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Overactive bladder syndrome

Management and treatment options

Background

Overactive bladder syndrome is a symptom-based clinical diagnosis. It is characterised by urinary urgency, frequency and nocturia, with or without urge urinary incontinence. These symptoms can often be managed in the primary care setting.

Objective

This article provides a review on overactive bladder syndrome and provides advice on management for the general practitioner.

Discussion

Overactive bladder syndrome can have a significant effect on quality of life, and affects 12–17% of the population. Prevalence increases with age. The management of overactive bladder syndrome involves exclusion of underlying pathology. First line treatment includes lifestyle interventions, pelvic floor exercises, bladder training and antimuscarinic agents. Failure of conservative management necessitates urology referral. Second line therapies are more invasive, and include botulinum toxin, neuromodulation or surgical interventions such as augmentation cystoplasty or urinary diversion.

Keywords

overactive urinary bladder; urological diseases; urinary incontinence

Overactive bladder syndrome (OBS) is a symptom complex consisting of urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence (Table 1). It is not explained by metabolic (eg. diabetes) or local pathological factors (eg. infection, stones, urothelial cancer).^{1–5} Urgency is the key symptom of OBS.⁶

Clinical significance

In Australia, prevalence of urinary incontinence has been reported at 42% and the incidence of urge-only incontinence at 16%.⁷ Worldwide prevalence of OBS is 12.8% for women and 10.8% for men.⁸ The prevalence of all incontinence increases with age.^{7,8} Appropriate management can decrease both morbidity and costs.⁹

When compared with demographically matched controls, patients with OBS have:^{10,11}

- significantly less work productivity
- less sexual satisfaction and more erectile dysfunction
- higher rates of depressive symptoms
- significantly poorer mental health
- poorer quality of sleep.

Postmenopausal women with urge incontinence have a significantly higher risk of falling and sustaining a fracture than women without urge incontinence.⁴

Causes

The symptoms of OBS have many potential causes and contributing factors. Normal storage of urine is dependent on spinal reflex mechanisms that activate sympathetic and somatic pathways to the urethral outlet and tonic inhibitory systems in the brain that suppress the parasympathetic excitatory outflow to the urinary bladder.⁴

The normal bladder fills like a compliant balloon, with pressure lower than urethral resistance. Initiation of urination decreases urethral resistance and phasic contraction of the detrusor muscle empties the bladder.⁴

Overactive bladder symptoms are usually associated with involuntary contractions of the detrusor muscle, which can result in urge incontinence, depending on the response of the sphincter.⁴ The most common cause of OBS is detrusor overactivity (DO);^{2,12} 64% of all patients with OBS have DO on cystometry, and 69% of men and 44% of women with urgency have DO.¹ Detrusor overactivity is thought to result not only from efferent (motor) hyper function/dysfunction but also most likely by afferent (sensory) noise. Patients with OBS seem to respond to antimuscarinic treatment irrespective of the presence of DO.¹³

Risk factors for OBS include vaginal birth delivery,¹⁴ with 40% of parous women experiencing

urge urinary incontinence, older age, obesity and chronic constipation.¹⁵ Childhood urinary symptoms in women have been found to be independently associated with adult lower urinary tract symptoms, specifically urgency, frequency and nocturia.¹⁶

Diagnosis

Overactive bladder syndrome is a diagnosis of exclusion. A focused history, including past history of urogenital disorders, in combination with physical examination of the genitourinary system and relevant pelvic examinations should be performed as there are multiple conditions that can cause or contribute to symptoms of overactive bladder.^{4,17} Initial and secondary investigations are listed in *Table 2*.

Postvoid residual volume (PVR)² is best measured with ultrasound (bladder scan or formal ultrasound), with the upper limit of normal being 30 mL.² An initially raised PVR requires confirmation before being considered significant² as it can be subject to error.

Increased PVR may contribute to urinary frequency and nocturia, and commencing

anticholinergic medications in a patient with increased PVR may worsen bladder function and potentiate urinary retention.¹⁸

A frequency/volume chart can exclude 24-hour polyuria due to diabetes insipidus, and nocturnal polyuria. It is an invaluable tool in OBS as it gives a better picture of the pattern of voiding than can be obtained from the symptoms alone.¹ Three-day voiding diaries are as reliable as seven-day diaries.² Information obtained should include number of voids in daytime, night time, 24 hour period, volume of urine over 24 hours, maximum voided volume, average voided volume, median maximum voided volume, and nocturnal urine volume. An assessment of severity of incontinence in terms of leakage episodes and pad usage² can also be obtained.

Secondary investigations should be considered in patients with neurological disease, refractory OBS, or those in whom initial investigations raise the suspicion of an underlying problem that may require further evaluation or treatment¹⁹ (*Table 3*).

Urodynamic testing aims to demonstrate incontinence objectively and differentiate between

different types of incontinence, so that the most effective method of treatment can be selected. Urodynamic investigations should also be used to demonstrate the presence of specific abnormalities before undertaking complex reconstructive urological procedures.²⁰

Urine cytology, performed on three voided specimens obtained on three separate days, has a variable sensitivity for the detection of urothelial carcinoma.²¹ Urine cytology is effective for screening for high grade lesions (sensitivity at least 90%, specificity 98–100%) and carcinoma in situ. However, it is unreliable for detection of well differentiated, low grade lesions.²¹

Cystoscopy is indicated in patients with sterile haematuria and risk factors for bladder cancer, and in patients with recurrent urinary tract infections. Carcinoma in situ and other intravesical abnormalities can be assessed via cystoscopy. The possibility of prostate cancer should also be considered in men and assessed based on prostate-specific antigen, digital rectal examination findings and relevant risk factors.⁴

Table 1. Definitions of overactive bladder syndrome

Detrusor overactivity	A urodynamic observation characterised by involuntary spontaneous or provoked detrusor contractions during the filling phase ^{2,12}
Nocturnal polyuria	An excess (>20–30%) proportion of urine excretion at night ²
Polyuria	>40 mL urine/kg body weight during 24 hours
Postvoid residual volume	The volume of fluid remaining in the bladder at the completion of micturition ²
Urgency	A sudden, compelling desire to void that is difficult to defer ^{2,6}
Urinary frequency	>8 micturitions/24 hours
Urgency urinary incontinence	Involuntary loss of urine associated with urgency ²

Table 2. Investigations for overactive bladder syndrome

Initial investigations⁴²
<ul style="list-style-type: none"> • Urinalysis to exclude infection, haematuria and glycosuria • Urinary tract ultrasound and measurement of postresidual volume • Frequency/volume chart for at least 3 days • Bladder diary for a minimum of 3 days
Secondary investigations¹⁹
<ul style="list-style-type: none"> • Urine cytology • Urodynamic testing • Cystoscopy • Imaging of upper urinary tract or spine

Table 3. Indications for urodynamic assessment¹⁷

Suspicion of occult diagnosis that may alter management
<ul style="list-style-type: none"> • Bladder outlet obstruction • Detrusor hyperactivity with impaired contractility • Impaired bladder compliance • Dysfunctional voiding • Mixed incontinence
Risk of upper urinary tract deterioration
<ul style="list-style-type: none"> • History of pelvic irradiation • Radical pelvic surgery (abdomino-perineal resection, radical hysterectomy) • Spina bifida • Neurogenic voiding dysfunction (eg. multiple sclerosis, spinal cord injury)
Other
<ul style="list-style-type: none"> • Failed or unsatisfactory response to empiric medical therapy • Uncertain diagnosis • Unaware incontinence • Prior lower urinary tract surgery (eg. transurethral resection of prostate, anti-incontinence surgery) • Irreversible, potentially morbid intervention planned (ie. augmentation cystoplasty)

Treatment

Principles of treatment are to reduce urinary incontinence by changing patient behaviour and teaching continence skills.²²

Up to one-third of women with urge only incontinence can undergo spontaneous resolution at 2 years.⁸ As OBS is a symptom complex, ‘no treatment’ is an acceptable choice for some patients and caregivers.²³

First line therapy

This can be initiated in the primary care setting. It includes a combination of lifestyle interventions (Table 4), bladder training and behavioural modification. Antimuscarinic medications can be added if these measures fail to control symptoms.^{1,8,20,23,24}

Behavioural treatments (Table 5) have been shown to be effective in older adults, reducing leakage by 50–80%.²⁵ Behavioural training requires a highly motivated patient, and 20–30% will become dry. As behavioural treatments work gradually at first and rely on patient self management, it is important to follow patients regularly to see sustained behavioural changes.²⁵

Bladder training (Table 6) has been found to reduce daily urinary frequency and lower daily urinary incontinence compared to antimuscarinics alone.²⁶

In women with cognitive impairment, prompted and timed voiding toileting programs are recommended.²⁰

Table 4. Lifestyle interventions^{1,22}

- Altering fluid intake – decreasing to reduce incontinence and frequency, increasing to improve urine concentration
- Smoking cessation
- Dietary modification to eliminate possible bladder irritants (eg. reducing caffeine, alcohol and carbonated beverages). Caffeine is a mild diuretic and bladder irritant, and reducing intake can reduce both urge and stress incontinence
- Weight reduction – central obesity places pressure on the bladder and may worsen urge incontinence²⁵
- Regulating bowel function to avoid constipation and straining during bowel movements

Medical noninvasive pharmacotherapy

In the primary care setting, patients presenting with typical overactive bladder symptoms can be treated empirically with an antimuscarinic agent and obtain clinical benefit without the need for invasive urodynamic procedures²⁷ (Table 7).

Human bladder contraction is mediated mainly

through stimulation of muscarinic receptors in the detrusor muscle by acetylcholine.¹² Antimuscarinic agents act during the filling/storage phase of the micturition cycle by inhibiting afferent (sensory) input from the bladder, and directly inhibiting smooth muscle contractility.²⁴ They are competitive antagonists, so with massive release of acetylcholine during micturition the drug effect is decreased and the muscle can contract.^{1,9}

Table 5. Behavioural training as first line therapy

Goal	To improve control by teaching the patient to inhibit or interrupt detrusor contractions
Method	<p>Pelvic floor muscle training with or without biofeedback. Mastering a voluntary contraction of the pelvic floor muscles will help to increase pressure within the urethra, inhibit detrusor contractions and control leakage of urine. Coaching and verbal feedback during vaginal examination can be as effective as biofeedback and electrical stimulation</p> <ul style="list-style-type: none"> • An initial approach is by verbal explanation of the technique reinforced with written materials • An effective verbal explanation of proper contraction of the pelvic floor muscles is to tell the patient to tighten up the muscles that they use to hold in flatus. These muscles can also be identified during a pelvic or digital rectal examination • An effective exercise prescription for older adults is to contract and relax their pelvic floor muscles for 2 seconds with 15 repetitions, three times per day. Patients should gradually increase the duration of squeeze/relaxations by about 1 second per week, until they achieve 10 second contractions and relaxations. At this point they can begin a maintenance prescription of 10 second contractions and relaxations with 10 repetitions once a day • Freeze and squeeze: <ul style="list-style-type: none"> – when a sense of urgency occurs, instead of rushing to the bathroom, stay still and repeatedly tighten the pelvic floor muscles without relaxing them until the urgency is gone. Walk to the bathroom at a normal pace • Repeat as needed <p>A maintenance program is essential to maintain strength and effectiveness</p> <p>At least 3 months of supervised pelvic floor muscle training is required to see benefits</p> <p>Continence management is often best guided by a continence trained professional (eg. nurse or physiotherapist)</p>

Table 6. Bladder training as first line therapy

Goal	To modify bladder function, reduce voiding frequency, increase bladder capacity and eliminate detrusor overactivity by using scheduled voiding rather than voiding in response to urgency
Method	<ul style="list-style-type: none"> • The bladder diary is reviewed with the patient, and the longest comfortable interval between voiding is chosen. This interval is the starting point • Patients are instructed to empty the bladder on waking and then each time during the day when the interval is reached, and again before going to bed • If the patient feels the urge to void during the interval, patients are instructed to use urge suppression techniques, such as distraction or relaxation techniques or self affirming statements, to get them through to the scheduled voiding time • After 1–2 weeks, increase the time interval by 15 minutes, gradually increasing the interval between voids • Patients are also encouraged to sit down and take five slow deep breaths, concentrating on the breathing and not the bladder sensation <p>A minimum of 6 weeks training is required to see benefits</p>

Antimuscarinic medications

Controlled release compounds are generally better tolerated than immediate release formulations, with similar efficacy. The majority of adverse events associated with antimuscarinic agents are due to inhibition of muscarinic receptors in organs other than the bladder^{7,28} (Table 8).

If treatment with an antimuscarinic fails due to inadequate symptom control or unacceptable adverse effects, a second antimuscarinic (or duloxetine) can be trialled before considering second or third line therapies²³ and a urological opinion. Dry mouth and constipation should be managed before abandoning effective antimuscarinic therapy.²³

A Cochrane review²⁹ evaluated anticholinergic medications versus nonpharmacologic treatment of OBS. Symptomatic improvements were more common in patients on anticholinergic drugs compared with bladder training (RR 0.73; 95% CI: 0.59–0.90), and the combination of anticholinergics with bladder training was associated with more improvement than bladder training alone (RR 0.55; 95% CI: 0.32–0.93). There is no clear evidence that one anticholinergic is better than another for treatment of OBS.²⁹

Effects in the elderly

Cognitive dysfunction including memory loss and attention deficits are particular side effects in the elderly.⁷

Antimuscarinic medications differ in their propensity to cause central nervous system adverse events due to differences in lipophilicity and crossing of the blood-brain barrier. Oxybutinin may be the most likely to cross the blood-brain barrier.¹³

The use of anticholinergics should be carefully weighed against the potential cognitive risks in the older adult population,²⁴ as long term exposure to anticholinergics may be associated with increased Alzheimer type pathology.³⁰

The newer antimuscarinics for OBS – darifenacin, solifenacin and tolterodine – have a significantly reduced impact on cognition compared with traditional agents. Similarly, oxybutinin transdermal gel does not seem to adversely affect cognition.³¹ Despite this, their use in the elderly

Table 7. Medications available in Australia and proven to be effective for overactive bladder syndrome

Drug	Adverse effects	Notes
Oxybutynin CR 5–15 mg/day	<ul style="list-style-type: none"> • Dry mouth (68%) • Constipation (10%) 	Dose response observed Take 1 hour before food
Oxybutynin transdermal 3.9 mg twice weekly	<ul style="list-style-type: none"> • Itchiness at site (14%) • Erythema at site (8%) • Dry mouth (7%) • Constipation (2.1%) 	Transdermal delivery reduces the typical anticholinergic side effects of dry mouth and constipation
Tolterodine 2 mg twice per day	<ul style="list-style-type: none"> • Dry mouth (23%) • Constipation (6%) • Dry eyes (4%) 	Dose dependent effect with immediate release Safe in men with bladder outlet obstruction Expensive, not subsidised on the PBS ^{3,2}
Solifenacin 5–10 mg/day	<ul style="list-style-type: none"> • Dry mouth (26%) • Constipation (12%) • Blurred vision (5%) 	Steady state at 10 days due to long half-life
Darifenacin 7.5–15 mg/day	<ul style="list-style-type: none"> • Dry mouth (35%) • Constipation (21%) 	Steady state 4–5 hours Dose response Safety, efficacy and tolerability maintained with long term use Not subsidised on the PBS
Vaginal oestrogen (topical) 0.5 g cream nightly for 2 weeks then twice per week	<ul style="list-style-type: none"> • Increased risk of breast cancer • Breast discomfort and pain • Local reactions 	For postmenopausal women with vaginal atrophy Contraindications: past history of breast cancer
Duloxetine 40 mg twice per day increasing to 60 mg twice per day after 4 weeks (for stress urinary incontinence)	<ul style="list-style-type: none"> • Nausea (31%) • Dry mouth (16%) • Constipation (14%) • Insomnia (13%) • Fatigue (11%) 	Efficacy for stress and mixed stress and urge incontinence Can be used if anticholinergics are contraindicated for overactive bladder syndrome ³³ TGA indicated and PBS subsidised in Australia for major depressive disorder

Table 8. Antimuscarinic agents: when to think twice

Absolute contraindications
<ul style="list-style-type: none"> • Closed angle glaucoma: anticholinergic medications substantially increase intraocular pressure which may threaten vision if not treated urgently⁴¹
<ul style="list-style-type: none"> • High doses in ulcerative colitis can lead to paralytic ileus
<ul style="list-style-type: none"> • A history of impaired gastric emptying or urinary retention¹⁰
Think twice
<ul style="list-style-type: none"> • Elderly patients: <ul style="list-style-type: none"> – central adverse effects include sedation, confusion, delirium, cognitive impairment and psychotic symptoms⁴² – signs of toxicity include urinary retention, agitation, hallucinations, seizures, cardiac arrhythmias and heart block⁴² – close monitoring is required²⁰
<ul style="list-style-type: none"> • Patients who are on other medications metabolised via the hepatic cytochrome P450 (CYP450) family (eg. warfarin, omeprazole, erythromycin, fluoxetine)¹⁷
<ul style="list-style-type: none"> • Men with bladder outlet obstruction: <ul style="list-style-type: none"> – 45–50% will have concurrent detrusor overactivity¹³ – combination treatment with antimuscarinic agents and an alpha-blocker should be used with caution

may still contribute to cognitive impairment and appropriate monitoring is recommended.

Prescribing in the elderly

Oxybutinin can be started at 2.5 mg twice per day. The morning dose can be increased or a lunchtime dose added depending on severity and timing of symptoms. The maximum dose is 5 mg three times per day.³² High doses are often not well tolerated due to dry mouth, gritty eyes, exacerbation of gastrointestinal reflux and constipation.

Nonantimuscarinic medications

Duloxetine (a serotonin noradrenaline reuptake inhibitor) can be effective in both stress and mixed stress and urge incontinence.³³ However, it is currently only Therapeutic Goods Administration (TGA) indicated and Pharmaceutical Benefits Scheme (PBS) subsidised in Australia for major depressive disorder. In clinical practice, most women discontinue duloxetine within 4 weeks due to adverse effects (Table 7).

Failure of conservative and medical treatments warrants urology referral for further investigation with urodynamics, and more invasive therapies may be considered.^{1,4}

Second line therapy

Intravesical botulinum toxin A (BoNT/A) prevents acetylcholine release at the neuromuscular junction, resulting in temporary chemodenervation and muscle relaxation for up to 6 months.³⁴ The technique is to place multiple injections under cystoscopic guidance directly into the detrusor.³⁵

Complete continence can be achieved in 40–80% of patients and bladder capacity improved by 56% for up to 6 months.³⁶ Maximal benefit is between 2 and 6 weeks, maintained over 6 months. The injections can be repeated.³⁵

Third line therapy

Sacral nerve stimulation involves an implantable electrode in the S3 foramen continuously stimulating the S3 nerve root, in order to stimulate the pudendal nerve. A temporary wire is initially placed under local anaesthetic for 5–7 days in both sides and a voiding diary is kept. An improvement of >50% in any parameters will enable a permanently implanted S3 lead on the side with the best clinical response. There is a potential benefit for up to 5 years in patients with OBS.³⁷

Current indications for sacral nerve stimulation include refractory urge incontinence, refractory urgency and frequency, and idiopathic urinary retention.³⁸

In augmentation cystoplasty, the bladder is enlarged by incorporating a variety of different patches into the native bladder, usually patches of bowel still attached to their mesentery (ileum, caecum or sigmoid colon).³⁹ Indications for bladder augmentation include a small, contracted bladder and a dysfunctional bladder with poor compliance.⁴⁰

Urinary diversion should be considered only when conservative treatments have failed, and if sacral nerve stimulation and augmentation cystoplasty are not appropriate or unacceptable to the patient.²⁰

Key points

- Overactive bladder syndrome is a symptomatic diagnosis consisting of urinary frequency, urgency and nocturia, with or without urge urinary incontinence.
- There is a significant impact on quality of life, which can lead to depression and affect relationships. Patients are often too embarrassed to discuss symptoms with their GP.
- Pathology such as urinary infection, diabetes, bladder stones, malignancy or an underlying neurological cause should be excluded.
- Initial treatment consists of a combination of lifestyle interventions, pelvic floor exercises, bladder training and antimuscarinic medications.
- Care should be taken when prescribing antimuscarinic therapy in the elderly.

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