfoundation.org
International Continence Society: www.icsoffice.org

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ABBREVIATED PRESCRIBING INFORMATION

Presentation: Vesicare® film-coated tablets containing 5 mg or 10 mg solifenacin succinate. **Indication:** Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in patients with overactive bladder syndrome. **Dosage:** *Adults:* Recommended dose: 5 mg once daily. If needed, the dose may be increased to 10 mg once daily. *Children and adolescents:* Should not be used. **Contraindications:** Lactation. Urinary retention, severe gastrointestinal condition (including toxic megacolon), myasthenia gravis or narrow-angle glaucoma and in patients at risk for these conditions. Patients hypersensitive to the active substance or to any of the excipients, or undergoing haemodialysis, or with severe hepatic impairment, or with severe renal or moderate hepatic impairment and on treatment with a potent CYP3A4 inhibitor. Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption. **Warnings and Precautions:** Pregnancy. Assess other causes of frequent urination before prescribing. Use with caution in patients with clinically significant bladder outflow obstruction at risk of urinary retention, gastrointestinal obstructive disorders, risk of decreased gastrointestinal motility, autonomic neuropathy, severe renal or moderate hepatic impairment (doses not to exceed 5 mg), concomitant use of a potent CYP3A4 inhibitor, hiatus hernia/gastroesophageal reflux and/or patients currently taking medicines that can cause or exacerbate oesophagitis. **Interactions:** Use with other anticholinergics may result in more pronounced therapeutic effects and undesirable effects. Allow one week after stopping Vesicare® before commencing other anticholinergic therapy. Therapeutic effect may be reduced by concomitant administration of cholinergic receptor agonists. Can reduce effects of stimulators of gastrointestinal tract motility. If used concomitantly with ketoconazole or other CYP3A4 potent inhibitor, maximum dose should be 5 mg due to 2-3 fold increase in AUC of Vesicare®. Pharmacokinetic interactions are possible with other CYP3A4 substrates with higher affinity and CYP3A4 inducers. **Adverse Effects:** Dry mouth, blurred vision, constipation, nausea, dyspepsia, abdominal pain, colonic obstruction, urinary retention hallucinations, confusional state. In worldwide postmarketing experience, QT prolongation and Torsade de Pointes have been reported in association with solifenacin use, but the frequency of events and the role of solifenacin in their causation cannot be reliably determined. *Prescribers should consult the Summary of Product Characteristics in relation to other side effects.* **Basic NHS Cost:** Vesicare® 5 mg blister packs of 30 tablets £27.62; Vesicare® 10 mg blister packs of 30 tablets £35.91. **Legal Category:** POM. **Product Licence Number:** Vesicare® 5 mg PL 00166/0197; Vesicare® 10 mg PL 00166/0198. **Date of Revision:** January 2010. **Further information available from:** Astellas Pharma Ltd, Lovett House, Lovett Road, Staines TW18 3AZ. Vesicare® is a Registered Trademark. For full prescribing information please refer to the Summary of Product Characteristics. **For medical information phone** 0800 783 5018.

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk
Adverse events should also be reported to Astellas Pharma Ltd. Tel: 0800 783 5018.

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