# Pharmacological management of overactive bladder syndrome

**Bardsley, A.**



**Original citation:**
Bardsley, A. (2014) Pharmacological management of overactive bladder syndrome. Independent Nurse, volume 2013 (19): 19-21. DOI: 10.12968/indn.2013.19.19

http://dx.doi.org/10.12968/indn.2013.19.19

Mark Allen Healthcare

Title: The pharmacological management of overactive bladder syndrome

Author: Alison Bardsley RGN, MSc, DN, PGCert HE

Title: Senior Lecturer Adult Nursing, Course Director for Non-medical Prescribing

Place of work: Coventry University

## Introduction

Overactive bladder (OAB) is a syndrome which affects around 12% of men and women, with incidence increasing with age around 70-80% of people are affected by the age of 80 (1). Patients' with OAB present with symptoms of urgency, increased daytime frequency and nocturia (2). Around 33% of people with OAB will exhibit urinary incontinence, which affects women more than men. OAB has a significant negative effect on patient's quality of life and can lead to social isolation and depression (3 and 1). Overactive bladder syndrome with urge incontinence is associated with early institutionalisation, financial cost and increased morbidity and mortality (4)

## Function of the Lower Urinary Tract

The function of the lower urinary tract (LUT) is to store and intermittently release urine, and requires the co-ordination of smooth and striated muscles in the bladder and bladder neck, urethra and urethral sphincter within the bladder outlet. Coordination between these organs is mediated by a complex neural control system located in the brain, spinal cord and peripheral ganglia. The average adult bladder can hold around 350-500mls of urine. The sensation of bladder fullness occurs when the bladder is around half full (200mls), but results in no increase of pressure from the detrusor muscle until the bladders capacity is reached.

## Nervous control of micturition (see figure 1)

Voluntary control of voiding requires interaction between the autonomic (mediated by the sympathetic and parasympathetic nerves) and somatic efferent pathways (mediated by pudendal nerves). When the bladder stretches during filling, the sympathetic nerves enable the detrusor to relax and the internal sphincter to contract. To initiate voiding, the parasympathetic nervous system is triggered to contract the detrusor muscle and relax and open the internal sphincter. The relaxation and opening of the external sphincter is under voluntary somatic nerve control.

Sympathetic innervations arise in the T11-L2 region of the spinal cord and enter the base of the bladder and urethra via the hypogastric nerve and inferior mesenteric plexus. Parasympathetic innervations arise from S2-S4 spinal segments and travel in sacral roots and pelvic nerves to the pelvic area and bladder wall, which is where the postganglionic

nerves supplying parasympathetic innervations to the bladder arise. Somatic nerves that supply the straited muscle within the external urethral sphincter arise from S2-S4 motor neurons and pass through the pudendal nerves (5).

Receptors and Neurotransmitters

Co-ordination of voiding involves four principle neuro transmitters: glutamate, serotonin, noradrenaline and acetylcholine. The parasympathetic neurons and somatic nerves primarily use acetylcholine (ACh) , while in the sympathetic neurons the neurotransmitter is noradrenaline.

Acetylcholine (ACH) is released from parasympathetic postganglionic axons in the pelvic nerves, which initiates bladder contraction by stimulating the M³ muscarinic receptors in the bladder smooth muscle. Sympathetic postganglionic neurons release noradrenaline (NA), which activate β³adrenergic receptors to relax the bladder smooth muscle and stimulate $\alpha_1$adrenergic receptors which contract the smooth muscle of the urethra maintaining closure during filling. Acetycholine is also released from somatic axons within the pudendal nerves, which produces contraction of the external sphincter by activating nicotinic cholinergic receptors. Bladder smooth muscle is also excited by ATP released from the parasympathetic postganglionic nerves, while nitric oxide relaxes the smooth muscle of the urethra.

Glutamate is the principle neurotransmitter in the spinal cord which activates ACh release stimulating the nicotinic receptors in the striated urethral sphincter. This action is thought to be enhanced by serotonin and noradrenaline.

There are 5 types of muscarinic acetycholine receptor (mAchR) isotopes which are specialised to different tissues and functions. These receptors are found in various organs around the body and activation can lead to various actions summarised in Table 1. The presence of muscarinic and nicotinic receptors in the bladder and urethra is the focus of pharmacological treatment options of overactive bladder

Figure 1 Innervations of the bladder and pelvic floor (Bardsley, A. (2012) 'Drug Therapies for post-menopausal urinary incontinence'. *Nurse Prescribing* 10 (8), 384-391)

*Fig 1*

Innervations of the bladder and pelvic floor

*Stimulation of sympathetic neurons →relaxation detrusor and contraction of internal sphincter*

*Stimulation of parasympathetic neurons →contracted detrusor*

*Stimulation of somatic neurons →contraction of external sphincter and pelvic floor*

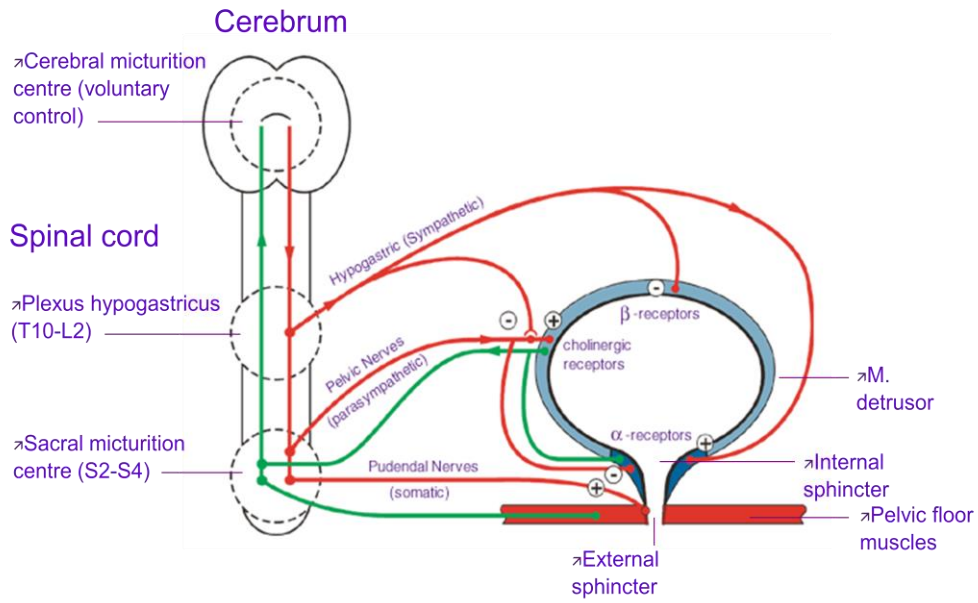

Table 1 (6)

| Type of mAchR | Organ | Action |
|---|---|---|
| M1 | Brain, salivary glands, sympathetic ganglia | Cognitive functions |
| M2 | Heart, Hind brain, smooth muscle | Decrease in heart rate |
| M3 | Smooth muscle, salivary glands, eye | Smooth muscle contraction<br>Salivary secretion |
| M4 | Brain | Unknown but possible CNs effect |
| M5 | Brain, Eye | Unknown but possible CNs effects |

Overactive Bladder and Urge Incontinence

When a bladder becomes overactive there are involuntary contractions of the bladder wall during the filling phase of micturition. For some people an overactive bladder is idiopathic, however for many the cause is related to a known neurogenic condition such as multiple sclerosis. The symptom of an urgent, sudden and compelling need to void is the most bothersome and usually drives the other symptoms of OAB.Urgency urinary incontinence is defined as the complaint of involuntary leakage of urine accompanied by or preceded by the urgent need to void (7,4). Frequency denotes the need to void too often during waking hours, and is usually defined as more than 8 times in 24hours. However the ICS do not asign a particular figure as increases in daytime frequency can be subjective and a bladder voiding diary should be maintained to confirm (7).

Assessment

The clinical diagnosis of OAB is based on an holistic history, which must include a baseline frequency volume chart. Baseline charts should be completed for a minimum of 3 days, covering work and leisure time (8). A urinaylsis should be undertaken to rule out infection and if blood is present in the urine culture, patients should be investigated for bladder cancer. Post void residual urine volume should be assessed using a bladder scan (8). Significant post void residual urine can lead to symptoms of urgency and frequency and is a particular issue for those patients with an underlying neurogenic condition. Urodynamic assessment is not required prior to commencing conservative treatment.

Treatment options

Lifestyle interventions, behavioural therapy and pharmacotherapy are the main first line options for treating OAB and include establishing normal voiding patterns, reducing bladder irritants such as caffeine, management of fluid intake, weight control, regularising bowel

habits and smoking cessation (9). Combining behavioural modifications with pharmacotherapy is shown to enhance the effectiveness (10, 4).

Pharmacotherapy

The updated NICE guidelines (8): Urinary Incontinence: the management of urinary incontinence in women recommend that before patients are started on medication for OAB the following should be discussed

- The likelihood of success and associated common adverse effects
- The frequency and route of administration
- That some adverse effects such as dry mouth and constipation may indicate that treatment has starting to have an effect
- That they may not see the full benefits until they have been taking the treatment for 4 weeks

The following anticholinergic medicines are currently available in the UK.

- Darifenacin
- Oxybutynin – available in immediate release, extended release, transdermal and topical gel formats
- Tolterodine – available in immediate release and extended release formulations
- Trospium – available in immediate and extended release formulations
- Propiverine - available in immediate and extended release formulations
- Solifenacin
- Fesoterodine

When choosing a drug for the treatment of OAB, NICE (8) recommend starting with oxybutinin (immediate release), tolteradine (immediate release) or darifenacin (once daily preparation). However oxybutinin should not be offered to frail older patients due to the risk of adverse effects. All patients should be reviewed at 4 weeks following the start of treatment and if the first line treatment is ineffective or not well tolerated a higher dose or an alternative drug should be offered, having considered the most cost-effective alternative. Referral to a multi-disciplinary secondary care team should only be made if drug treatment is unsuccessful or the patient wishes to discuss alternative options.

How do anticholinergic medications work?

Anticholinergic medications act as agonists, inhibiting the binding of acetycholine on the muscarinic receptors within the detrusor muscle, which reduces the involuntary nerve messages that lead to uncontrolled contractions of the detrusor and increase the bladders ability to store urine. The action and metabolism of anticholinergic agonists varies depending on the affinity of an individual drug to a particular muscarinic or nicotinic receptor within the detrusor. Anticholinergic medications are also used to reduce OAB associated nocturia.

## Precautions in prescribing anticholinergic medications

As anticholinergic medications target M receptors, they are associated with a number of side effects including constipation, dry mouth, blurred vision and somnolence, with more serious events including cognitive and cardiac side effects, as these receptors are present elsewhere within the body (see table 1) (11). For older people there may be central nervous system (CNS) effects, for example cognitive disturbances which range from sedation, inability to concentrate, memory impairment and delirium. This high side effect profile is associated with poor concordance, with a reported 43-83% discontinuation rate and over half of patients never refilling the initial prescription (12).

When considering using anticholinergic medications for the treatment of OAB, the prescriber must consider coexisting conditions, for example poor bladder emptying. Anticholinergic medications are metabolised by the liver and excreted through the kidneys, so care should be taken in patients with renal and hepatic impairment. Concomitant use of other medications with anticholinergic effects such as antihistamines may also increase the risk of adverse effects (11). Low doses should always be prescribed initially to minimise the adverse effects (8).

## Oestrogens

Muscle mass generally decreases with age. The urethral mucosa forms a watertight seal aiding continence and evidence suggests that the urethra is hormonally sensitive with oestrogen having an advantageous effect (13). However the role of oestrogen replacement in treating incontinence associated with OAB is unclear (8). Systemic oestrogens are associated with an increased risk of systemic adverse effects for example thromboembolism (8). Following a review of the current available evidence NICE (8) recommend that systemic oestrogen (hormone replacement therapy) should not be offered for the treatment of urinary incontinence, but intravaginal oestrogen can aid post menopausal women with vaginal atrophy (13).

## Botulinum toxin

Botulinum toxin (type A) is a neurotoxin, derived from the bacteria *Clostridium botulinum*. One action of Botulinum toxin is to inhibit the release of acetycholine from the pre-synaptic cholinergic nerve endings, which temporarily paralysis the muscle into which it is injected, leading to decreased muscle contractibility (1). The toxin is injected directly into the detrusor muscle under cystopic guidance, and can be repeated every 6-12months. NICE (8) recommend the use of botulinum toxin A with OAB when patients have not responded to other conservative treatment options and the patient has been reviewed by a multidisciplinary team (MDT). Patients must be counselled prior to treatment on the risks and benefits, which include the absence of evidence on the duration of effects and the long term efficacy and risks (8). One of the main adverse effects of injecting botulinum toxin A into the bladder is that it can cause paralysis of the detrusor muscle leading to large residual

urines as the bladder is unable to empty fully. Therefore all women who are offered Botox injections must be willing and able to undertake self catheterisation prior to the procedure (8).

Where OAB sypmtoms do not respond to conservative and pharmacological options or injection of botulinum toxin, or where patients areunable to perfrom intermittent self cathetrisation, percutaneous sacral nerve stimulation (P-SNS) can be offered (8). The principle of neurostimulation is that exciting the sacral reflex pathway at the S3 nerve root will inhibit the reflex behaviour of the bladder and so reduce detrusor overactivity.

## Conclusion

Incontinence associated with overactive bladder syndrome is common and can affect the physical, psychological and social well being of individuals. Alongside lifestyle and behavioural modifications, the main treatment option is pharmacological. The revised NICE guidelines provide recommendations for the use of pharmacological treatment.

## References:


1. Andersson KE et al. Pharmacological Treatment of Urinary Incontinence. In: Abrams P., ed. *Incontinence. 4th International Consultation on Incontinence.* Paris: Health Publications Ltd, 2009; pp. 631-700.

2. International Continence Society Fact Sheets: A Background to Urinary and Faecal Incontinence, 2013. *www.ics.org.* [Online]
[Accessed 27th October 2013].

3. Miu D et al. Etiology and predictors of urinary incontinence and its effects on quality of life. *Geriatrics Gerontology International,* Volume 10, 2010; pp. 177-182.

4. National Collaborating Centre for Women's and Children's Health and Women's, National Institute for Health and Clinical Excellence (NICE). *Urinary Incontinence; The Management of Urinary Incontinence in Women.,* London: Royal College of Obstertricians and Gynaecologists Press, 2006.

5. Fowler C et al. The neural control of micturition. *Nat Rev Neuroscience, 2008;* 9(6), pp. 453-466.

6. Abrams, P et al. 2009. *4th International Consultation on Incontinence: Recomendations of the International Scientific Committee: Evalation and Treatment of Urinary Incontinence, Pelvic Organ Prolapse and Faecal Incontinence,* Paris: International Continence Society, 2009.

7. Abrams P et al. The standardisation of terminology in lower urinary tract function: a report from the standardisation sub-comittee of the International Continence Society. *Urology,* Volume 2003; 61, pp. 37-49.

8. National Institute for Health and Care Excellence. *The management of urinary incontinence in women: Clinical guideline 171,* London: National Institute for Health and Care Excellence, 2013.

9. Wyman JF et al. Practical aspects of lifestyle modifications and lifestyle interventions in the treatment of overactive bladder and urgency urinary incontinence. *The International Journal of Clinical Practice, 2009;* Volume 63, pp. 1122-3.

10. Burgio KL. Behavioural treatment options for urinary incontinence. *Gastroenterology, 2004;* Volume 126, pp. S82-9.

11. Robinson, D., and Cardozo, L. Antimuscarinic drugs to treat overactive bladder *British Medical Journal.2012; 344doi: 10.1136/bmj.e2130*

12. Sexton, C.C et al. Persistence and adherence in the treatment of overactive bladder syndrome with anticholinergic therapy: a systematic review the literature. *International Journal of Clinical Practice.* 2011; (65) 567-85

13. Moehrer B et al. Oestrogens for urinary incontinence in women. *Cochrane Database Systematic Review, 2003;* 2(CD001405.).