Understanding the impact of overactive bladder from a patient perspective

Thomas Lackner and Karen Reed

Abstract

Objective: To educate pharmacists about the clinical presentation and treatment of overactive bladder, as well as its far-reaching impact on patient well-being.

Data source: Information presented at the symposium Understanding the Impact of Overactive Bladder from a Patient Perspective, which was presented at APhA2009, the American Pharmacists Association Annual Meeting & Exposition, on April 4, 2009, in San Antonio, TX.

Summary: Overactive bladder is a disruptive and embarrassing disorder that affects an estimated 33 million men and women in the United States. The characteristic symptoms—urgency, frequency, nocturia, and urge incontinence—affect patients’ productivity at home and at work, interfere with social relationships and sexual intimacy, and compromise physical functioning. Treatment that combines lifestyle interventions, behavioral treatments, and pharmacologic therapy with antimuscarinic agents can decrease symptoms and lead to improved quality of life for many patients.

Conclusion: Overactive bladder is a highly prevalent condition that remains both underdiagnosed and undertreated. Pharmacists can make an important contribution to improved management of overactive bladder by identifying patients who have symptoms of overactive bladder, educating them about available nonpharmacologic and pharmacologic therapies, and monitoring therapy to ensure optimal treatment outcomes.

Keywords: Overactive bladder, pharmaceutical care, counseling (patient).


Learning objectives

- Summarize the pathophysiology, clinical presentation, and treatment of overactive bladder.
- Differentiate between overactive bladder and stress incontinence.
- Identify patients who may have undiagnosed or untreated overactive bladder.
- Use effective and appropriate communication techniques to engage patients in discussions about overactive bladder.
- Compare and contrast the impact and management of overactive bladder in older patients and younger patients.

ACPE Activity Type: Application-Based

ACPE Activity Type: Application-Based

www.pharmacytoday.org
Overactive bladder is a symptom-based syndrome defined as urgency, with or without urge incontinence, usually with frequency and nocturia. Although the prevalence of overactive bladder increases markedly with advancing age, it is neither a normal nor an inevitable consequence of aging. Overactive bladder affects all aspects of patients’ lives, including physical, psychological, domestic, social, occupational, and sexual function. Because many patients are too embarrassed to discuss their symptoms, they often attempt to manage or hide them with a variety of elaborate and lifestyle-altering coping mechanisms. Treatment involves a combination of lifestyle interventions, behavioral treatments, and pharmacologic therapy aimed at decreasing bothersome symptoms, preventing possible consequences and complications, and improving the patient’s quality of life. Antimuscarinic agents are the primary pharmacologic therapy for overactive bladder; they are considered efficacious, safe, and well tolerated.

**Analysis:** Pharmacists are ideally positioned to identify and counsel patients with overactive bladder. Recognizing patients who might benefit from treatment is an important initial step. When patients report symptoms consistent with overactive bladder, pharmacists should review the medication profile to identify potentially reversible causes of lower urinary tract symptoms. Pharmacologic therapy with antimuscarinic agents is an option for patients with diagnosed overactive bladder if nonpharmacologic interventions prove to be inadequate for controlling symptoms or if patients express a preference for drug therapy. Patients respond differently to various antimuscarinic agents; thus, no single “best” drug for the treatment of overactive bladder exists. All patients should be educated about the common adverse effects of antimuscarinic agents, the likely delay between initiation of therapy and maximal therapeutic effect, and the need for continual drug administration. Therapy should be modified as needed to achieve an acceptable balance between efficacy and adverse effects. Throughout therapy, pharmacists should be alert for problems that can arise when antimuscarinic agents are used in patients with coexisting conditions such as Alzheimer’s disease, constipation, gastroesophageal reflux disease, osteoporosis, and vision abnormalities.

**Figure 1.** Relationships among overactive bladder and urge, stress, and mixed incontinence

Of overactive bladder in the United States comes from the National Overactive Bladder Evaluation (NOBLE) program, a computer-assisted telephone interview study. In NOBLE, the overall prevalence of overactive bladder was found to be 16.9% in women and 16.0% in men. This translates to approximately 33 million affected adults, which is greater than the number of adults with diabetes and greater than the combined totals for osteoporosis, Alzheimer’s disease, and Parkinson’s disease.

NOBLE also found that the prevalence of overactive bladder increases markedly with advancing age in both men and women. However, the condition is neither a normal nor an inevitable consequence of aging.
Normal bladder function and overactive bladder

Overactive bladder is expensive. The total annual cost associated with overactive bladder is estimated at more than $12 billion; this amount (derived from NOBLE study data) includes the direct costs of routine care and treatment, consequence costs (i.e., costs attributable to complications of overactive bladder, longer hospital stays, and nursing home admissions), and indirect costs (i.e., lost productivity). The total cost of overactive bladder is comparable with the total cost reported for conditions such as osteoporosis and gynecologic and breast cancers. More than 70% of the costs associated with overactive bladder ($9.1 billion) are borne by community-dwelling adults compared with $3.5 billion incurred by institutionalized elderly patients (≥65 years of age).

Normal bladder function and overactive bladder

Normal bladder function in adults involves two discrete processes: (1) bladder filling and storage and (2) bladder emptying. These events alternate in a continuous cycle (the micturition cycle).

The urinary bladder is a hollow, spheroidal organ composed of smooth muscle (the detrusor muscle) and connective tissue. During the filling and storage phase of the micturition cycle, the bladder expands passively to accommodate a continuously increasing volume of urine with little or no change in bladder pressure. When the micturition cycle switches to the bladder emptying phase—at an appropriate time and under voluntary control—a highly coordinated contraction of the detrusor muscle expels urine at high pressure.

Urine passes through the base (neck) of the bladder to the outside of the body via the urethra. During bladder filling, the urethra is held closed by the internal and external urethral sphincters. The internal sphincter is not a true anatomic sphincter; it is an area of involuntary smooth muscle at the junction of the bladder neck and the urethra that operates in concert with supportive structures of the pelvic floor to keep the proximal urethra closed. The external sphincter, in contrast, is a circularly oriented layer of striated skeletal muscle that is under voluntary control. The external sphincter plays an active role in maintaining urinary continence.

The micturition cycle is controlled by a complex system of neural circuits in the brain, spinal cord, and peripheral ganglia. These circuits coordinate the activity of the smooth muscle in the detrusor and internal urethral sphincter with that of the striated muscle in the external urethral sphincter. Bladder filling and storage is under sympathetic control; stimulation of alpha-adrenergic receptors in the bladder neck causes the internal sphincter to contract, while stimulation of beta-adrenergic receptors in the bladder body relaxes the detrusor muscle. Somatic outflow to the external urethral sphincter keeps the sphincter contracted and the urethra closed. Bladder emptying is under parasympathetic control; stimulation of cholinergic receptors initiates a sustained, coordinated contraction of the detrusor muscle and induces relaxation of the internal sphincter. Inhibition of somatic outflow allows the external urinary sphincter to relax, thereby opening the urethra and allowing urine to flow out of the bladder.

Overactive bladder is usually attributed to detrusor overactivity—involuntary detrusor contractions that occur during the bladder filling and storage phase. However, not all patients with overactive bladder have evidence of detrusor overactivity during urodynamic testing. The causes of overactive bladder are likely multifactorial.

Overactive bladder versus stress incontinence

Patients with stress incontinence experience small amounts of urine leakage during sudden increases in intraabdominal pressure, such as those that occur with coughing, laughing, sneezing, exercise, or other physical exertion. In contrast to urge incontinence, stress incontinence is not the direct result of bladder dysfunction; instead, urine leakage occurs because the urethral sphincteric mechanisms do not remain tightly closed when bladder pressure exceeds urethral pressure. Stress incontinence usually reflects weakness of, or some degree of damage to, the urethra, sphincters, or muscles, nerves, and connective tissue of the pelvic floor. The distinguishing features of overactive bladder and stress incontinence are listed in Table 1.

Stress incontinence affects as many as 40% of women, with a peak incidence between 45 and 49 years of age. Common risk factors include pregnancy and vaginal delivery, pelvic surgery, and chronic abdominal straining (e.g., chronic constipation). Obese women (body mass index ≥ 30 kg/m²) are twice as likely to develop stress incontinence as normal-weight women. Decreasing estrogen levels at menopause and pelvic organ prolapse may contribute to stress incontinence in middle-aged women.

Stress incontinence also occurs in men, most commonly after prostatic surgery (particularly radical prostatectomy) that causes injury to the urethral sphincteric mechanisms.

Overactive bladder versus benign prostatic hyperplasia

In men, symptoms of urgency, frequency, and nocturia may be related to overactive bladder or benign prostatic hyperplasia. Symptoms related to benign prostatic hyperplasia occur when the enlarged prostate presses on the bladder neck and obstructs the urethra; the resulting increase in urethral resistance causes compensatory changes in bladder function. Approximately 50% of men with some type of prostatic obstruction also have detrusor overactivity.
Overactive bladder: patient perspective

Prostatic obstruction in prostatic hyperplasia also produces voiding symptoms such as hesitancy, straining, a slow or intermittent urine stream, and a feeling of incomplete bladder emptying. Patients may develop urinary retention with subsequent overflow incontinence (the term used to describe leakage of urine associated with urinary retention).

Consequences and complications of overactive bladder

Left untreated or treated inadequately, overactive bladder can lead to a number of adverse consequences and complications. In NOBLE, patients with overactive bladder reported considerably more urinary tract infections and a greater risk of being injured in a fall than age- and sex-matched control patients. In another study that included more than 6,000 older women, participants who experienced urge incontinence at least once per week had a 26% increase in the risk of falls and a 34% increase in the risk of fractures. Patients typically are injured as they hurry to reach the toilet (especially during the nighttime) or because they slip on a puddle of urine.

Incontinent patients may experience skin problems ranging from irritation to pressure ulcers. Incontinence-associated dermatitis is an inflammatory condition that occurs when urine comes into contact with skin, particularly when incontinence products are used to manage urine leakage. Excessive moisture makes the skin more susceptible to overgrowth by organisms such as Candida albicans or Staphylococcus species, which can lead to skin breakdown and infection.

Dehydration is a possible consequence of inadequate fluid intake. Patients with overactive bladder may deliberately restrict their consumption of fluids in a misguided attempt to reduce or control their symptoms. Although taking in smaller amounts of liquid does decrease the amount of urine in the bladder, that urine may be highly concentrated and irritating and can subsequently exacerbate symptoms of urgency and frequency. Dehydration also predisposes patients to urinary tract infections and is a recognized cause of transient (reversible) incontinence.

Nocturia can contribute to disturbed sleep in patients and their partners. Patients with nocturia report both a lack of energy and chronic fatigue.

Effect of overactive bladder on patients

Patients with overactive bladder have a considerably poorer quality of life than age-matched populations. All aspects of patients’ lives are affected, including physical, psychological, domestic, social, occupational, and sexual function.

Several studies have identified urgency as the most bothersome symptom of overactive bladder. The unpredictable and uncontrollable nature of urgency episodes, coupled with the fear of urine loss, compel many patients to limit or abandon activities they have enjoyed for much of their lives, such as shopping, playing sports, traveling, dining out, or attending movies or religious services. As a result, patients can become socially isolated and may be reluctant to leave their homes.

“What’s the cost to patients? They put their lives on hold, that’s what happens.”

Karen Reed

In some patients, urgency or urge incontinence can become a conditioned reflex that is triggered by certain events. For example, “key-in-the-lock syndrome” is a term applied to symptoms that occur when patients approach the door to their home. Other common triggers include the sound of running water, seeing a bathroom sign, and washing dishes or clothes.

The symptoms of overactive bladder take their toll on family members and lead to strained relationships. In a recent study of the impact of overactive bladder on family members, a variety of frustrations became evident in the comments made by participants. Examples include:

- “She had to stop to go to the bathroom every 15 minutes. And she’d go and then she’d have to go right again. It’s annoying to stop and wait for her to go to the bathroom every 15 minutes.”
- “Another thing is when if you have a kid, especially a little boy who wants to play ball with his dad, and dad has to keep going to the bathroom. ... At first, his father was into activities with his son, but since this problem he hasn’t been. It interrupts family day.”

Many patients attempt to manage or hide their overactive bladder symptoms with a variety of elaborate and lifestyle-altering coping mechanisms. For example, patients may become preoccupied with “toilet mapping”: immediately searching out...
OVERACTIVE BLADDER: PATIENT PERSPECTIVE

Table 2. Examples of coping mechanisms commonly adopted by patients with overactive bladder

<table>
<thead>
<tr>
<th>Coping Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediately searching out restrooms when in a new place, or locating toilets in advance of travel (“toilet mapping”)</td>
</tr>
<tr>
<td>Limiting daily travel to places and routes where the locations of nearby restrooms are known</td>
</tr>
<tr>
<td>Urinating frequently to stay “in control” (defensive voiding)</td>
</tr>
<tr>
<td>Sitting closest to the door for easier access to the restroom</td>
</tr>
<tr>
<td>Sitting on the aisle at the theater and on planes to have easier access to the restroom</td>
</tr>
<tr>
<td>Drinking less fluid</td>
</tr>
<tr>
<td>Limiting fluid intake in the evenings</td>
</tr>
<tr>
<td>Limiting social, physical, and outdoor activities</td>
</tr>
<tr>
<td>Avoiding sexual intimacy</td>
</tr>
<tr>
<td>Wearing absorbent products (e.g., adult incontinence pads or diapers)</td>
</tr>
<tr>
<td>Carrying extra clothes and absorbent products in case of a wetting accident</td>
</tr>
<tr>
<td>Wearing dark, baggy clothing to hide wet spots or conceal absorbent products</td>
</tr>
</tbody>
</table>

Identifying patients with overactive bladder

Health care providers, including pharmacists, typically do not ask patients about lower urinary tract problems. One survey that investigated coping strategies and health care seeking in adults with overactive bladder found that it was the patient who initiated the topic of urinary problems in 90% of discussions between a patient and a health care provider. Even when patients do bring up the subject, as many as 30% receive no assessment of their symptoms and the majority (80%) are not treated.

Reality check

Patients aren’t the only ones who are reluctant to discuss bladder control problems. Polling questions posed to symposium participants revealed the following:

- 48% of participants would feel uncomfortable raising bladder control issues with patients.
- 78% of participants would wait for a patient to ask them about bladder control problems—they would not initiate the conversation.
- 40% of participants would be uncomfortable approaching a patient who was looking at incontinence products to ask about bladder control issues.

Community pharmacists are ideally positioned to identify patients who may have undiagnosed or untreated overactive bladder. Pharmacists should pay particular attention to patients who may have undiagnosed or untreated overactive bladder. Examples of questions that help to elicit information about symptoms of urgency, frequency, urge incontinence, and stress incontinence, as well as possible contributing factors, are presented in Table 3. Patients who report symptoms consistent with overactive bladder should be encouraged to express their concerns to a primary care provider; a complete diagnostic evaluation is needed to rule out other potential causes.

“If a health care provider won’t help a patient with suspected overactive bladder, the patient may need to think about finding a new provider. I’ve said that many times to my patients with diabetes—we also need to say it to patients about their overactive bladder.”

Karen Reed

Despite their impaired quality of life, an estimated 40% of patients with overactive bladder do not mention their symptoms to their health care provider. Possible reasons for this reticence include:

- Embarrassment.
- The belief that symptoms are a normal part of aging.
- The belief that symptoms are self-limiting or too “mild” to warrant treatment.
- A lack of awareness of available treatments.
- The perception that available treatments are not effective or cause too many adverse effects.
- Concern about possible high costs of treatment.

-toilets in new locations or identifying bathroom facilities in advance of travel (e.g., by visiting websites such as www.thebathroomdiaries.com). Other common coping strategies are listed in Table 2.

Overactive bladder poses particular problems for patients who are still in the workforce, especially patients who cannot access the bathroom “at will” (e.g., teachers, factory workers). Patients often harbor concerns about the myriad implications of their symptoms for job seeking and job performance. Disturbed sleep from nocturia can affect daytime functioning and work productivity. Patients may dread having to walk past colleagues on their frequent trips to the restroom. Women with urge incontinence have reported using disposable items not intended for urine control (e.g., sanitary napkins, panty liners, tissues) to hide their condition.

The psychological toll of overactive bladder can be severe, as patients struggle to cope with feelings of embarrassment, shame, annoyance, guilt, and apathy. Anxiety and depression are common among patients with overactive bladder. Patients also report having low self-esteem, feeling unattractive, perceiving themselves as a burden to caregivers, and fearing that they smell of urine. Some patients simply deny that they have a problem.

Despite their impaired quality of life, an estimated 40% of patients with overactive bladder do not mention their symptoms to their health care provider. Possible reasons for this reticence include:

- Embarrassment.
- The belief that symptoms are a normal part of aging.
- The belief that symptoms are self-limiting or too “mild” to warrant treatment.
- A lack of awareness of available treatments.
- The perception that available treatments are not effective or cause too many adverse effects.
- Concern about possible high costs of treatment.

Despite their impaired quality of life, an estimated 40% of patients with overactive bladder do not mention their symptoms to their health care provider. Possible reasons for this reticence include:

- Embarrassment.
- The belief that symptoms are a normal part of aging.
- The belief that symptoms are self-limiting or too “mild” to warrant treatment.
- A lack of awareness of available treatments.
- The perception that available treatments are not effective or cause too many adverse effects.
- Concern about possible high costs of treatment.

If a health care provider won’t help [a patient with suspected overactive bladder], the patient may need to think about finding a new provider. I’ve said that many times to my patients with diabetes—we also need to say it to patients about their overactive bladder.”

Karen Reed
Creating a dialogue with patients

Symposium speaker Karen Reed offered the following suggestions for improving communications with patients who are coping with overactive bladder:

- Make sure your patients “know their pharmacist.” The theme of American Pharmacists Month is “Know Your Medicine, Know Your Pharmacist.” Patients know their hairdresser, they know their doctor, and they know their mechanic. If they don’t know you, they are not going to talk about their overactive bladder. You have to come out from behind that counter and introduce yourself—let patients know your name—and cultivate a relationship with the patient. It will be a relationship you will never regret.

- Consider offering medication therapy management (MTM) services. Patients realize four important benefits from MTM services: (1) a clear understanding of their medications; (2) a thorough review of all their medications, including their dietary supplements, herbal remedies, vitamins, minerals, and natural products; (3) a personal medication record; and (4) a medication-related action plan. Through MTM services, you can help patients get started on becoming active participants in their care. The MTM interaction also provides a perfect opportunity for patients to open up to you in a private environment and talk about overactive bladder.

- Seize opportunities to ask patients about bladder problems. By asking the right questions, you’ll find out whether the patient has a problem with overactive bladder. When counseling a patient about prescription or nonprescription medications, consider asking, “Are you ever wet?” Plain and simple. You might think, “I couldn’t ask somebody that”—but it isn’t that difficult. If you just ask them, they will answer you.

### Table 3. Sample questions for evaluating overactive bladder and incontinence

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you get sudden urges to go to the bathroom that are so strong you can’t ignore them?</td>
<td>How often do you go to the bathroom?</td>
</tr>
<tr>
<td>How often do you go to the bathroom?</td>
<td>Do you avoid places that you think won’t have a nearby restroom?</td>
</tr>
<tr>
<td>When you’re in an unfamiliar place, do you make sure you know where the restroom is?</td>
<td>Do you ever have to get up at night to go to the bathroom? How frequently?</td>
</tr>
<tr>
<td>Do you leak urine when you cough, sneeze, or stand?</td>
<td>Do you leak urine on the way to the bathroom?</td>
</tr>
<tr>
<td>How much water and other beverages do you drink during the day? What kinds of beverages?</td>
<td>How often do you have an “accident”? When you have an “accident,” is it a small or large amount?</td>
</tr>
<tr>
<td>Do you currently use any products, such as pads, diapers, or undergarments, for protection?</td>
<td>How often do you go to the bathroom?</td>
</tr>
<tr>
<td>How often do you have an “accident”? When you have an “accident,” is it a small or large amount?</td>
<td>How much of a bother are your symptoms to you?</td>
</tr>
</tbody>
</table>

### Table 4. DRIP mnemonic for reversible causes of incontinence

| D: Dehydration, delirium, depression, dietary factors |
| R: Renal failure, restricted mobility, retention (urinary retention) |
| I: Infection (urinary tract, prostate), inflammation (atrophy vaginitis/urethritis), impaction (fecal) |
| P: Pharmaceuticals, polyuria (hyperglycemia, hypercalcemia, peripheral edema) |

By definition, a person is not considered to have overactive bladder until other possible causes and pathologies have been excluded. Some patients who report episodes of incontinence may be experiencing transient incontinence from potentially reversible or ameliorable conditions or factors. The mnemonic DRIP (Table 4) aids in recalling common causes of transient incontinence. Pharmacists should be aware that a wide variety of drugs can affect urinary function; cholinesterase inhibitors, diuretics, lithium, and drugs that cause peripheral edema (e.g., nonsteroidal anti-inflammatory drugs, thiazolidinediones) are most likely to precipitate urgency and frequency.

### Treatment

The goals of treatment for overactive bladder are multifold. Primary goals are to decrease bothersome symptoms, prevent possible consequences and complications, and improve the patient’s quality of life. Ideally, these goals are achieved in the most cost-effective manner possible for the patient while avoiding adverse effects of therapy.

Treatment options for overactive bladder encompass lifestyle interventions, behavioral treatments, and pharmacologic therapy. Pharmacologic agents are considered to be an adjunct to, rather than a replacement for, nonpharmacologic approaches.

### Lifestyle interventions

Substances that irritate the bladder lining could contribute to symptoms of urgency and frequency. Thus, a common strategy for managing overactive bladder is to reduce or eliminate potential bladder irritants from the diet. These include caffeine, carbonated beverages, acidic fruits and juices (e.g., citrus, tomato), highly spicy foods, and artificial sweeteners (particularly aspartame). Caffeine and alcohol have diuretic effects that can lead to increased frequency.

A normal fluid intake—approximately 48 to 64 fl oz/day—is recommended for most patients with overactive bladder. Patients with nocturia usually benefit from modifying the timing of fluid intake (e.g., limiting fluid intake 2 to 3 hours before bedtime).

Weight reduction can improve both urge incontinence and stress incontinence in patients who are overweight. Because smoking is believed to contribute to stress incontinence (through chronic coughing) and urgency (through the effects of nicotine on the bladder), smoking cessation is advised for patients who smoke.
Environmental interventions can help to protect patients from falls. Examples include arranging furniture to ensure an unobstructed pathway to the bathroom and installing nightlights in the homes of patients with nocturia.

Behavioral treatments

Behavioral treatments are recommended as first-line therapy for overactive bladder. Key techniques with which pharmacists should be familiar are timed (or scheduled) voiding, bladder training, and pelvic floor muscle training.

Timed voiding involves having the patient void on a fixed schedule (e.g., every 2 hours) during waking hours, regardless of whether the patient senses the need to void. It is a passive intervention that seeks to circumvent episodes of incontinence with frequent bladder emptying. Timed toileting is used most commonly in long-term care settings or for patients who have impaired mobility or cognition.

Bladder training (also known as bladder retraining) is an active intervention that incorporates patient education, a timed toileting regimen with gradual increases in the time between voids, and urge inhibition techniques that help the patient suppress the initial urge to void. The initial scheduled interval between voids is very short, usually only about 1 hour. Patients use urge inhibition techniques if they feel the need to void between scheduled voids. The initial interval is increased by 15 to 30 minutes each week until the patient achieves a more normal pattern of voiding every 3 to 4 hours.

Pelvic floor muscle training consists of repetitive, episodic contractions of the pelvic floor muscles (i.e., Kegel exercises) performed over time. This technique seeks to enhance the patient’s ability to control urinary urgency and inhibit detrusor contractions by increasing the strength, bulk, and function of the pelvic floor muscles. Pelvic floor muscle training also is an important strategy for managing stress incontinence. Because patients often have a difficult time identifying and isolating the correct muscles, pelvic floor muscle training should be taught by a qualified health professional. Many patients benefit from biofeedback-assisted training.

Pharmacologic therapy

Antimuscarinic agents are the primary pharmacologic therapy for overactive bladder. The highly coordinated contraction of the detrusor muscle that occurs during the bladder emptying phase of the micturition cycle is mediated by the neurotransmitter acetylcholine. Antimuscarinic agents exert their effects primarily by preventing acetylcholine from binding to M2 and M3 muscarinic receptors in the bladder wall. Through this and possible additional mechanisms, antimuscarinic agents reduce detrusor activity and improve bladder capacity.

A recent systematic review and meta-analysis concluded that antimuscarinic agents are efficacious, safe, and well tolerated treatments for overactive bladder. Data were extracted from 83 trials involving more than 30,000 patients. Meta-analysis revealed moderate but important improvements compared with placebo in the following measures:

- Number of incontinence episodes per day (0.4–1.1 fewer episodes).
- Number of micturitions per day (0.5–1.3 fewer micturitions).
- Number of urgency episodes per day (0.64–1.56 fewer episodes).
- Volume voided per micturition (13–40 mL more volume).

Some patients with incontinence returned to continence by the endpoint of each study.

In terms of efficacy, no “best” agent for the treatment of overactive bladder exists. The currently available antimuscarinic agents (Table 5) are considered clinically equivalent, with similar efficacy at the most commonly prescribed doses. Individual patient response to antimuscarinic agents is highly variable; successive trials with different agents may be required to maximize effectiveness.

Although some patients may begin to see improvements in their symptoms as early as the first week after treatment is initiated, the full benefits of antimuscarinic therapy may not be realized for several weeks. Patients should be educated about this possible delay to ensure that unrealistic treatment expectations do not lead to nonadherence, especially because adverse effects may be experienced soon after therapy is initiated.

Maximizing antimuscarinic therapy for overactive bladder often involves striking a tolerable balance between symptom relief and adverse effects. Mucaric receptors are located throughout the body; because antimuscarinic agents are not selective for receptors in the bladder, they produce classic anticholinergic effects such as dry mouth, constipation, and blurred vision. Dry mouth is the most frequently reported adverse effect, affecting up to two-thirds of patients in some clinical trials. In some cases, dry mouth is so severe that patients describe having to use their fingers to pull their tongue off the roof of their mouth.

“If I were a patient taking [an antimuscarinic agent] and all that was happening was that I was having side effects, my first inclination would be, ‘This isn’t worth it. I’m going to stop the drug.’ Patients need to be informed that these drugs don’t always work right away and the maximal effect could take up to a few weeks or so.”

Thomas Lackner

Most of the antimuscarinic agents used for the treatment of overactive bladder are available as immediate or extended release tablets or capsules (Table 5). The extended release formulations generally are associated with lower rates of adverse effects. Oxybutynin also is available in transdermal gel and patch formulations. Oxybutynin undergoes extensive first-pass metabolism to N-desmethyl oxybutynin, an active metabolite that circulates at concentrations approximately 4 to 10 times greater than those of the parent compound. The metabolite is believed to contribute heavily to the high rate of adverse effects seen with immediate release oxybutynin. Transdermal administration of oxybutynin avoids this first-pass metabolism and results in substantially lower plasma concentrations of the active metabolite, which in turn yield substantially lower rates of
anticholinergic adverse effects. However, the patch can cause application-site reactions (e.g., pruritus, erythema) severe enough to require discontinuation of therapy; the gel formulation appears to offer improved skin tolerability.

Although the available antimuscarinic agents are considered to be clinically equivalent, they do differ from one another in chemical structure, molecular weight, lipophilicity, molecular charge, and other variables that affect drug activity and safety. Most antimuscarinic agents are tertiary amines; trospium is a quaternary amine. The tertiary amines are metabolized by the cytochrome P450 (CYP) system, primarily isoenzymes CYP2D6 and CYP3A4. As shown in Table 5, dosage adjustments generally are recommended when tertiary amines are administered concurrently with potent inhibitors of CYP3A4 such as antifungals (e.g., ketoconazole, itraconazole, miconazole) and macrolide antibiotics (e.g., erythromycin, clarithromycin).

Because the tertiary amines are metabolized in both the liver and kidneys, dosage reductions are recommended in patients with impaired hepatic or renal function (Table 5). The use of extended release trospium is not advised in patients with severe renal impairment because trospium is eliminated largely unchanged through the kidneys.

There is increasing concern about possible detrimental central nervous system effects during antimuscarinic therapy, such as dizziness, cognitive dysfunction (including memory loss), sleep disturbances, and delirium. These effects are of particular concern in older patients and may contribute to the widespread belief that antimuscarinic agents are underused in that patient population. For an agent to cause central nervous system effects, it must cross the blood–brain barrier. Darifenacin, oxybutynin, solifenacin, and tolterodine all possess characteristics that allow for drug passage into the brain: high lipophilicity, low molecular weight, and a low to moderate number of positively charged molecules. Oxybutynin should be especially likely to cross the blood–brain barrier. In contrast, trospium should be least likely to cross the blood–brain barrier because it is hydrophilic and has both a high molecular weight and high positive charge. Whether these differences in

Table 5. Antimuscarinic agents used in the treatment of overactive bladder

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Trade name</th>
<th>Dosage form (available strengths)</th>
<th>Usual dosage</th>
<th>Hepatic impairment</th>
<th>Renal impairment</th>
<th>Potent CYP3A4 inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darifenacin</td>
<td>Enablex</td>
<td>Extended release tablets (7.5 mg, 15 mg)</td>
<td>7.5–15 mg once daily</td>
<td>Moderate: 7.5 mg once daily</td>
<td>None</td>
<td>7.5 mg once daily</td>
</tr>
<tr>
<td>Fesoterodine</td>
<td>Toviaz</td>
<td>Extended release tablets (4 mg, 8 mg)</td>
<td>4–8 mg once daily</td>
<td>Severe: do not use</td>
<td>4 mg once daily</td>
<td>4 mg once daily</td>
</tr>
<tr>
<td>Oxybutynin</td>
<td>Ditropan</td>
<td>Immediate release tablets (5 mg)</td>
<td>5 mg two to four times daily</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Ditropan XL</td>
<td>Extended release tablets (5 mg, 10 mg, 15 mg)</td>
<td>5–30 mg once daily</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Oxytrol</td>
<td>Transdermal system (36 mg)</td>
<td>One patch applied twice weekly (every 3 to 4 days)(^b)</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Gelnique</td>
<td>Topical gel (10%)</td>
<td>1 g (1.14 mL) of 100 mg/g gel applied once daily to the thigh, abdomen, or upper arm/shoulder</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Solifenacin</td>
<td>VESIcare</td>
<td>Extended release tablets (5 mg, 10 mg)</td>
<td>5–10 mg once daily</td>
<td>5 mg once daily</td>
<td>5 mg once daily</td>
<td>5 mg once daily</td>
</tr>
<tr>
<td>Tolterodine</td>
<td>Detrol</td>
<td>Immediate release tablets (1 mg, 2 mg)</td>
<td>1–2 mg twice daily</td>
<td>Severe: 1 mg once daily</td>
<td>1 mg once daily</td>
<td>1 mg once daily</td>
</tr>
<tr>
<td></td>
<td>Detrol LA</td>
<td>Extended release capsules (2 mg, 4 mg)</td>
<td>2–4 mg once daily</td>
<td>Severe: 2 mg once daily</td>
<td>2 mg once daily</td>
<td>2 mg once daily</td>
</tr>
<tr>
<td>Trosplum</td>
<td>Sanctura</td>
<td>Immediate release tablets (20 mg)</td>
<td>20 mg twice daily 1 hour before meals(^c)</td>
<td>None</td>
<td>20 mg once daily at bedtime(^a)</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Sanctura XR</td>
<td>Extended release capsules (60 mg)</td>
<td>60 mg once daily in the morning, 1 hour before meal</td>
<td>Severe: use with caution</td>
<td>Do not use(^a)</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviation used: CYP, cytochrome P450.

\(^a\)Creatinine clearance <30 mL/minute.
\(^b\)Each patch delivers oxybutynin 3.9 mg/day.
\(^c\)A dosage of 20 mg once daily may be considered in patients ≥75 years of age if twice-daily administration is not tolerated.
molecular characteristics translate into clinically meaningful differences in adverse effects requires additional study. In one recent randomized, double-blind, placebo-controlled trial, 4 weeks of treatment with oral extended release oxybutynin 5 mg once daily did not impair cognition or cause delirium in older female nursing home residents with urge incontinence and mild to severe cognitive impairment.

Pharmacists should be aware of some potentially serious problems that can arise when antimuscarinic agents are used in patients with coexisting disease states. Examples of patient groups that might be affected include

- **Patients with or at risk for osteoporosis who are being treated with oral bisphosphonates.** Antimuscarinic therapy decreases saliva production and reduces the amount of saliva that flows down the esophagus with swallowing. These effects may increase the risk of bisphosphonate-induced esophageal ulceration.

- **Patients with gastroesophageal reflux disease (GERD).** Because bicarbonate in swallowed saliva helps to neutralize acid in refluxed material, decreased production of saliva secondary to antimuscarinic therapy may exacerbate reflux symptoms. Diminished salivation also can prolong the amount of time that the esophagus is exposed to refluxed acid. Antimuscarinic agents can delay gastric emptying, which may contribute to GERD symptoms; this effect is of greatest concern in patients with uncontrolled acid reflux symptoms or complicated disease.

- **Patients with dementia who are being treated with cholinesterase inhibitors or memantine.** Antimuscarinic agents directly antagonize the pharmacologic effect of cholinesterase inhibitors and memantine. Thus, concurrent use may dilute the benefits of both types of drugs. In clinical practice, an antimuscarinic agent may be prescribed to treat new-onset or worsening urinary incontinence in a patient already being treated with a cholinesterase inhibitor or memantine. However, incontinence is a possible adverse effect of both cholinesterase inhibitors and memantine; a safer initial approach is to reduce the dose of those agents when possible.

- **Patients with constipation.** Antimuscarinic agents can worsen existing constipation through both direct and indirect effects. An example of an indirect effect is the patient who loses interest in eating because of dry mouth. Patients may not produce sufficient saliva to break food down into components that interact with the taste buds; as a result, food does not taste as good and becomes less appealing.

- **Patients with vision abnormalities.** Blurred vision is a common adverse effect of antimuscarinic agents. Antimuscarinic therapy is contraindicated in patients with uncontrolled narrow-angle glaucoma. Pharmacists should pay close attention to a patient’s overall anticholinergic load (i.e., the possible additive response from multiple agents with anticholinergic effects). A greater anticholinergic load can result in a greater incidence of adverse effects, including a higher risk of cognitive dysfunction and delirium in older patients. One approach to estimating a patient’s anticholinergic load is the anticholinergic risk scale (ARS)—a categorical list that ranks the anticholinergic potential of commonly prescribed medications on a 3-point Likert-type scale (0, no or low risk; 3, high anticholinergic potential). The ARS score is the sum of points for all medications used by the patient. The anticholinergic drug scale is a similar measure for assessing medication-related anticholinergic burden.

Antimuscarinic therapy usually must be continued indefinitely. Although limited evidence indicates that patients with well controlled symptoms might be able to taper their medication dose or even have extended drug holidays, the data are insufficient to support those recommendations. Pharmacists should make a special effort to counsel patients about the need for ongoing adherence. In particular, pharmacists should watch for patients who use antimuscarinic agents solely on an as-needed basis (e.g., before social events or long journeys) in the mistaken belief that such use is adequate and effective.

**“I wish I had a dollar for every patient who’s told me she takes her [antimuscarinic agent] before she goes out for lunch with her daughter. It doesn’t work that way, now, does it?”**

Karen Reed

**Conclusion**

Overactive bladder is a highly prevalent and disruptive disorder. Pharmacists can contribute to improved patient outcomes by identifying potentially reversible causes of lower urinary tract symptoms and recommending and monitoring drug therapy. Pharmacologic therapy with antimuscarinic agents is an option when nonpharmacologic interventions prove to be inadequate for controlling symptoms or when patients express a preference for drug therapy. Patients respond differently to the various antimuscarinic agents; thus, there is no single “best” drug for the treatment of overactive bladder exists. After efficacy, considerations for selecting a specific agent include the potential for adverse effects, patient convenience, and cost. Therapy should be modified as needed to achieve an acceptable balance between efficacy and adverse effects.

**References**


Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract symptoms and recommending and monitoring drug therapy. Pharmacologic therapy with antimuscarinic agents is an option when nonpharmacologic interventions prove to be inadequate for controlling symptoms or when patients express a preference for drug therapy. Patients respond differently to the various antimuscarinic agents; thus, there is no single “best” drug for the treatment of overactive bladder exists. After efficacy, considerations for selecting a specific agent include the potential for adverse effects, patient convenience, and cost. Therapy should be modified as needed to achieve an acceptable balance between efficacy and adverse effects.

**References**


Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract symptoms and recommending and monitoring drug therapy. Pharmacologic therapy with antimuscarinic agents is an option when nonpharmacologic interventions prove to be inadequate for controlling symptoms or when patients express a preference for drug therapy. Patients respond differently to the various antimuscarinic agents; thus, there is no single “best” drug for the treatment of overactive bladder exists. After efficacy, considerations for selecting a specific agent include the potential for adverse effects, patient convenience, and cost. Therapy should be modified as needed to achieve an acceptable balance between efficacy and adverse effects.

**References**


Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract symptoms and recommending and monitoring drug therapy. Pharmacologic therapy with antimuscarinic agents is an option when nonpharmacologic interventions prove to be inadequate for controlling symptoms or when patients express a preference for drug therapy. Patients respond differently to the various antimuscarinic agents; thus, there is no single “best” drug for the treatment of overactive bladder exists. After efficacy, considerations for selecting a specific agent include the potential for adverse effects, patient convenience, and cost. Therapy should be modified as needed to achieve an acceptable balance between efficacy and adverse effects.

**References**


Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract symptoms and recommending and monitoring drug therapy. Pharmacologic therapy with antimuscarinic agents is an option when nonpharmacologic interventions prove to be inadequate for controlling symptoms or when patients express a preference for drug therapy. Patients respond differently to the various antimuscarinic agents; thus, there is no single “best” drug for the treatment of overactive bladder exists. After efficacy, considerations for selecting a specific agent include the potential for adverse effects, patient convenience, and cost. Therapy should be modified as needed to achieve an acceptable balance between efficacy and adverse effects.

**References**


Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract symptoms and recommending and monitoring drug therapy. Pharmacologic therapy with antimuscarinic agents is an option when nonpharmacologic interventions prove to be inadequate for controlling symptoms or when patients express a preference for drug therapy. Patients respond differently to the various antimuscarinic agents; thus, there is no single “best” drug for the treatment of overactive bladder exists. After efficacy, considerations for selecting a specific agent include the potential for adverse effects, patient convenience, and cost. Therapy should be modified as needed to achieve an acceptable balance between efficacy and adverse effects.

**References**


Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract symptoms and recommending and monitoring drug therapy. Pharmacologic therapy with antimuscarinic agents is an option when nonpharmacologic interventions prove to be inadequate for controlling symptoms or when patients express a preference for drug therapy. Patients respond differently to the various antimuscarinic agents; thus, there is no single “best” drug for the treatment of overactive bladder exists. After efficacy, considerations for selecting a specific agent include the potential for adverse effects, patient convenience, and cost. Therapy should be modified as needed to achieve an acceptable balance between efficacy and adverse effects.

**References**


CPE Credit:
To obtain 2.0 contact hours of continuing pharmacy education credit (0.2 CEUs) for “Understanding the impact of overactive bladder from a patient perspective,” go to www.pharmacist.com and take your test online for instant credit. CPE processing is free. A Statement of Credit will be awarded for a passing grade of 70% or better. You have two opportunities to successfully complete the posttest. Pharmacists who complete this exercise successfully before April 4, 2012, can receive credit.

The American Pharmacists Association is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. The ACPE Universal Activity Number assigned to the program by the accredited provider is 202-000-09-114-H01-P.

Participants in the live version of this activity, “Understanding the impact of overactive bladder from a patient perspective,” which was presented at APhA2009, the American Pharmacists Association Annual Meeting & Exposition, on April 4, 2009, are not eligible for CPE credit for this home-study activity.

“Understanding the impact of overactive bladder from a patient perspective” is a home-study continuing education activity for pharmacists developed by the American Pharmacists Association and supported by an independent educational grant from Pfizer, Inc.
Assessment Questions

Instructions: The assessment test for this activity must be taken online; please see “CPE Processing” below for further instructions. There is only one correct answer to each question. This CPE will be available online at www.pharmacist.com/education no later than June 15, 2009.

1. Which of the following represents a sudden, compelling desire to pass urine that is difficult to defer?
   a. Urge
   b. Urgency
   c. Frequency
   d. Urge incontinence

2. Patients may be considered to experience frequency if they void more than how many times per day?
   a. 4
   b. 6
   c. 8
   d. 10

3. Approximately what percentage of patients with overactive bladder experience urge incontinence?
   a. 25%
   b. 33%
   c. 50%
   d. 90%

4. The prevalence of overactive bladder is:
   a. Substantially higher in women than in men.
   b. About the same in men and women.
   c. Substantially higher in men than in women.
   d. Not known at this time.

5. What is the percentage of patients with overactive bladder who are between 35 and 65 years of age?
   a. 10%
   b. 25%
   c. 33%
   d. 50%

6. Contraction of the detrusor muscle is caused by
   a. Parasympathetic stimulation of cholinergic receptors.
   b. Somatic outflow to the detrusor muscle.
   d. Sympathetic stimulation of beta-adrenergic receptors.

7. Overactive bladder usually is caused by:
   a. Detrusor overactivity.
   b. Detrusor underactivity.
   c. Overactive urethra.
   d. Underactive urethra.

8. A patient who complains of leaking small amounts of urine when she coughs or sneezes is most likely experiencing:
   a. Overactive bladder with urge incontinence
   b. Stress incontinence
   c. Overflow incontinence
   d. Mixed incontinence

9. Which of the following is not recognized as a possible consequence of overactive bladder?
   a. Bladder cancer
   b. Dermatitis
   c. Falls and fractures
   d. Sleep disturbances

10. Which symptom usually is identified by patients with overactive bladder as most bothersome?
    a. Frequency
    b. Nocturia
    c. Urge incontinence
    d. Urgency

11. Which of the following questions is most likely to identify a patient who experiences urgency?
    a. How often do you go to the bathroom?
    b. Do you leak urine on the way to the bathroom?
    c. Do you get sudden urges to go to the bathroom that are so strong you can’t ignore them?
    d. Do you leak when you cough, sneeze, or stand?

12. Lifestyle interventions for patients with overactive bladder may include all of the following except
    a. Avoiding bladder irritants (e.g., acidic fruits and juices).
    b. Drinking as little fluid as possible.
    c. Losing weight.
    d. Stopping smoking.

13. The primary pharmacologic agents for the treatment of overactive bladder are
    a. Alpha-adrenergic agonists.
    b. Antimuscarinic agents.
    c. Topical estrogens.
    d. Tricyclic antidepressants.
14. Which of the following agents is most likely to cause dry mouth?
   a. Darifenacin
   b. Immediate release oxybutynin
   c. Extended release tolterodine
   d. Solifenacin

15. Which of the following agents is considered to be least likely to cross the blood–brain barrier?
   a. Fesoterodine
   b. Oxybutynin
   c. Tolterodine
   d. Trosipium

16. Antimuscarinic agents directly oppose the pharmacologic effect of which of the following medications?
   a. Alpha-adrenergic agonists
   b. Bisphosphonates
   c. Cholinesterase inhibitors
   d. Histamine H₂-receptor antagonists

The following case applies to questions 17 through 20:
You notice E.W., a 75-year-old black woman, hovering near the pharmacy counter. She waits until several other patients leave and no one else is around, then approaches you somewhat timidly. She asks quietly, “What do you think is the best pad to buy for wetting accidents?” As you start to talk with E.W., you learn that she has not discussed her urinary incontinence with her physician. In answer to your questions, E.W. reports voiding 14 to 17 times per day and 2 to 3 times during the night. She needs to void 1 to 2 minutes after awareness of the urge to urinate and is then immediately incontinent; she loses large amounts of urine. E.W. drinks 11 to 12 cups of fluid per day, including 4 cups of caffeinated coffee and tea. She denies problems with leakage when she coughs or sneezes.

Medications: Amlodipine 10 mg once daily, celecoxib 200 mg as needed, omeprazole 20 mg before breakfast, risedronate 35 mg once per week, spironolactone 50 mg once daily, multivitamin once daily

Comorbidities: Hypertension, hypokalemia, osteoporosis, osteoarthritis, gastroesophageal reflux disease

17. What is E.W.’s most likely diagnosis?
   a. Overactive bladder with urge incontinence
   b. Stress incontinence
   c. Mixed incontinence (urge plus stress incontinence)
   d. Transient incontinence

18. Which (if any) of E.W.’s medications could be contributing to her symptoms?
   a. Celecoxib
   b. Multivitamin
   c. Risedronate
   d. Spironolactone

19. Which of the following recommendations could you make immediately to E.W. to help with her symptoms?
   a. Decrease fluid intake to 6 to 8 cups per day, spread out over the day
   b. Switch to decaffeinated coffee and herbal tea
   c. Limit or stop drinking fluids after dinner
   d. All of the above alternatives are correct.

20. The usual adverse effects of antimuscarinic agents could make E.W. more likely to experience problems with which of the following medications?
   a. Amlodipine
   b. Celecoxib
   c. Risedronate
   d. Spironolactone

CPE Processing:
Get your documentation of credit now! Completing a posttest at www.pharmacist.com/education is as easy as 1-2-3.
1. Go to Online CE Quick List and click on the title of this activity.
2. Log in. APhA members enter your user name and password. Not an APhA member? Just click “Create one now” to open an account. No fee is required to register.
3. Successfully complete the CPE exam and evaluation form to gain immediate access to your documentation of credit.

Live step-by-step assistance is available Monday through Friday 8:30 am to 5:00 pm ET at APhA Member Services at 800-237-APhA (2742) or by e-mailing InfoCenter@pharmacist.com.