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TOLTERODINE FOR SYMPTOMS ASSOCIATED WITH OVERACTIVE BLADDER: A NIGHTTIME DOSING REGIMEN MAINTAINS EFFICACY AND IMPROVES TOLERABILITY

Hypothesis / aims of study

Overactive bladder (OAB) is a highly prevalent condition characterized by urinary urgency, frequency, and urge incontinence. Effective treatments exist, and muscarinic antagonists, including tolterodine tartrate (TOL), are first-line therapies. Studies have shown that TOL has proven efficacy and better tolerability compared with other antimuscarinics. The standard treatment regimen is daytime dosing. The study design of 2 recent clinical trials allowed us to assess the potential benefits of nighttime dosing for further reducing the adverse events (AEs) associated with antimuscarinic therapy.

Study design, materials and methods

We pooled data collected from two 12-week placebo (PBO)–controlled trials of TOL extended release (ER; 4 mg once daily) for OAB symptoms in patients with frequency (mean ³8 micturitions/24 h), nighttime frequency (mean ³2.5 micturitions/sleep cycle), and urgency with or without incontinence for ³6 months. Patients were instructed to take study drug within 4 hours of going to sleep. Objective endpoints (ie, changes in the number of micturitions/24 h, volume per void) were quantified from information recorded in 7-day diaries. Information for subjective endpoints (ie, patient perception of severity of urgency, overall treatment benefit, satisfaction with treatment, willingness to continue treatment) was obtained from patients by the investigator. Severity of urgency was assessed using a 5-point scale: 1=None (I felt no need to empty my bladder but did so for other reasons); 2=Mild (I could postpone voiding as long as necessary without fear of wetting myself); 3=Moderate (I could postpone voiding for a short time without fear of wetting myself); 4=Severe (I could not postpone voiding but had to rush to the toilet to not wet myself); 5=Urge incontinence (I leaked before arriving at the toilet). Withdrawal rates and AEs were recorded for the duration of both studies.

Results

In total, 850 PBO- and 848 TOL ER–treated patients contributed data to this analysis. By week 12, patients who received TOL ER showed statistically significant improvements on objective measures of efficacy, including a reduction in the number of micturitions/24 h and an increase in urine volume per void compared with PBO. Nighttime frequency was reduced among patients taking TOL ER; however, this was not a statistically significant difference relative to PBO. On subjective measures, patients who received TOL ER reported significant improvements in their perception of overall treatment benefit, satisfaction with treatment, and willingness to continue treatment compared with PBO (Table). Commonly reported AEs in both treatment groups included dry mouth (4% PBO, 11% TOL ER), constipation (2% PBO, 3% TOL ER), and blurred vision (1% PBO, 1% TOL ER). However, the rates from nighttime TOL ER dosing were reduced compared with those reported in a previously published study that used a daytime TOL ER regimen (dry mouth, 23%; constipation, 6%; blurred vision, 3%) [1].

Interpretation of results

The findings suggest that the efficacy of TOL ER for alleviating OAB symptoms is maintained with nighttime dosing. In addition, nighttime dosing may also reduce patient reporting of common AEs because these events are likely to occur during sleep.

Concluding message

Patients who have effectively managed their OAB symptoms with daytime dosing of TOL ER might consider a nighttime regimen to further reduce the potential occurrence of antimuscarinic effects such as dry mouth.

Table. Summary of Objective and Subjective Efficacy Measures With Nighttime Dosing

	Change From Baseline		Treatment Difference	
Objective efficacy measure	**PBO (n=850)**	**TOL (n=848)**	**LSM (SEM)**	***P* Value**
Severity of urgency, LSM (SEM)	–0.03 (0.02)	–0.11 (0.02)	–0.08 (0.02)	0.0004

	% Change From Baseline		Treatment Difference		
Objective efficacy measure	**PBO (n=850)**	**TOL (n=848)**	**%**	**95% CI**	***P* Value[b]**
Micturitions/24 h,[a] Median	–10.0	–14.6	–3.7	–5.5 to –1.8	0.0001
Micturitions/night,[a] Median	–20.0	–22.2	–1.9	–4.6 to 0.6	0.1768
Volume voided/micturition, Median	1.8	10.7	6.6	4.3 to 9.0	<0.0001

	% Responding "Yes"		Treatment Difference		
Subjective efficacy measure	**PBO (n=850)**	**TOL (n=848)**	**%**	**95% CI**	***P* Value[c]**
Overall treatment benefit	53.1	62.2	9.8	5.1 to 14.6	0.0001
Satisfied with treatment	54.9	62	8	3.3 to 12.7	0.001
Willingness to continue	48.8	57.4	8.4	3.5 to 13.3	0.0009

CI=confidence interval; LSM=least squares mean; PBO=placebo; SEM=standard error of the mean; TOL=tolterodine.
[a]Level of urgency, 1–5.
[b]Wilcoxon test.
[c]Chi-square test.

Reference:

1. Tolterodine once-daily: superior efficacy and tolerability in the treatment of the overactive bladder. Urology 2001;57:414–421.

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