Overactive bladder syndrome

Management and treatment options

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Background
Overactive bladder (OAB) is a common syndrome in the community characterised by unstable bladder contractions, resulting in urinary urgency, frequency and nocturia in the absence of detectable disease. Large studies suggest that >10% of the general population is symptomatic.

Objective
The aim of this article is to summarise the stepwise treatment for OAB that seeks to improve patient quality of life and reduce patient and health system costs.

Discussion
OAB is a diagnosis of exclusion that begins with a targeted history and examination of the urogenital system with the aim of assessing the burden of disease on the patient. First-line treatment comprises conservative measures including weight reduction, a decrease in exposure to bladder stimulants, fluid optimisation and pelvic floor exercises. Pharmacological treatments for OAB include anticholinergic medications such as oxybutynin. If the patient is unresponsive to pharmacological treatment, a review by a urology specialist is appropriate. Recommendations may include minimally invasive procedures such as intravesical botulinum toxin A injections, reserving the invasive procedures for patients in specific circumstances.

OVERACTIVE BLADDER (OAB) is a common syndrome characterised by unstable bladder contractions, resulting in urinary urgency, frequency and nocturia (defined in Table 1). Classically, patients with OAB report difficulty suppressing the urge to urinate. OAB is frequently associated with urge incontinence. Associated urge urinary incontinence is common, with large American and European studies suggesting that >10% of the general population is symptomatic, with those aged >65 years being twice as likely to be affected.[1] The associated sequelae of OAB, including urinary incontinence, have a negative impact on the quality of life of affected individuals.[2] The effects of urinary incontinence are not isolated to the patient. Increased burden may be felt by the caregiver, thereby affecting the caregiver's relationship with the patient. Further, untreated urinary incontinence may increase the risk of urinary tract infection (UTI) and may cause significant surrounding inflammatory changes.[2]

Many patients downplay their symptoms of OAB and do not raise the issue with health practitioners.[1] While OAB may be difficult to completely cure, symptoms can be effectively reduced, and quality of life can be improved without excessive cost or morbidity.[3–5] Since a previous review published in 2012,[6] considerable changes have occurred in recent years with respect to management regimens for patients with OAB and urge urinary incontinence. The aim of this article is to summarise these updated strategies.

Causes

The symptoms of OAB are typically associated with detrusor overactivity. By definition, OAB is idiopathic – although multiple risk factors have been identified.[5] Such risk factors may be modifiable or non-modifiable.[5] Identification of these is critical as reduction of exposure represents a pertinent facet of the initial treatment of OAB.

Pertinent key differential diagnoses must be considered and excluded prior to the diagnosis of OAB being confirmed.[6] Specifically, a neuropathic bladder from diseases of the central nervous system may result in neurogenic detrusor overactivity, a disease process that is high risk and requires complex urological input. Similarly, urothelial carcinoma of the bladder can result in irritative voiding and patients presenting with voiding dysfunction; therefore, symptoms similar to OAB may be the first signs of high-grade bladder cancer. A more comprehensive differential diagnosis for OAB is listed in Table 2.

Assessment of OAB

OAB is a diagnosis of exclusion beginning with a targeted history and examination of the urogenital system with an aim to assess the burden of disease facing the patient and affecting their quality of life (refer to Table 2).

It is important to complete comprehensive history-taking, assessing pertinent past medical history, quantification of local symptoms, urge

incontinence and obstetric history. Specific details of incontinence should be interrogated to exclude other types of incontinence. Use of validated questionnaires – such as the OAB questionnaire (OAB-q) to assess patient quality of life with urge incontinence, or the International Consultation on Incontinence Questionnaire Overactive Bladder Module (ICIQ–OAB) to assess severity and burden – assist in providing a baseline from which treatment efficacy can be determined.[4]

It is imperative to rule out sinister or reversible conditions that may have similar symptomatic presentations such as UTI, urolithiasis and bladder cancer (as outlined in Table 2).[3] Neurological disease should also be excluded. Examination is directed to the abdomen (comprising a pelvic examination including investigation of sensation in the perineum), as well as a gross neurological examination to exclude neurological disease. Patients with macroscopic haematuria should be promptly referred for exclusion of urothelial carcinoma.[7,8]

Initial investigations include routine blood examination and urinalysis to exclude infective causes of incontinence and to detect haematuria and glycosuria.[9] Urine cytology should strongly be considered – particularly in patients at high risk of bladder cancer if there has been a recent onset of symptoms. Early appropriate imaging would include ultrasonography of the urinary tract with a post-void residual measurement. Completion of a bladder diary can provide useful objective information regarding fluid intake (including irritants such as caffeine and alcohol) and urinary volumes, as well as assist in quantifying incontinence episodes and identifying reversed diurnal rhythm.

On the basis of initial investigations, urological referral may be considered to complete additional investigations including cystoscopy or urodynamics.

Treatment of OAB

Once a diagnosis of OAB has been made, most patients can progress through a stepwise treatment path from conservative options to medical and finally surgical treatments. Each step should be trialled for

Table 1. Definition of symptoms of overactive bladder

Term	Definition
Urinary urgency	Inability to defer voiding
Urge incontinence	Urgency causing non-voluntary urinary incontinence
Urinary frequency	Eight or more voids per 24 hours
Nocturia	Awakening to void ≥1 instance per night

Table 2. Risk factors and differential diagnosis for overactive bladder (OAB)

Risk factors and contributory factors for OAB	
Non-modifiable risk factors	• Age • Sex (female) • Metabolic syndrome • Post-menopausal • Benign prostatic hyperplasia • Pelvic organ prolapse in women
Modifiable risk factors	• Alcohol • Smoking • Obesity • Caffeine intake (coffee, tea, energy drinks) • Carbonated beverages • Spicy foods • Bladder stones
Important differential diagnosis for OAB	
Neurological (neurogenic detrusor overactivity)	• Stroke • Multiple sclerosis • Dementia • Diabetic neuropathy • Spina bifida • Spinal trauma • Reversed diurnal rhythm
Malignancy	• Urothelial carcinoma (including carcinoma in situ)
Lower urinary tract	• Recurrent urinary tract infection • Bladder outlet obstruction (including benign prostatic hyperplasia, urethral stricture) • Foreign body in lower urinary tract (eg eroded synthetic mesh) • Overflow incontinence
Systemic pathologies	• Obstructive sleep apnoea • Congestive heart failure • Diabetes resulting in polyuria
Medicine	• Diuretics • Anticholinergics • Narcotics

a period of at least four weeks. Following progression to the next step of the treatment regimen, it is critical to continue the preceding steps. A management algorithm is outlined in Figure 1.

Step 1: Conservative management

Conservative measures are a reasonable first-line management strategy depending on the burden of disease faced by the patient. Communication with and education of the patient, and potentially caregivers, is important with early management. It is necessary to actively engage the patient to agree on interventions or modifying behaviours that are feasible. Close compliance with conservative measures has an efficacy of 50%.[10] Specifically, conservative measures include:[4,11]

- treatment of modifiable risk factors (eg weight reduction)
- reduction of exposure to bladder stimulants (eg alcohol, caffeine, smoking, carbonated beverages)
- constipation avoidance – aiming for soft stools passing every 1–2 days; patient increasing daily fibre intake; potentially using stool softeners and laxatives
- fluid optimisation – restricting fluid intake to 6–8 glasses of water per day; avoiding pre-bed hydration by two hours if polydipsia is identified in the voiding diary or if high intake prior to bed is resulting in nocturia
- pelvic floor exercises – bladder training with physiotherapy
- containment devices (eg incontinence pads)
- bladder training – scheduling voiding times; using urge control techniques – when feeling the urge to urinate, the patient contracts pelvic floor musculature for 10 seconds or for a burst of five rapid activations until the urgency is relieved.

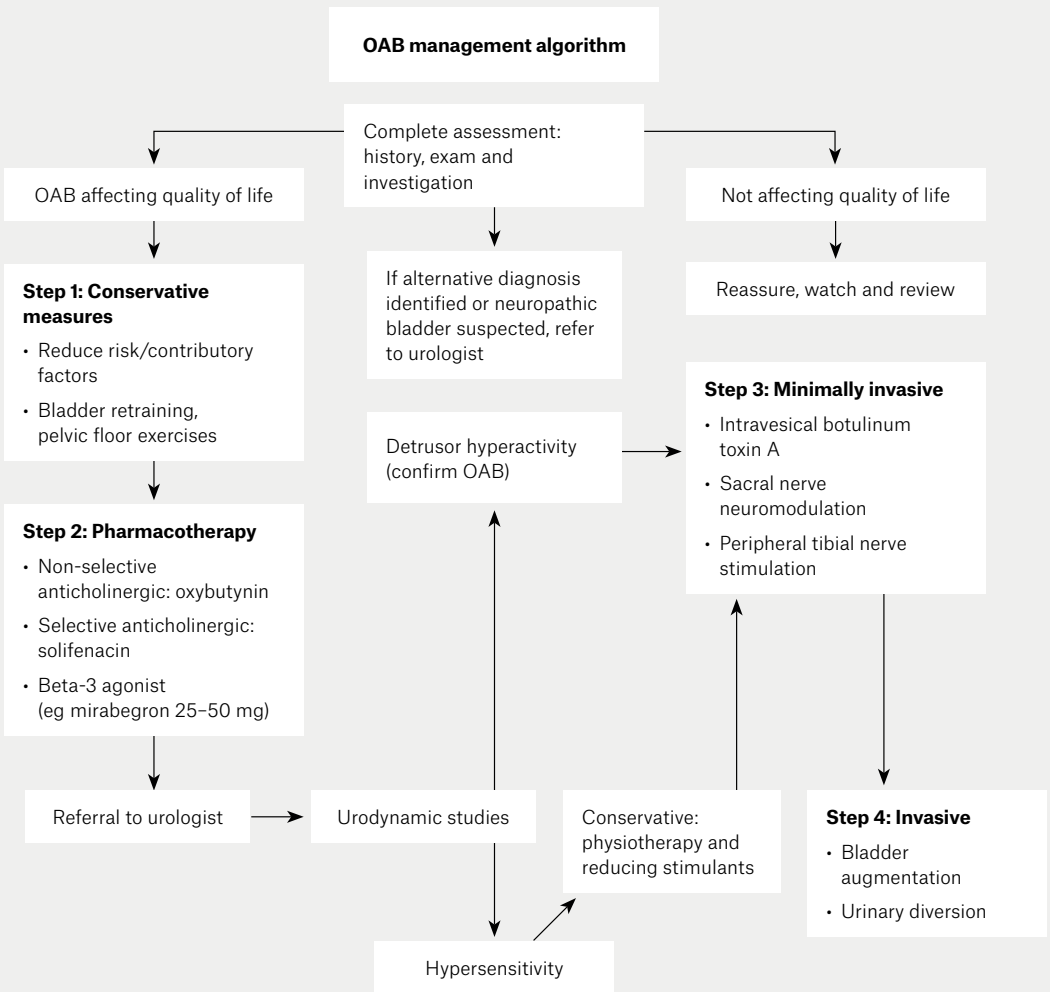

Figure 1. Management algorithm for overactive bladder; treatment moves to the next level (ie more invasive) treatment form if treatment goals are not met after the appropriate duration

MSU, midstream urine; OAB, overactive bladder; USS KUB, ultrasonography of kidney, ureters, bladder

Topical oestrogen is often used in the post-menopausal female population. There is significant overlap in the diagnosis of OAB and the genitourinary syndrome of menopause, and the use of vaginal oestrogen in this setting is efficacious in the treatment of urinary incontinence by improving urinary urgency, frequency and bladder capacity.[12] Care should be taken when prescribing topical oestrogen for patients with a history of breast or endometrial malignancy.

Step 2: Pharmacotherapy

Anticholinergic therapy

Anticholinergic medications block the acetylcholine neurotransmitter synapse in the central and peripheral nervous systems, inhibiting parasympathetic activity, thereby reducing the involuntary movement of smooth muscles such as those present in the bladder.[13,14] Multiple anticholinergic medications are available for use in clinical practice (Table 3). Such medications include non-selective agents (oxybutynin, tolterodine) or more-selective agents (solifenacin, darifenacin).[13,14]

Non-selective agents are effective, with a success rate of >65%.[15] Unfortunately, these agents have several adverse effects that can make them relatively poorly tolerated. Fewer than 35% of patients are adherent to anticholinergic medications at 12 months post-commencement.[13,14] Dry mouth is a common complaint on starting the medication, and other bothersome side effects related to its mechanism of action include constipation and dry eyes.[15] Anticholinergic agents, primarily non-selective agents, should also be used cautiously in older patients because of their effects on cognitive function and possible interaction with other medications.[16] Prescribers should be aware that these agents are contraindicated for patients with glaucoma.[13,14]

If there is a good therapeutic response to oral oxybutynin but it is poorly tolerated because of systemic side effects, a common solution is to prescribe topical oxybutynin patches 3.9 mg/24 hours, which are better tolerated because of the lack of hepatic metabolites. However, they can also cause a bothersome local skin reaction.[13,14]

More-selective agents have an improved tolerability profile at an increased expense. These agents are selective for the M3 receptor and therefore have fewer systemic side effects and remarkable efficacy at the level of the bladder. Solifenacin is commonly prescribed in Australia.

Beta-3 agonist therapy

Beta-3 adrenergic receptor agonists upregulate sympathetic activity, thereby promoting detrusor smooth muscle relaxation and consequently reducing muscle spasms.[15] The current commercially available β3 adrenoceptor agonist is mirabegron (Table 3). It works via a different path to anticholinergic agents by relaxing the detrusor muscle, allowing higher bladder volumes before the need for urination. Significant improvements are typically seen at week four after initiation of treatment, and improvements are maintained at 12 months. Given its action on the sympathetic system, mirabegron should be used cautiously in patients with difficult-to-control hypertension and a prolonged QT interval.[13–15]

Studies have shown it is both safe and efficacious to prescribe an antimuscarinic agent and β3 adrenoceptor agonist synergistically for patients that are refractory to monotherapy.[15]

Advanced treatment options for OAB

Step 3: Minimally invasive options

Intravesical botulinum toxin A

Botulinum toxin A bladder injections administered via cystoscopy into the wall of the bladder inhibit muscle contractions and suppress bladder activity. The treatment is typically effective for 6–12 months,[17] but the procedure can be repeated. Half of the patients treated with intravesical botulinum toxin A reported improvement in symptoms of OAB.[17] The disadvantages of this treatment are its temporary nature, the need for a general anaesthetic (although local anaesthetic treatment is becoming more commonly available in Australia) and the small risk of iatrogenic urinary retention requiring temporary catheterisation (5%).[17]

Table 3. Pharmacotherapy agents

Medication class	Agent	Route, dose	PBS listing	Adverse effects
Anti-cholinergic, non-selective	Oxybutynin	Oral, 5 mg three times daily	Yes	Dry mouth, constipation, blurred vision, drowsiness, delirium
		Topical, 3.9 mg/24 hours	Yes	Skin reaction, dry mouth, constipation, blurred vision, drowsiness, delirium
Anti-cholinergic, M3 selective	Solifenacin	Oral, 5–10 mg daily	No, $50–65 per month	Severe hepatic impairment
Beta-3 agonist	Mirabegron	Oral, 25–50 mg daily	No, $50–65 per month	Hypertension, long QT syndrome

PBS, Pharmaceutical Benefits Scheme

Sacral nerve stimulation

For sacral nerve stimulation, surgeons implant an electrode in the S3–S4 sacral foramen with the aim of manipulating the sensory pathway of the bladder innervation.[18] As defined by patient voiding diaries, 90% of patients showed >50% improvement of symptoms.[18] Of the reported complications, one-third of patients may require surgical revision within the first year because of pain (and, less commonly, infection) or transient electric shock.[18] The sacral nerve stimulation battery will run out a few years after implantation and require replacing. The implants are expensive, and public hospital accessibility is limited.

Peripheral tibial nerve stimulation

For peripheral tibial nerve stimulation (PTNS), an electrode is inserted into the skin 5 cm above the medial malleolus. By way of an electrode, a retrograde stimulation is generated through the tibial nerve to the sacral plexus. The nerve is increasingly stimulated until great toe flexion, toe abduction or leg extension, at which time the amplitude is reduced by one level and the treatment continues for 30 minutes. Treatment is repeated weekly for up to 12 sessions. The response to therapy is typically observed within six treatments. Adverse effects include pain, which is typically mild, and bleeding. PTNS is contraindicated in patients with pacemakers/defibrillators, those who are pregnant or those with prior nerve damage affecting the tibial nerve or pelvic floor.[11]

Step 4: Invasive surgical options

When conservative and minimally invasive treatments have failed, bladder augmentation cystoplasty may be considered to treat urge incontinence caused by neurogenic bladder dysfunction, significantly contracted bladder caused by inflammatory conditions, interstitial cystitis and reconstruction after bladder injury.[19] This procedure involves bladder enlargement by adding a piece of bowel into the bladder wall. It can be attractive as a definitive solution to the underlying problem; however, if the patient is responding well to less invasive treatments, those treatments should be continued to avoid major surgery. Apart from the risks associated with major abdominal surgery, there is a poorly defined rare risk of malignancy at the ileo-vesical junction, and patients may void varying amounts of mucus secreted from the implanted small bowel.

Patients with intractable incontinence who are not fit for augmentation or other diversions may benefit from a long-term large-bore (18–24 FG) suprapubic catheter. The suprapubic catheter is associated with similar infection rates and resulting complications as long-term urethral catheterisation.[20] Patients will also need to be able to care, or have carers able to care, for a leg bag and night bag.[20]

In extreme cases of severe OAB refractory to all other treatment, urinary diversion in the form of an ileal conduit with or without cystectomy may be considered after thorough counselling in a high-volume centre.[19,21]

When to refer

Referral to a urologist should be considered for patients where:

- a significant alternative diagnosis has been identified, such as neurological disease or urothelial carcinoma
- there are red flag symptoms such as haematuria, recurrent UTIs or progressive renal compromise
- there is high risk of significant alternative diagnosis; for example, the patient has an extensive smoking history, atypical or abnormal urine cytology, or previous urological malignancy
- OAB is refractory to medical treatments
- there are features of urological compromise, such as severe incontinence, recurrent UTIs, hydronephrosis or progressive decline in renal function.

Early referral should also be considered for a patient who has had a number of urological surgeries, such as women with urethral slings.

Conclusion

OAB is a common syndrome in the Australian community. It adversely affects the elderly and is debilitating for patients physically, psychologically and socially. Following diagnosis, there is a spectrum of treatment options available to patients and medical practitioners to consider in a stepwise approach. If conservative and pharmacological treatments are not therapeutic, or if an alternative diagnosis is suspected, referral to a urologist for complete assessment is recommended.

Key points

- OAB is a common condition in Australia that disproportionately affects the elderly.
- The definition of OAB is symptom based, and a diagnosis is made in the absence of an identifiable disease.
- For the majority of patients, a stepwise treatment of OAB begins with a wide range of conservative measures, offering the patient both lifestyle modifications and control techniques on the basis of the patient's history and engagement in treatment.
- In combination with conservative treatment, pharmacotherapy is the mainstay of treatment for OAB, with multiple anticholinergic agents and a new β3 agonist available.
- If conservative treatment and pharmacotherapy do not improve symptoms, minimally invasive treatments such as botulinum toxin A injections, sacral nerve neuromodulation and peripheral tibial nerve stimulation can be trialled.
- In extreme cases of severe OAB that is refractory to all other treatment, urinary diversion in the form of an ileal conduit with or without cystectomy may be considered after thorough counselling in a high-volume centre.

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