Current and Future Approaches to Treating

Urinary Incontinence

Pharmacologic, Surgical, and Behavioral Treatment of Urge and Stress Incontinence

Reports from the meetings of the American College of Obstetricians and Gynecologists, the American Geriatrics Society, and the American Urological Association

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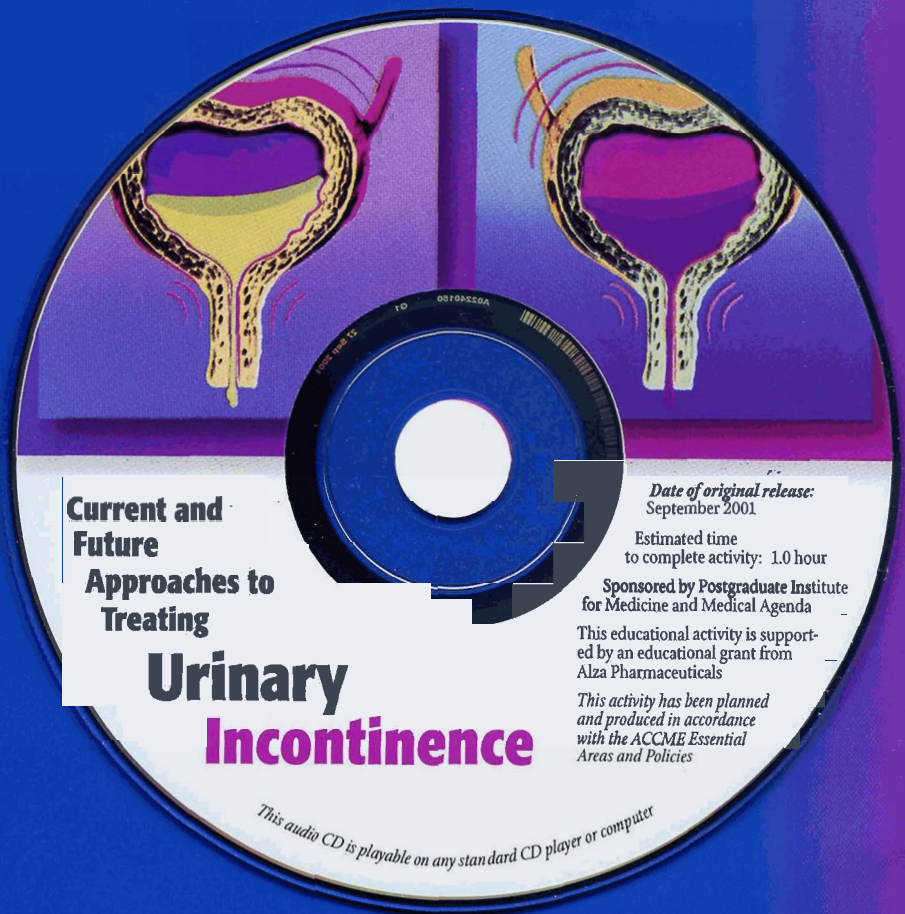

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Audio CD Contents

Track 1 OBJECT Study: Comparison of Oxybutynin Extended-Release and Tolterodine for the Treatment of Overactive Bladder

Track 2 OBJECT Study Adverse Events: Comparison of Extended-Release Oxybutynin and Tolterodine for the Treatment of Overactive Bladder

Track 3 The Selective Alpha Blocker Tamsulosin in Neurogenic Lower Urinary Tract Dysfunction

Track 4 Transvaginal Radio Frequency Bladder Neck Suspension to Treat Genuine Stress Incontinence

Track 5 Quality of Life Following Implantation of a Sacral Neuromodulator

Track 6 Non-pharmacologic and Pharmacologic Management of Urinary Incontinence in the Elderly

Track 7 The Knack: Timed Pelvic Muscle Contraction to Reduce Cough-Related Urine Loss

Track 8 Behavioral and Pharmacologic Therapies for Urge Incontinence

Track 9 Advanced Drug Delivery Systems and Future Treatments for Overactive Bladder

Track 10 Pharmacokinetics of Intravesical Oxybutynin

Track 11 Detrusor Overactivity Index: Establishing Criteria for Measuring the Severity of Overactivity

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This Continuing Medical Education activity consists of several articles presenting some of the latest information on the management of urge and stress urinary incontinence. The information was derived from presentations and interviews at the 2001 annual meetings of the American College of Obstetricians and Gynecologists, the American Geriatrics Society, and the American Urological Association. The articles include information on current management, recent research findings, and future directions for the treatment of urinary incontinence.

The producers or sponsors of this activity are not affiliated with the above organizations, and the organizations have not participated in the development of the activity nor do they endorse it.

OBJECT Study: Comparison of Oxybutynin Extended-Release and Tolterodine for the Treatment of Overactive Bladder

Primary Author (Interviewed):
Peter Sand, M.D.
Northwestern University Medical School, Chicago, IL

In brief: *The first large, randomized, double-blind study to compare the two most commonly prescribed drugs for urinary incontinence shows that oxybutynin extended-release is more efficacious than tolterodine, with an equivalent side effect profile. A 10-mg daily dose of oxybutynin extended-release was significantly more effective than a 4-mg daily dose of tolterodine in reducing urge incontinence, total incontinence, and micturition frequency. The incidence of adverse events, including central nervous system ones, was low and not statistically different between the two treatment groups.*

The **aim** of the study, known as OBJECT (Overactive Bladder: Judging Effective Control and Treatment), was to compare two of the leading medications for treatment of overactive bladder: oxybutynin extended-release and tolterodine.

The **study population** consisted of 378 patients with urge incontinence or mixed urge and stress incontinence, recruited from 37 doctors' practices. The mean age was 59.0 years (range 21–87). Patients with 7–50 episodes of urge incontinence per week and 10 or more voids in 24 hours were enrolled. Females made up 83% of the study population, which accurately reflects the gender distribution of overactive bladder patients in the general population. Study subjects were randomized 1:1 to oxybutynin extended-release or to tolterodine. The two treatment groups were not statistically different at baseline in terms of age, gender, or parameters of incontinence.

The **protocol** consisted of a prospective, randomized, double-blind, double-dummy parallel-group multicenter study. After a 2-week run-in and washout period, the patients were randomized to receive a daily dose of 10 mg extended-release oxybutynin or 4 mg tolterodine (2 mg twice a day) for 12 weeks. Patients completed daily urinary diaries and were evaluated for reduction of urge incontinence episodes, total urinary incontinence episodes, and frequency of micturitions. Safety and efficacy were assessed during office visits and through the daily urine diaries.

The **results** show that at 12 weeks oxybutynin extended-release was significantly more effective than tolterodine in reducing episodes of urge incontinence, total incontinence, and micturition frequency *(see Table 1)*. Both drugs resulted in statistically significant

Table 1.
Efficacy in Treating Urge Incontinence: Oxybutynin Extended-Release vs. Tolterodine

	Baseline		12 Weeks		
	Oxybutynin ER group*	Tolterodine group	Oxybutynin ER group	Tolterodine group	Significance**
Mean Urge Incontinence Episodes/Week	25.6	24.1	6.1	7.8	p = 0.03
Mean of Total Incontinence Episodes/Week	28.6	27.0	7.1	9.3	p = 0.02
Mean Micturition Frequency/Week	91.8	91.6	67.1	71.5	p = 0.02

* ER = extended-release

** Oxybutynin extended-release vs. tolterodine at 12 weeks.

reductions in the number of urge and total incontinence episodes and in micturition frequency compared to baseline.

Both treatments were well tolerated, and the incidence of adverse events was similar but with a trend toward less dry mouth among the oxybutynin extended-release patients. Dry mouth was the most common adverse event for these drugs. Other anticholinergic adverse events included constipation, impaired urination/urinary retention, and blurred vision. *(See Table 2.)*

Central nervous system adverse events included dizziness, somnolence, asthenia, insomnia, and nervousness. Less than 5% of patients suffered any one of these adverse events. Other adverse events were headache, dyspepsia, nausea, and vomiting. The incidence of total CNS adverse events in subpopulations was similar in older and younger patients, in patients naive to previous anticholinergic therapy, and in female patients. Overall, less than 7% of patients discontinued treatment because of adverse events.

The researchers **concluded** that oxybutynin extended-release (10 mg once daily) was significantly more effective than a 4-mg daily dose of tolterodine for all the efficacy end-points studied. Furthermore, the incidence of adverse events, including ones related to the central nervous system, was low and similar between the two treatment groups.

Commentary

Dr. Sand said that both of these drugs are excellent, actively-used agents. Most American physicians commonly prescribe these medications because patients prefer pharmacotherapy as a first treatment. He believes this study will help clinicians decide which drug to use. Dr. Sand noted that the head-to-head data show that at 12 weeks patients taking tolterodine had 28% more urge incontinence episodes and 31% more

Table 2.
Anticholinergic Adverse Events

	Oxybutynin ER*	Tolterodine
Dry mouth	28.1%	33.2%
Constipation	7.0%	6.2%
Impaired urination/ urinary retention	3.2%	3.1%
Blurred vision	2.2%	1.0%

* ER = extended-release

total incontinence episodes than patients taking oxybutynin extended-release.

Dr. Sand pointed out that in a study of a 4-mg, once-daily, long-acting dose of tolterodine, its overall efficacy in reducing incontinence episodes was 53%, which is equivalent to the 46–55% reduction in incontinence episodes with the 2-mg, twice-daily dose of the drug seen in several other studies. "So it's equal to what we've seen in all prior work looking at Detrol 2 milligrams b.i.d.," he said. "So I don't think the efficacy is any different [between the two forms of tolterodine]."

The clinical significance of the OBJECT trial is threefold. "A lot of people in urogynecology and female urology thought that oxybutynin was a stronger medication and would reduce urge incontinence episodes better than tolterodine," Dr. Sand said. Second, "I was also surprised to see that there was a significant difference in urinary frequency between them." Finally, he added that he was also surprised that oxybutynin extended-release appeared to cause less dry mouth than tolterodine. "We see in general clinical use that these drugs completely stop urge incontinence and urgency and frequency in 40% to 50% of patients," he said. "When people have been incontinent for 20 or 30 years and getting up four or five times a night to go to the bathroom, it just makes a huge difference in their lives."

The main **limitation** of the study is that it was only of 12 weeks duration, which may not reflect long-term treatment of a chronic condition such as urge incontinence. Another limitation is that specialists rather than primary care physicians enrolled the participants. ■

Disclosure

The study was supported by Alza Pharmaceuticals. Dr. Sand is a consultant to Alza, as well as to Pharmacia and other pharmaceutical companies engaged in incontinence research.

OBJECT Study Adverse Events: Comparison of Extended-Release Oxybutynin and Tolterodine for the Treatment of Overactive Bladder

Primary Author (Interviewed):
Rodney Anderson, M.D.
Professor of Urology, Stanford University, Stanford, California

In brief: *In a sub-analysis of the OBJECT study, comparing oxybutynin extended-release and tolterodine, the incidence of adverse events, including those of the central nervous system, was low and similar between the two treatment groups and among the three age groups studied.*

The **aim** of this sub-analysis of the OBJECT (Overactive Bladder: Judging Effective Control and Treatment) study was to compare the adverse events, including results by age, of two of the leading medications for treatment of overactive bladder—oxybutynin extended-release and tolterodine.

The **study population, protocol,** and overall efficacy **results** are the same as above in "OBJECT Study: Comparison of Oxybutynin Extended-Release and Tolterodine for the Treatment of Overactive Bladder," (primary author: Peter Sand, M.D.). Study subjects received either a 10 mg daily dose of oxybutynin extended-release or 2 mg of tolterodine twice a day. The study and sub-analysis reported clinical endpoints at 12 weeks of therapy.

The incidences of adverse events were not statistically different when comparing the two treatment groups, or across age groups, said Dr. Anderson. *(See Table 1.)* The

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