MANAGEMENT OF OVERACTIVE BLADDER WITH TRANSDERMAL OXYBUTYNIN IN A DIFFICULT-TO-TREAT PATIENT

Leslie Wooldridge, RNCS, MSN, GNP

Urology Associates, Grand Rapids, Michigan

ABSTRACT

BACKGROUND: Antimuscarinic agents such as oxybutynin and tolterodine relieve overactive bladder (OAB) symptoms. However, their use, particularly with higher doses, is limited by anticholinergic-mediated adverse events (AEs). Transdermal oxybutynin (OXY-TDS) provides continuous, consistent plasma oxybutynin concentrations while reducing levels of N-desethyloxybutynin (N-DEO, thought to be associated with anticholinergic AEs) compared with oral formulations. OXY-TDS has demonstrated efficacy, with levels of anticholinergic AEs comparable to those of placebo. This abstract reports on OXY-TDS used in a difficult-to-treat OAB patient.

PATIENT: A 90-year-old woman presented with OAB symptoms and incontinence that had worsened gradually over 10 years.

MEDICAL HISTORY: Symptoms included urgency, urinary leakage immediately after voiding or without warning, and voiding 12 times daily. Urinalysis was negative. Postvoid residual volume was 128 mL. Patient had a history of heart disease (treatment: furosemide 40 mg qd), skin cancer (in remission), hypothyroidism, and intermittent constipation. Physical examination revealed enlarged, inflamed urethral meatus; inflamed, friable vaginal walls; no cystocele, rectocele, or vaginal prolapse.

ASSESSMENT: Patient was diagnosed with OAB with urge incontinence.

TREATMENT PLAN: Initial treatment comprised coffee intake reduction of 2–3 cups/d, thus reducing total fluid intake from 10 to 7–8 cups/d; behavioral therapy; Kegel exercises; vaginal estrogen cream; 10 mg qd extended-release oral oxybutynin.

FOLLOW-UP: Patient was compliant with treatments but, after 1 month, her condition worsened and she experienced increased constipation. She was switched to 4 mg qd long-acting tolterodine and a fiber supplement was added, but her condition did not improve after another month of follow-up. Patient was switched from tolterodine to OXY-TDS 3.9 mg/d. After 1 month, patient's condition improved, with no complaints of anticholinergic AEs. Patient reported swimming 3 times a week, attending exercise classes twice a week, and enjoying meals without a feeling of urgency.

CONCLUSION: After failing oral therapies, patient improved during treatment with OXY-TDS. The use of OXY-TDS also resulted in greatly improved quality of life. OXY-TDS may be a safe, effective alternative to oral OAB therapies.

INTRODUCTION

- Overactive bladder (OAB) may affect more than 16% of adults in the United States; more than
 one third of these individuals also experience urge urinary incontinence, with 45% having
 mixed urge and stress incontinence.¹
- Although antimuscarincs, such as oxybutynin and tolterodine, are widely prescribed for the treatment of OAB, their use may be limited by anticholinergic-mediated adverse events (AEs), particularly dry mouth and constipation.²
- Anticholinergic AEs associated with oxybutynin are thought to be linked to high plasma concentrations of the active metabolite, N-desethyloxybutynin (N-DEO).³
- Oxybutynin transdermal system (OXY-TDS) bypasses first-pass presystemic metabolism, thus lowering plasma concentrations of N-DEO and decreasing anticholinergic AEs while maintaining the efficacy associated with oral oxybutynin.⁴⁻⁶
- This report details the treatment of an older female OAB patient who first received oral antimuscarinics but experienced anticholinergic AEs, then was treated successfully with OXY-TDS

PATIENT HISTORY

- The patient was a 90-year-old woman who presented with symptoms of OAB that had gradually worsened over 10 years.
- The patient was 5'5" tall, weighed 142 lbs, and had given birth 4 times.
- She reported daily fluid intake of 10 cups, including 5 cups of decaffeinated coffee.
- Her bladder diary indicated that she voided approximately 12 times daily (including twice nightly) and had about 8 (6 minor, 2 large) leakage episodes per day, resulting in a need to use 2 pads per day.

ASSESSMENT

• Based on the assessment, the patient was diagnosed with OAB with urge incontinence (Figure 1)

Figure 1. Patient history, objective information, subjective information, and assessi

Symptoms	Comorbid Conditions	Concomitant Medications	Urodynamics	Physical Examination
Urgency episodes (13 times daily) Urinary leakage Voiding 12 times daily Nocturia (2 times/night)	Heart disease Skin cancer (in remission) Hypothyroidism Intermittent constipation	Levoxyl® 88 mcg QD Lasix® 20 mg QD Relafen® 500 mg QD Coumadin® 2.5 mg QD Gen-Diltiazem SR® 240 mg QD Docusate 100 mg BID Cytotec® 100 mcg QD Calcium 600 mg QD FiberCon® BID	Urinalysis: negative Postvoid residual: 128 mL	Enlarged, inflamed urethral meatus Inflamed, friable vaginal walls No cystocele, rectocele, or vaginal prolapse



Diagnosis: OAB With Urge Incontinence

TREATMENT PLAN

 Based on the diagnosis, the initial treatment plan included both behavioral and pharmacologic therapy (Table 1).

Table 1. Initial Treatment Plan

Behavioral Modification Therapy

- Reduce coffee intake 2-3 cups/d, reducing overall fluids from 10 to 7.5 cups/d
- Avoid irritating foods and fluids, particularly grapefruit juice
- Practice toilet retraining at 2-hour intervals
- Practice urge reduction techniques with each urge to urinate

Pharmacologic Therapy

- Extended-release oral oxybutynin (10 mg/d)
- Estrogen cream (2 g, 3 times/wk)

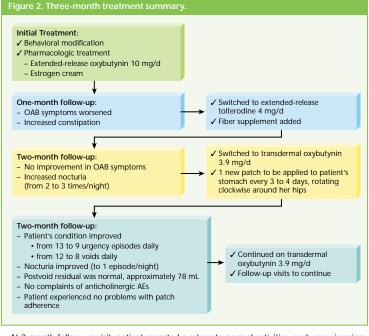
GENERAL VOIDING, KEGEL EXERCISE, AND URGE REDUCTION TECHNIQUES

- Double-void with each void
- Relax while urinating.
- Perform Kegel exercises daily.
- Begin with 30 Kegel exercises per day, 10 in each position: sitting, standing, lying down.
- To perform each Kegel, squeeze and hold for 10 seconds then relax for 10 seconds.
- Do 5 quick flicks or squeezes prior to performing the squeeze-and-hold exercises.
- Do not perform Kegel exercises when fatigued.
- When patients feel the urge to void, they are to:
- Stop what they are doing.
- Take a deep breath.
- Do a couple of quick Kegel exercises.
- Distract themselves from the thought of urinating.

PATIENT FOLLOW-UP

The patient was followed for 3 months (Figure 2).

• Patient was compliant with her treatment plan through each month.



 At 3-month follow-up visit, patient reported a return to normal activities, such as swimming, attending exercise classes, and enjoying meals without a feeling of urgency.

gure 3. Typical abdominal application of transdermal oxybutynin



- Patient should select a comfortable application site on the abdomen, hip, or buttock.
- Patch should be applied to a clean, dry, smooth area free of oils, lotions, or powders.
- Patch application should be rotated; patient should not apply new patch to the same site for at least 7 days.

CONCLUSIONS

- Oral antimuscarinic agents are the most commonly prescribed pharmacologic treatments for OAB, despite their poor tolerability.
- Oral oxybutynin, in particular, undergoes significant gastrointestinal and hepatic firstpass metabolism, producing high plasma levels of the primary active metabolite, N-DEO, which may be associated with anticholinergic-related AEs.
- Treatment with transdermal oxybutynin, which uses a delivery system that produces significantly less N-DEO than oral oxybutynin, was successful in this patient after she had failed to improve on oral extended-release formulations of both oxybutynin and tolterodine.
- This case demonstrates that transdermal oxybutynin is a safe, effective alternative to oral OAB therapies, yielding improvements in OAB symptoms, a lower incidence of anticholinergic-related AEs, and improved quality of life.
- Transdermal Oxybutynin may improve quality of life. At 3 month follow up, this patient reported being able to return to normal activities including swimming, exercise classes, and enjoying meals without urgency
- OXY-TDS provides an additional option for gerontological nurse practitioners for the treatment of OAB through twice weekly dosing and reduced anticholinergic AEs

REFERENCES

- Stewart WF, Van Rooyan JB, Cundiff GW, et al. Prevalence and burden of overactive bladder in the United States. World J Urol. 2003;20:327–336.
- 2. Wein AJ. Diagnosis and treatment of the overactive bladder. *Urology*. 2003;62(suppl 5B):20–7.
- Waldeck K, Larsson B, Andersson KE. Comparison of oxybutynin and its active metabolite, N-desethyloxybutynin, in the human detrusor and parotid gland. J Urol. 1997;157:1093–1097.
- Zobrist RH, Quan D, Thomas HM, Stanworth S, Sanders SW. Pharmacokinetics and metabolism of transdermal oxybutynin: in vitro and in vivo performance of a novel delivery system. *Pharm Res.* 2003;20:103–109.
- Dmochowski RR, Davila GW, Zinner NR, et al. Efficacy and safety of transdermal oxybutynin in patients with urge and mixed urinary incontinence. J Urol. 2002;168:580–586.
- Dmochowski RR, Sand PK, Zinner NR, Gittelman MC, Davila GW, Sanders SW. Comparative efficacy and safety of transdermal oxybutynin and oral tolterodine versus placebo in previously treated patients with urge and mixed urinary incontinence. *Urology*. 2003; 168:580–586.

Supported with funding from Watson Pharma, Inc.

Presented at the 23rd Annual National Conference of Gerontological Nurse Practitioners, Sept 29–Oct 3, 2004, Phoenix, Ariz.

