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Urinary Incontinence and Overactive Bladder in Seniors: Implications for the Long-Term Care Setting

AUDIENCE AND PURPOSE

This supplement has been designed to meet the needs of pharmacists, nurses, and nurse practitioners who care for elderly people in community and nursing home settings.

The purpose of this supplement is to review the key issues related to the prevalence, assessment, diagnosis, and management of urinary incontinence (UI).

Learning Objectives

- Discuss the prevalence, clinical effects, and costs associated with UI in community-based seniors and long-term care (LTC) residents
- Describe methods to identify, assess, and diagnose UI in the LTC setting
- Define methods to successfully manage UI and overactive bladder (OAB) in the LTC setting
- Discuss the results of the OBJECT trial and its implications on the treatment of UI and OAB
- Identify future methods that may improve the management of UI and OAB

Disclosure Statements

Mr. Jones discloses no relationships. Dr. Cranmer discloses relationships with Janssen, Purdue, Abbott, Ortho-McNeil, Novartis, Faulding, Ross, Lilly, and Aventis. Dr. Dmochowski discloses relationships with Ortho-McNeil and Pharmacia. Ms. Dornberger discloses no relationships. Ms. Helveston discloses no relationships. Dr. Herman discloses relationships with Pfizer, Eisai, and Wyeth.

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Written by MatureHealth Communications LLC

Urinary Incontinence and Overactive Bladder in Seniors: Implications for the Long-Term Care Setting

Clinical and Economic Implications of Urinary Incontinence for Community and Long-Term Care Settings

Table 1.

Prevalence of Urinary Incontinence

- In persons aged 15 to 64 years
  - men—1.5%–5%
  - women—10%–30%
- In persons aged 65 years and older
  - community setting—15%–30% overall, 30%–50% in women
  - homebound—approximately 50%
  - LTC setting—greater than 50%
  - in LTC setting, 27% of those admitted with continence were actually incontinent

Episodes occur daily or weekly

AHCPR Guidelines, 1999.

The prevalence of urinary incontinence (UI) in the United States is greater than commonly believed (Table 1), with approximately 10.4 million American women and 2.6 million men affected by this condition. Furthermore, UI often is underdiagnosed at the time of nursing home admission. While the prevalence of UI increases with age, it is not a normal part of the aging process. It is, however, often a precipitating factor in the decision to institutionalize an elderly person since the condition is commonly associated with dementia, fecal impaction, and inability to walk.

UI can have far-reaching physical, social, and economic consequences (Table 2). Often associated with social stigma and shame, this may result in prolonged anxiety that can lead to major depression. Patient embarrassment over this condition also results in underreporting and underdiagnosis; indeed, fewer than half of UI patients discuss the issue with their physicians. Sufferers isolate themselves socially, fearing loss of bladder control, leading to loss of independence, depression, and an overall decline in quality of life (QOL).

The frequent need to urinate can interfere significantly with activities of daily living (ADLs). Comorbid conditions, common in the elderly, can exacerbate the problem. Impaired mobility resulting from Parkinson's disease or stroke, reduced toilet accessibility, environmental barriers, and cognitive impairment can all complicate UI. Perhaps the greatest adjuvant concern with UI is the risk of falls. Long-term care (LTC) residents are at a higher risk for falls, especially at night, as a result of instability or slipping

Table 2.

Psychological Impact of Urinary Incontinence

- Social stigma, self-isolation, anxiety, and depression
- Lack of control over urinary function = loss of independence
- Fewer than 50% of people discuss this issue with their physicians
- Significantly underreported and underdiagnosed

while en route to the toilet or decreased stability when standing during unassisted toileting. All of these comorbidities may result in diminished QOL and higher downstream health care costs.

UI and Falls

Studies indicate that incontinence is an independent risk factor for falls and fractures. The prevalence of UI in community-based women over age 65 is estimated to be between 30% and 50%, and the prevalence of falls in this group is 19% to 42%, with a recurrence rate of 33% to 50%. Approximately 5% to 10% of these falls result in fractures. One study followed more than 6000 community-dwelling elderly women with urge UI for an average of 3 years to determine if urge UI is associated with risk of falls and nonspinal fractures.[1] The women's average age was 78 years, and 52% lived alone. Only 20% were in poor general health. The women reported falls and fractures using regularly mailed postcards (every 4 months) and a self-completed questionnaire to characterize the UI. Results of the study are shown in Table 3.

During follow-up, 55% of respondents reported at least 1 fall. About 20% reported at least 1 fall per year, and 5% reported an average of 3 or more falls per year. Statistical analysis of the data, adjusted for common risk factors for falls and fractures, showed an independent association between weekly or more frequent urge incontinence in community-dwelling older women, with a 26% increased risk of falls and a 34% increased risk of nonspinal, nontraumatic fractures. The authors suggest that since the risk of falling may have been increased by urinary frequency, nocturia, and rushing to the bathroom, early diagnosis and appropriate treatment of urge incontinence may lower the risk of fractures.

It is reasonable to expect that the incidence of UI-related falls, particularly nocturnal falls, would be greater in the

Table 3.

Does Urinary Incontinence Increase Risk for Falls and Fractures?

- Results—average 3-year follow-up
  - 55% reported falling
  - 8.5% reported fractures
  - 25% reported weekly or more frequent urge incontinence
  - 19% reported weekly or more frequent stress incontinence
  - 12% reported both types of incontinence
- Weekly or more frequent urge incontinence was associated independently with risk of falling and nonspinal, nontraumatic fractures
- Stress incontinence was not associated independently with falls or fractures

Brown et al. *JAGS*, 2000.

LTC setting than in the community setting. Patients recently moving to an LTC facility from the community setting face a change in bed type and an unfamiliar bathroom route, increasing the possibility of an incontinent episode. In fact, nursing home-based studies have reported increased falls among residents en route to the bathroom or while on the toilet.

Concomitant conditions, such as vertigo or osteoporosis, may contribute to falls and fractures in the LTC setting by predisposing residents to falling while getting out of bed, thereby leading to a greater incidence of fall-induced complications. In addition, cognitive impairment, a common condition in LTC residents, may precipitate a fall resulting from patients' inability to focus on multiple tasks. In other words, the urge to reach the bathroom may distract patients' focus on walking and lead to a fall.

Costs of UI in LTC Facilities

The economic costs associated with UI are significant, particularly in the LTC setting. Beyond the cost of adult diapers, other direct incidental costs associated with UI, such as labor, laundry, and waste disposal, are often underestimated when calculating the economic impact of UI in the LTC setting. The cost of medication for incontinence management may appear higher than changing adult diapers before these incidental costs are fully accounted for.

A recent study conducted at two large New Jersey nursing homes determined the cost of staff time and materials per incontinent resident for adult diaper changes over a 24-hour period.[2] Study results indicated that the average staff time invested for each incontinence-care episode was 3 minutes 33 seconds. Further, 20 pounds of dry wash were used for each resident with UI during each 24-hour period, contrasted with 8 pounds of dry wash per 24 hours for a continent resident. Laundry, labor, and material costs for incontinent residents were $17.21 per day per resident, or $6,281.65 per resident per year. Laundry (52%) and labor (36%) accounted for the greatest proportion of daily costs. Despite the significant totals, these numbers actually represent a "low bid" in that they did not include items such as Periguard®, a skin protectant antimicrobial ointment. Based on this study, the annual direct cost of incontinence in the United States may be as high as $11.2 billion in the community setting and $5.2 billion in nursing homes.

The economic implications of this study extend well beyond the most visible laundry, labor, and material costs. The cost of treatment for anxiety or depression, skin care consequences, and falls and fractures must be considered alongside the less tangible but significant consequences and costs of allied regulatory compliance, staff retention, and risk management concerns.

Classification of UI

The 5 major categories of incontinence are stress, overactive bladder (OAB)/urge, overflow, functional, and mixed incontinence.

Stress incontinence, defined as involuntary urine loss following increased intraabdominal pressure, may occur with coughing, laughing, or exercising. It often results from urethral hypermobility, usually caused by weak bladder neck support, or from lack of normal intrinsic pressure within the urethra. This form of UI most commonly occurs in women during the early postmenopausal period and between the ages of 55 and 75 years.

OAB/urge incontinence, or involuntary urine loss preceded by a strong urge to void whether or not the bladder is full, is characterized by urgency, frequency, dysuria, and nocturia. This problem is caused by lower urinary tract irritation or a neurological condition such as stroke, dementia, or a CNS illness, that prevents normal elimination. This problem occurs most often in people older than 75 years.

Overflow incontinence, involuntary urine loss caused by overdistension of the bladder, is associated with frequent or constant dribbling. Usually caused by an overactive bladder muscle and/or outlet obstruction, overflow incontinence may result from medications that reduce activity, from concomitant illness, such as diabetes, or from pelvic surgery.

Functional incontinence describes involuntary urine loss unrelated to urinary tract causes and is diagnosed by exclusion of other categories. This condition results from chronic physical or cognitive impairment that prevents patients from reaching a toilet. Impaired mobility, environmental barriers to toileting, or psychological impairment may be factors.

Mixed incontinence, the most common form of incontinence in the LTC setting, describes the combined conditions of stress incontinence and OAB. The condition is often caused by a fistula, which is a complication following hysterectomy or other surgery.

Risk Factors for UI

A variety of common geriatric conditions can increase the likelihood of UI. Impaired mobility or immobility resulting from stroke, hip fracture, obesity, impaired cognition, or delirium or dementia increases the risk of UI, and secondary conditions, such as low or excessive fluid intake or fecal impaction may result. Diabetes mellitus can increase the osmotic load in the kidneys, precipitating free water loss and the need to urinate. Other risk factors that can predispose a patient to UI include congestive heart failure and diuretic use, gastrointestinal disease, postmenopausal atrophic vaginitis due to estrogen depletion, pelvic muscle weakness, urinary tract infections (UTIs), and previous pelvic surgeries such as prostatectomy. Psychological problems, such as depression or anxiety disorders, as well as central nervous system (CNS) conditions, such as Parkinson's disease, may promote UI by interfering with the nervous system's signaling for bladder relaxation.

Both prescription and nonprescription medications can cause or exacerbate UI. Drug classes that can cause decreased bladder contractions resulting in retention include anticholinergics, antidepressants, antipsychotics, sedative-hypnotics, and antihistamines. Other drugs that may affect UI include CNS depressants, such as narcotics or alcohol, calcium-channel blockers, alpha-adrenergic agonists, beta-adrenergic blockers, caffeine, and diuretics.

Diagnosis and Assessment of UI

Assessing UI

UI management begins with classification and specific cause identification. This is accomplished by the maintenance of bladder records in the form of a 7-day voiding diary, which lists voiding time, incontinence incidents, voided urine amount, bowel movement occurrences, and fluid intake. The assessment should also include questions regarding the frequency, time, quantity, and triggers (eg, cough, specific exercise, laughter) of involuntary urine loss. It should also include a history of changes that occurred in the patient's life before the problem with involuntary urine loss occurred (such as surgery, injury, trauma, onset of illness, new medications), and recent changes in the patient's ability to carry out ADLs. The family or caregiver can provide most information for UI patients with dementia. The nurse's aide is often the best information source for current LTC residents.

The initial assessment should include an abdominal, rectal, and pelvic (women) or genital (men) exam, as well as a full physical exam, urinalysis, determination of volume status and postvoid residual (PVR), and assessment of the patient's functional toileting capabilities. Atrophic vaginitis, which might be treated with estrogen cream, may reflect additional estrogen-deficiency conditions, including osteoporosis. The urinalysis might detect UI-related conditions, including hematuria, glucosuria, pyuria, or bacteriuria (although bacteriuria has no effect on morbidity or mortality in chronically incontinent nursing home residents). Observation of patient voiding can reveal any discomfort or hesitancy. While a PVR determination by ultrasound is preferable because it is noninvasive and avoids the risk of urethral trauma, PVR by catheterization is an option. A PVR <50 mL is considered normal, while a PVR >100 mL is considered to be inadequate emptying. A PVR between 50 mL and 100 mL requires clinical judgment in determining treatment, based on the responses to the assessment questions and the patient's mental and physical status. For the frail elderly, for example, a much larger benchmark capacity of 200 mL may be indicated. Since patient input may influence the results of a single determination, multiple PVR measures should be considered.

Unless the diagnosis is uncertain, the patient is a surgery candidate, or comorbid conditions (such as recurrent UTIs or possible prostate cancer) are indicated, the value of urodynamic, endoscopic, or imaging tests is questionable. A urology referral is rare unless the patient is hospitalized for another condition.

Since medications may contribute to incontinence, the resident's medication history should be reviewed. Drugs that have been associated with impaired micturition include anticholinergics, antihistamines, gastrointestinal antispasmodics, anti-Parkinson's disease medications, antidepressants, muscle relaxants, and narcotics. Alpha-blockers can induce UI, and drugs that can cause decreased bladder contractions with retention-precipitating or aggravating UI-include anticholinergics, antidepressants, antipsychotics, sedative-hypnotics, and antihistamines. Other drugs that affect UI include CNS depressants, such as narcotics or alcohol, calcium channel blockers, beta-adrenergic blockers, caffeine, diuretics, and alpha-adrenergic agonists and antagonists.

Nursing Assessment

The minimum data set (MDS) 2.0, a standardized nursing home resident assessment tool, provides an outcome measure that determines the patient's nursing care needs, functional abilities, cognitive function, physical capability, and nursing care plan. Resident assessment must take place within 14 days of admission, and the nursing care plan must be developed and initiated within 24 hours of assessment analysis. The health care team responsible for the assessment includes the nurse, dietitian, physical therapist, social worker, and occupational therapist, with input from nurse's aides and pharmacists. Ongoing assessments should be performed by a multidisciplinary team, incorporating input from all caregivers. Behaviors should be recorded during all shifts and over a period of time to determine changes in behavior patterns. Facilities whose employees have a more established history with residents are more likely to notice and report small changes in residents' abilities, particularly cognitive abilities. Table 4 summarizes MDS sections that focus primarily on UI, but other sections also may impact the results directly or indirectly.

Nurses should perform ongoing resident assessment to note changes in bowel and bladder habits, risk for falls, and need for additional aids, such as geri-pads. Nurses should also determine each resident's pattern of incontinent voiding to encourage resident toilet use.

Table 4.

MDS: Sections Focusing on Urinary Incontinence

- Section B—Cognitive Patterns
  - B5: cognitive skills for daily decision making
- Section G—Physical Functioning and Structural Problems
  - G1i: toilet use
  - G1j: personal hygiene
- Section H—Continence in Last 14 Days
- Section I—Disease Diagnoses
- Section J—Other Health Conditions
- Section K—Oral/Nutritional Status

Section J, Other Health Conditions, may contribute in assessing the patient's incontinence or severity relative to the presence of comorbid conditions, such as dementia or congestive heart failure. UI severity, with or without comorbid dementia, is difficult to quantify. For example, an inaccurate report of the number of adult diapers used by the resident at the time of admission may occur because incontinent elderly patients may not have their diapers changed as often as necessary, since they may not realize they are wet.

Strategies for Success in Managing UI

All caregivers' input should be considered in establishing the care plan. Treatment goals should be attainable and individualized. For example, total dryness may be unfeasible or unrealistic for a very aged patient. Regular proactive follow-up that includes recording of behavior changes and appropriate plan modification is essential, whether or not it seems necessary. Finally, staff troubleshooting for problems should be an ongoing preventive strategy.

Current Methods for Managing UI and OAB

Defining Goals

The first step in UI management is to define the treatment goals (Table 5).

While total dryness may be unrealistic, maximizing QOL by reducing the number of incontinent episodes, keeping patients as dry and comfortable as possible, improving ADLs, and diminishing social isolation without impinging on the patient's cognitive process is an attainable goal. This goal may entail avoiding drugs that impair micturition, such as the commonly used agent diphenhydramine. Because it is inexpensive, diphenhydramine is commonly prescribed, even though it has been associated with sedation that can result in falls, hip fractures, and incontinence.

Another QOL issue, the maintenance of skin integrity, is particularly important in preventing decubitus ulcers, which are often associated with incontinence.

Managing Comorbidities

While identification of incontinence type and formulation of individualized patient treatment goals and strategies are important, managing comorbidities is also crucial in UI, even if they are not completely correctable. Diabetes and pain should be controlled and the patient's cognitive abilities should be assessed to determine the appropriateness of imposing behavior modification approaches. Continuous assessment of the patient's status will help to determine the management course.

Behavior Modification

If behavior modification becomes part of the UI care plan, the assessment team must address several issues. First, both the resident's ability to comply and compliance issues with the family and staff must be evaluated. In particular, the staff must be educated to understand and appropriately deal with the resident's condition.

Dietary issues, including ethnic preferences, can affect resident behavior and even comorbidities. Since a patient's fluid preferences for either carbonation or caffeine can affect UI, serving decaffeinated beverages may help decrease incontinence incidences as well as reduce a patient's agitation.

While the elderly resident with UI may independently institute fluid management in an effort to control the problem, increased risk of dehydration may result. Regardless of UI, residents should drink at least 7 to 8 glasses of fluid daily.

The resident's previous lifestyle may also contribute to the UI management plan. If, for example, an individual worked nights before retirement, the staff should monitor behavior and activity changes. Another consideration may be accessibility of the resident's clothing. For example, simplifying the voiding process by replacing buttons or

Table 5.

Define the Treatment Goal

- Manage the comorbidities causing incontinence
- Decrease the number of episodes
- Eliminate all episodes
- Improve ADLs and QOL
- Diminish social isolation
- Maintain skin integrity

even zippers with Velcro® closures can facilitate continence management.

In addition, the staff should evaluate the resident's daytime environment, including bathroom proximity, as well as the times and methods of fluid intake.

Quality Indicators

State surveyors of LTC facilities review 9 separate quality indicators that directly relate to UI. These are: prevalence of falls; incidence of cognitive impairment; prevalence of bladder or bowel incontinence; prevalence of occasional or frequent bladder or bowel incontinence without toileting plan; prevalence of indwelling catheter; prevalence of fecal impaction; prevalence of UTI; prevalence of bedfast residents, and incidence of decline in late-loss ADLs. Surveyors likely will flag any resident for whom more than one of these quality indicators have been noted. Facilities must show a daily plan, implemented by all levels of care personnel, that appropriately addresses UI problems.

Based on this information, the cost of addressing these initial measures must be considered against the cost of potential quality indicator violations if a LTC facility fails to manage UI properly.

Management Strategy

UI management should proceed from the least to the most invasive strategy based on a step-management approach. Behavior modification goals center around 2 general principles: (1) maintain a regulated bladder volume and (2) increase the CNS's and pelvic floor mechanism's ability to inhibit detrusor contractions and incontinence. Behavior modifications include prompted voiding with toileting assistance; individualized habit training; scheduled toileting to promote bladder retraining; relaxation training; pelvic muscle exercises, and biofeedback. Even a patient with mild Alzheimer's disease can be trained in toilet habits and prompted voiding, at least until the disease progresses to a point at which personal maintenance is no longer practical. Pelvic muscle or Kegel exercises also may or may not be feasible in an institutional setting. Biofeedback and relaxation may be effective for cognitively intact patients, such as those in an assisted living facility, but probably will be ineffective in a skilled nursing facility.

Bladder retraining requires adequate staffing; however, such staff is sometimes unavailable or undertrained due to rapid staff turnover.

Since pelvic muscle rehabilitation involves timed voiding, concentration on reducing and/or preventing urges, use of Kegel exercises, and biofeedback, only a LTC facility resident with good cognition would be a candidate for this therapy.

Regulations on the use of containment devices, such as absorbent pads and adult briefs, are specific to each state, city, and facility. Usually the most effective—particularly during behavior modification training—are adult briefs that can be pulled down. When necessary, the newer generations of condom catheters are preferable to indwelling catheters for male incontinent residents; however, these can be very costly and can be harmful to the patient if applied incorrectly.

Surgical procedures should be a last resort after all other options have failed, but LTC facilities very rarely resort to them. Surgery is more likely to enhance QOL in the community setting, even with comorbidities. Surgery may be useful to correct some types of obstructions, but given the comorbid diseases suffered by most LTC residents, the potential complications of surgical intervention often outweigh the potential benefits. Occasionally, LTC facilities perform transurethral resection of the prostate (TURP); however, observable benefit may take several months and detrusor overactivity that produces persistent incontinence may obfuscate results.

Pharmacologic Management

Behavior management and pharmacologic management of UI are mutually supportive therapies since neither used alone will work for all residents. Therapeutic decision-makers must consider possible UTI, fecal impaction, vitamin and mineral deficiencies, as well as overall nutrition needs, detrusor underactivity (incomplete bladder emptying), and concomitant medication complications. For example, up to 30% of patients starting on an ACE inhibitor will experience coughing episodes, creating risk for an incontinence episode. Calcium channel blockers may cause suppression of the detrusor muscle contraction and hypotension, while diuretics pose obvious problems.

Since UI-related depression can be drug induced, intervention with appropriate drug therapy modifications may reduce the likelihood of resulting psychological and social sequelae. Delirium, dementia, and depression, the "3 Ds," may complicate identification of this problem and compromise the patient's ability to anticipate, communicate, or act upon a pending incontinent episode.

Pharmacologic therapy for UI rapidly reduces the frequency of micturition and incontinent episodes; however, the impact on quality indicators and staff utilization time for administering drugs in multiple daily doses and for monitoring or correcting adverse drug reactions must be considered.

Anticholinergics and antispasmodics are the "gold standard" for treating OAB. Tricyclic antidepressants, especially imipramine, have some potential, particularly for nocturia, and may benefit residents who have multiple indications for its use.

Atrophic vaginitis should be treated with topical estrogen. For women whose pelvic floor may have been weakened by multiple pregnancies or who were on estrogen replacement therapy (ERT) before entering the facility, ERT should be considered. Both ERT and alpha-adrenergic agonists are appropriate for women with stress incontinence.

Although pharmacologic strategies are unreliable, they may be considered as potential remedies for UI. Overflow incontinence may be alleviated with alpha-adrenergic antagonists or antiandrogens (finasteride). Phytotherapy, such as saw palmetto, may be used, and cholinergic agents may help to eliminate residual urine, although success with this approach is unlikely.

Drug Therapy Selection and Initiation

Drugs must be selected on established efficacy for the patient's specific incontinence type, considering that an FDA-approved indication for the drug is necessary to ensure reimbursement from the state Medicaid board. The potential for adverse effects due to concomitant medications or comorbidities must be considered when 2 agents with equivalent efficacy and different risk profiles are considered.

Dosing issues also will influence drug interventions. Dosage forms must accommodate for the patient's ability to swallow as well as related considerations. Once-daily dosing frequency will simplify daily medication passes. Consideration of medication costs should include the adverse event profile, the potential added cost of medication-related problems, as well as staff costs to support multiple daily dosing.

Medication therapy should be started with a single agent at its lowest recommended dose, and be increased gradually until the desired effect is achieved or adverse effects become intolerable. Adequate time for full efficacy should be allowed. Generally, combination drug therapy is as effective as monotherapy, but the combination of behavior and drug therapy is often synergistic.

Currently, the 2 standard medication benchmarks for OAB treatment are oxybutynin extended-release tablets (Ditropan XL®) and tolterodine tablets (Detrol®). (Recently, Detrol® LA, an extended-release formulation for tolterodine, has been introduced.) Both are FDA approved for UI. Appropriately monitored, the adverse drug effects are manageable. Following is a brief comparative summary of the 2 drugs.

In the only head-to-head study, oxybutynin extended-release tablets were shown to be more effective than tolterodine tablets in controlling OAB. Most studies demonstrated that while tolterodine and extended-release tolterodine decrease urinary frequency and possibly increase the voided urine quantity, they fail to show statistically significant decreases in incontinence episodes. The pharmacokinetics and adverse-effect profile of oxybutynin extended-release tablets and extended-release tolterodine tablets in patients older than 65 years is similar to that in younger patients. Extended-release tolterodine tablets do carry a dosage limitation (2 mg/d) for patients with reduced hepatic or renal function, and a warning regarding drug-drug interactions with CYP3A4 inhibitors, such as macrolides or antifungal preparations. Oxybutynin extended-release tablets should be used with caution in patients with hepatic or renal impairment. Similar adverse-effect profiles for both drugs reflect their anticholinergic action, with dry mouth, constipation, and CNS effects such as headache and somnolence predominating.

One important difference between the drugs is the delivery system. Delivery technology differences produce differences in pharmacokinetics, pharmacodynamics, drug interactions, and dosing convenience. The Ditropan XL® OROS® formulation is designed to improve the medication's clinical profile. OROS® technology provides an osmotically active polymeric push compartment and a drug compartment surrounded by a semipermeable membrane with a laser-drilled delivery orifice. This technology regulates medication blood levels over 24 hours, avoiding peaks that may increase side effects and dips that may diminish efficacy. Maintaining consistent blood levels over a 24-hour period decreases the likelihood of adverse effects.

In contrast, the delivery technology for Detrol® LA comprises multiple tiny beads of drug, coated in varying thicknesses of soluble material to promote dissolution at different times. Alkaline environments promote rapid absorption, with peak plasma levels achieved in 2 to 6 hours. According to approved prescribing information, dosing for extended-release tolterodine is once a day. Co-medication with an antacid, an H_2 blocker, a proton pump inhibitor, or any other drug that increases the gastric pH, could shift tolterodine blood levels, increasing the potential for side effects.

Oxybutynin extended-release tablets are absorbed in the distal small intestine and the large intestine, with peak plasma concentrations achieved in 12 hours and a 24-hour dose interval. Neither gastric pH nor food affects the tablet's rate of drug delivery, allowing once-daily dosing. Oxybutynin extended-release tablets are metabolized primarily by the cytochrome P450 enzyme system in the liver and gut wall, and its metabolic clearance is predictable.

The OBJECT Trial

Overactive Bladder: Judging Effective Control and Treatment

Antimuscarinic treatment with immediate-release oxybutynin chloride tablets has provided satisfactory efficacy for OAB over the last 30 years. However, anticholinergic effects (such as dry mouth) reduced patient compliance rates, leading to discontinuations. The OBJECT study was designed to directly compare the efficacy and tolerability of oxybutynin extended-release tablets and tolterodine tablets on episodes of urge or total incontinence and frequency of micturition.

In clinical practice, oxybutynin extended-release tablets are usually titrated to dose levels that produce an optimal balance between efficacy and tolerability, while tolterodine tablets are usually prescribed as a fixed, 4-mg dose. To establish a benchmark comparison between the 2 medications, the OBJECT study used a fixed-dose regimen of both drugs—10 mg/d (qd) of extended-release oxybutynin (Ditropan XL®) or 4 mg/d (2 mg bid) of tolterodine (Detrol®), reflecting the doses used in 90% of patients throughout the United States.

OBJECT was a 12-week, prospective, randomized, double-blind, double-dummy, parallel-group study, enrolling 378 patients at 37 study sites in the United States.[3] Eligible patients were ambulatory (not institutionalized) and had 7 to 50 episodes of urge incontinence per week and 10 or more micturitions per day. Patients who had other causes of incontinence, had delivered a child, or had undergone pelvic, vaginal, bladder, or prostate surgery within 6 months before entering the study were excluded. Also excluded were patients who would be at medical risk if administered an antimuscarinic agent, those who had taken a study drug within the previous month, pregnant women, patients incapable of following study protocol, patients incapable of swallowing medications whole, or patients with a history of alcohol or drug abuse problems. Medications used for the treatment of OAB, or any anticholinergic agents, had to be discontinued before entering the study. However, patients previously treated for OAB could be included.

Table 6.

Efficacy Parameters*

Parameters	Extended-release oxybutynin (n=160)	Tolterodine (n=172)	*P* value
Urge incontinence episodes/wk			
Baseline	25–147	24.1–14.5	0.24†
End of study	6.1–9.7	7.8–11.1	0.03‡
(95% CI)	(4.4–7.3)	(6.7–9.5)	
Total incontinence episodes/wk			
Baseline	28.6–17.9	27.017.0	0.34†
End of study	7.1–12.0	9.313.4	0.02‡
(95% CI)	(5.2–8.6)	(8.0–11.3)	
Micturition freq. episodes/wk			
Baseline	91.8–22.6	91.6–20.2	0.86†
End of study	67.1–22.1	71.5–20.5	0.02‡
(95% CI)	(64.6–70.0)	(69.1–74.2)	

*Actual end of study (12-week) mean (± SD) values are reported based on the number of subjects who completed the study. Baseline mean ± SD values include only those patients who completed the study. CI=confidence interval.
†Wilcoxon rank sum test.
‡Testing and CI construction were done on the values adjusted for baseline and stratum in an analysis of covariance model.

Appell et al. *Mayo Clin Proc.* 2001.

The study participants initially included 315 women and 63 men, divided into 2 comparable treatment groups. Mean age for both groups was 59 years; women represented 82% and 84% of the oxybutynin extended-release tablet and the tolterodine tablet groups, respectively. Prior OAB treatment was reported for 41% and 38% of the oxybutynin extended-release tablet and the tolterodine tablet groups, respectively. At baseline, patients in each treatment group experienced a mean weekly frequency of 25 urge incontinence episodes and 28 total incontinence episodes. Mean weekly micturition frequency was 93 in the oxybutynin extended-release tablet group and 92 in the tolterodine tablet group.

Following baseline examinations and screening, eligible patients were stratified according to severity of urge incontinence at baseline. Within each severity stratum, patients were randomized to receive either a oxybutynin extended-release tablet 10 mg daily or tolterodine tablets 2 mg twice daily for 12 weeks. To ensure blinding of all concerned, study medications were distributed in a double-blind and double-dummy fashion. Seven-day urinary diaries were kept for all participants during each evaluation period (weeks 2, 4, 8, and 12) to document the number of micturitions, the number and nature of incontinence episodes, nocturnal voids, and nocturnal incontinence. The number of urge incontinence episodes at 12 weeks, adjusted for baseline and reported in the diaries represented the primary outcome measure. Also evaluated were the number of total incontinence episodes and micturition frequency at 12 weeks adjusted for baseline.

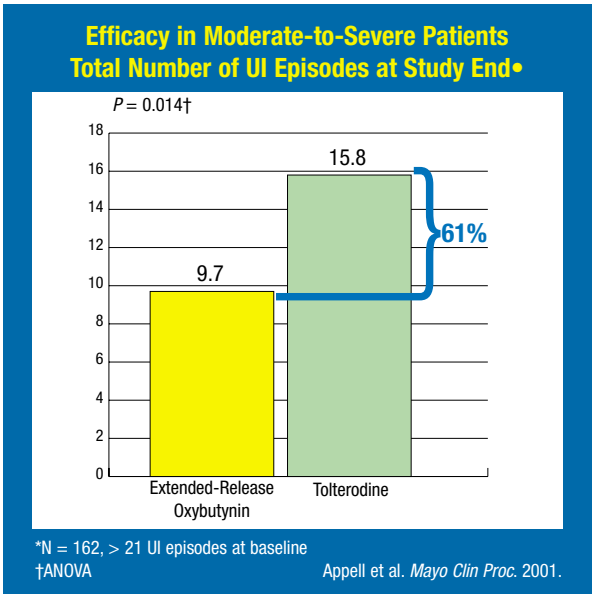
Three hundred thirty-two patients, 276 women and 56 men, completed the study; 46 discontinued early. Fourteen patients in the oxybutynin extended-release tablet group and 15 in the tolterodine tablet group cited adverse events as a reason for discontinuation. Urinary diary data were provided for both baseline and 12 weeks by 160 patients in the oxybutynin extended-release tablet group and 172 in the tolterodine tablet group. The OBJECT study omitted a placebo arm because both drugs had been compared to placebo in previous trials submitted for FDA marketing approval. No previously treated patients introduced bias, and the double-blind, randomized study design limited potential for treatment selection bias. Furthermore, 60% of patients in both study arms were naive to treatment, and the protocol allowed for non-naive patients to have responded to previous treatment.

Table 6 compares efficacy of the 2 agents. At the end of the 12-week study, tolterodine tablets averaged 28% more urge episodes than those taking oxybutynin extended-release tablets (7.8 episodes vs 6.1 episodes, respectively; $P = 0.03$). Similarly, the tolterodine tablet group averaged 31% more total incontinence episodes at 12 weeks compared to the oxybutynin extended-release tablet group (9.3 vs 7.1 episodes, respectively; $P = 0.02$). In the tolterodine tablet group, micturition frequency was 7% greater compared to the oxybutynin extended-release tablet group (71.5 vs 67.1 episodes, respectively; $P = 0.02$).

Included in the OBJECT trial were 162 persons with moderate-to-severe UI. The most dramatic efficacy difference occurred in this group, in which the tolterodine tablet group showed a 61% greater difference in incontinence episodes compared to the oxybutynin extended-release tablet group (9.7 vs 15.8; $P = 0.014$) (Figure 1).

The study indicated that both drugs substantially reduced the frequency of micturitions per week. Furthermore, continuation of treatment likely would result in continued

Figure 1.



frequency decrease. Both drugs reduced the number of incontinence episodes compared to baseline in almost all patients (96.2% of the oxybutynin extended-release tablet group and 95.0% of the tolterodine tablet group).

This trial also indicated statistically significant reductions in urge and total incontinence episodes and in micturition frequency within age groups younger than 65 years, 65 to 74 years, and older than 74 years. Safety and efficacy also appeared statistically similar among the 3 age groups.

For both treatment groups, anticholinergic and CNS side effects were comparable (Tables 7 and 8), and the incidence of side effects was similar across age groups.

Twenty-eight percent of oxybutynin extended-release tablet patients reported dry mouth, compared to 33% of tolterodine tablet patients. CNS side-effect rates and other adverse events were low in both treatment groups and comparable across all age groups. Importantly, neither group reported confusion or cognition problems. Discontinuation rates also were similar for both treatment groups—7.6% in the oxybutynin extended-release tablet group and 7.8% in the tolterodine tablet group.

Table 7.

Anticholinergic Side Effects, %

Event	Extended-Release Oxybutynin	Tolterodine	*P* value*
Dry mouth (total)	28.1	33.3	0.316
Dry mouth (mod-sev)	10.2	10.9	0.869
Constipation	7.0	6.2	0.837
Urinary retention	3.2	3.1	1.000
Blurred vision	2.2	1.0	0.440

*Fisher's Exact Test.

Appell et al. *Mayo Clin Proc.* 2001.

The OBJECT trial supports the use of Ditropan XL® in the management of OAB. Future studies may provide head-to-head comparisons between Ditropan XL® and Detrol® LA.

Future Trends in the Management of UI and OAB

As advancements in understanding of the CNS and peripheral nerve neuroanatomy and histopathology and their interrelationships continue, more precisely targeted drugs and devices are being developed.

One new device, InterStim® SNS, is a sacral nerve stimulator, which is used to treat urinary urge incontinence, urinary retention, and significant urgency and frequency symptoms. Sacral nerve stimulation modulates the neural reflexes in the bladder, sphincter, and pelvic floor, which control voiding. The 2-stage therapy involves an acute test stimulation procedure followed by permanent system implantation if the acute test is effective. The procedure is used only after behavioral and other interventional and drug therapies have failed. Similar to the success rate of pacemaker technology, the implant was successful in more than 70% of patients after 6 months, and effectiveness was retained in 60% after 12 months. Side effects were technical and included lead migration, technical problems, pain, and suspected device malfunction. However, the device is completely removable if necessary. Since the device development is in its infancy, it is currently very expensive, but it provides hope for greatly improved QOL in the future.

New advanced drug-delivery systems include transdermal, intravaginal, and intravesical delivery. The transdermal system, currently in phase III trials, eliminates every-12-hour dosing, reduces medications passes, bypasses first-pass metabolism, allows administration of smaller doses to achieve the same effects as larger doses, and increases patient tolerance. Possible disadvantages include local skin irritation and, in patients over age 75, lack of adequate skin hydration to allow drug penetration. The product under study contains an enhancing agent to force the anticholinergic agent through the skin.

Another new delivery system, UROS infusor technology, allows continuous intravesical drug delivery over 1 month. The device, which is placed directly into the bladder, releases low doses of drug locally (eg, 0.5 mg of oxybutynin), producing effects similar to much higher doses (eg, 15-mg dose of immediate-release oxybutynin) either orally or transdermally administered. This system offers significantly reduced potential for side effects. Since the system is invasive, however, it would be reserved for patients who cannot tolerate oral drug delivery.

Table 8.

CNS Side Effects, %

Event	Extended-Release Oxybutynin	Tolterodine	*P* value*
Dizziness	4.9	4.1	0.807
Somnolence	4.3	1.6	0.133
Asthenia	1.6	3.6	0.338
Insomnia	0.5	1.6	0.623
Nervousness	0	1.0	0.499

*Fisher's Exact Test.

Appell et al. *Mayo Clin Proc.* 2001.

New drug types have been developed to exploit muscarinic receptor selectivity. Darifenacin, for example, is a selective antagonist for the M3 receptor, which mediates bladder contraction. A recently completed large-scale clinical trial showed this drug to have a single-dose effect on urodynamic parameters.

Another drug category is the quaternary amines, of which tropsium hydrochloride is an example. The pharmacologic effect of this drug is similar to probanthine but with less extensive side effects and little to no CNS effect. However, the drug may cause more marked GI side effects.

A novel use of capsaicin, capsicum pepper extract, may emerge based on an understanding of the vanilloid receptors, which have a role in initiating micturition. There are 2 types of receptor fibers: myelinated and unmyelinated. Myelinated fibers allow for normal bladder function, while the unmyelinated C fibers perceive pain and are unmasked when the bladder receives a noxious stimulus such as infection. Capsaicin instillation desensitizes the C fibers by altering potassium- and calcium-channel activity.

This process has been shown to improve long-term bladder function in a modest percentage of patients. Unfortunately, in some cases pain is intensified initially when the capsaicin is instilled, the procedure requires general anesthesia. RTX (resiniferatoxin), a capsaicin analogue, has also been used, with much less pain and a dramatic effect on bladder capacity, urgency, and frequency. Currently, appropriate delivery systems for this drug are being researched.

Many possibilities for future drug development and delivery are being explored. While numerous receptor subtypes are active in the physiology of voiding, their interactions are unknown. Understanding the function of sensory afferents will play an increasingly important role in understanding the physiology of voiding. While complete drug receptor specificity remains a mystery, the potential for new drugs and delivery vehicles currently is being explored, and the years ahead may produce some new and exciting approaches to UI management.

Summary

There is a high prevalence of UI in the LTC setting. This illness has a significant impact on residents' morbidity, ADLs, and QOL. In order to successfully manage UI in seniors, it is important to first correctly diagnose and assess the type and severity of UI. Prior to initiating therapy, the treatment goals should be defined. Once defined, there are a number of options available to effectively meet the treatment goals for the various types of UI. UI management should be initiated with the least invasive approaches first. Behavioral and pharmacologic management should be used together, since neither one alone has been demonstrated to be effective for all residents. New therapies and devices are currently in development that should improve the management of UI in the future.

Selected References: 1. Brown JS, Vittinghoff E, Wyman JF, et al. Urinary incontinence: does it increase risk for falls and fractures? Study of Osteoporotic Fractures Research Group. *J Am Geriatr Soc.* 2000; 48:721-725. 2. Frenchman IB. Cost of urinary incontinence in two skilled nursing facilities: a prospective study. *Clin Geriatr.* 2001;9:49-52. 3. Appell RA, Sand P, Dmochowski R, et al. Prospective randomized controlled trial of extended-release oxybutynin chloride and tolterodine tartrate in the treatment of overactive bladder: results of the OBJECT Study. *Mayo Clin Proc.* 2001;76:358-363.

Additional References Available Upon Request.

Post-Test

Please circle your answers on this post-test form. Copies will be accepted.

This course qualifies for continuing pharmacy, nurse practitioner, and nurse credit, which will be awarded via mail within 4 weeks after submission of a successfully completed program post-test. A passing grade of 70% is required. Any participant who fails the examination may be re-examined one additional time. In order to apply for continuing pharmacy education credit, please circle the correct answers on this post-test form. Include a check in the amount of $10.00 made out to the appropriate CE provider. Place the completed post-test form and check in an envelope, affix stamp, and mail to the appropriate address listed below:

Pharmacist continuing education credit:

Rutgers, The State University of New Jersey
Ernest Mario School of Pharmacy
Office of Continuous Education
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Nurse Practitioner continuing education credit:

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250 East Broad Street
Westfield, New Jersey 07090

A check should be made out to MatureHealth Communications.

Nurse continuing education credit:

Rutgers, The State University of New Jersey
College of Nursing
Center for Professional Development
175 University Avenue, Conklin Hall 244
Newark, New Jersey 07102-1814

A check should be made out to Rutgers, The State University of New Jersey, College of Nursing.

Copies of this form will be accepted.

Post-Test Questions

1. The prevalence of UI in the LTC setting is
   a. 20%–30%
   b. 30%–40%
   c. 40%–50%
   d. greater than 50%

2. The psychological impact of UI includes all the following except:
   a. social stigma
   b. increase in independence
   c. self-isolation
   d. depression

3. Approximately what percentage of falls result in fractures?
   a. 5%–10%
   b. 10%–20%
   c. 30%–40%
   d. 40%–50%

4. The estimated direct cost of incontinence in nursing homes in the United States is approximately:
   a. $5 million
   b. $5 billion
   c. $1 million
   d. $1 billion

5. The initial assessment for UI should include:
   a. a full physical exam
   b. urinalysis
   c. determination of postvoid residual
   d. all the above

6. The treatment goals for UI include:
   a. manage comorbidities associated with incontinence
   b. decrease the number of episodes
   c. improve ADLs
   d. all the above

7. If behavior modification becomes part of the UI care plan, the first step should be to:
   a. define the available resources
   b. identify available pharmacotherapy
   c. evaluate the resident's ability to comply
   d. all the above

8. To ensure reimbursement from the state Medicaid board, drugs selected to manage a patient's specific incontinence should be based on:
   a. cost
   b. established efficacy for specific UI type
   c. dosage form
   d. dosing schedule

9. Medication therapy should be started with:
   a. a single agent
   b. the maximum recommended dose
   c. combination therapy
   d. all the above

10. The OBJECT study found that at the end of the 12 weeks, compared to tolterodine, oxybutynin extended-release tablets were statistically significantly more effective for reducing:
    a. urge incontinence episodes
    b. total incontinence episodes
    c. micturition frequency
    d. all the above

Signature _____

Name _____

Specialty _____

Street Address _____ **Box/Suite** _____

City _____ **State** _____ **Zip** _____

Phone (____)_____ **Fax (____)** _____

E-mail _____

Program Evaluation

1. How would you rate this program overall?
   a. excellent
   b. good
   c. fair
   d. poor

2. To what degree has this program improved your knowledge of the subject matter?
   a. extensively
   b. moderately
   c. somewhat
   d. not at all

3. How relevant was the program content to your practice?
   a. very relevant
   b. relevant
   c. somewhat relevant
   d. not relevant

4. How effectively did the program meet the learning objectives?
   a. very effectively
   b. effectively
   c. somewhat effectively
   d. not at all

5. The program was free from undue commercial bias:
   a. strongly agree
   b. agree
   c. disagree
   d. strongly disagree

6. As a result of this CE program, what changes, if any, will you make in your practice?_____
   _____
   _____
   _____

7. Please list any other specific CE offerings that would be of interest to you._____
   _____
   _____
   _____