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EFFICACY AND SAFETY OF TOLTERODINE IN A PREDOMINANTLY CONTINENT POPULATION OF MALE PATIENTS WITH OVERACTIVE BLADDER AND NOCTURIA

Hypothesis / aims of study

Tolterodine extended release (TER) is indicated for overactive bladder (OAB), characterized by the symptoms of urinary urgency with or without urgency urinary incontinence (UUI), usually with frequency and nocturia. We evaluated the efficacy and safety of night-time TER dosing in predominantly continent male patients with OAB and nocturia. Data were stratified according to the urgency rating associated with each micturition to investigate the efficacy of TER for OAB (urgency-related) micturitions.

Study design, materials and methods

This was a post hoc analysis of data from two 12-week placebo (PBO)–controlled trials of night-time (≤4 h before bed) TER (4 mg QD) dosing in patients with urinary frequency (≥8 micturitions/24 h) and nocturia (mean ≥2.5 episodes/night). Efficacy was evaluated using 7-day micturition diaries. Patients also recorded their sleep cycle and the time of each awakening associated with a micturition or UUI episode. All micturitions during the sleep cycle were considered nocturia. Urgency associated with each micturition was recorded using a 5-point urgency rating scale: 1 = "I felt no need to empty my bladder but did so for other reasons," 2 = "I could postpone voiding as long as necessary without fear of wetting myself," 3 = "I could postpone voiding for a short time without fear of wetting myself," 4 = "I could not postpone voiding but had to rush to the toilet in order not to wet myself," and 5 = "I leaked before arriving at the toilet." [1] By description, micturitions associated with an urgency rating of 1 and 2 were non-urgency; micturitions associated with a rating of 3 were borderline urgency (were or were not associated with urgency depending on how the patient interpreted "a short time"), and micturitions associated with ratings of 4 and 5 were clearly associated with urgency. A rating of 5 was counted as a UUI episode and a micturition. Individual patient micturitions were categorized as: total micturitions (urgency rating 1–5), non-OAB micturitions (1–2), OAB micturitions (3-5), and severe OAB micturitions (4–5). All adverse events (AEs) were recorded.

Results

745 men (mean age, 64 y) were randomized to PBO (n=374) or TER (n=371). 73% of patients were continent (0 UUI episodes/wk at baseline). By week 12, night-time severe OAB micturitions were reduced significantly in TER vs PBO patients, as were 24-hour and daytime total, OAB, and severe OAB micturitions (**Table**). TER significantly reduced mean urgency rating (**Table**). AEs associated with TER vs PBO were low and included dry mouth (11% vs 4%), constipation (2% vs 2%), and urinary retention (1% vs 1%). Withdrawals (3% vs 4%) were also low.

Interpretation of results

These results demonstrated that TER significantly reduced night-time severe OAB micturitions and daytime and 24-hour OAB and severe OAB micturitions. TER did not affect non-OAB micturitions, which is consistent with its mechanism of action. These results strongly suggest that assessment of urgency associated with each micturition should be captured in micturition diaries. OAB-related micturitions may be the most meaningful objective endpoint for the evaluation of drug efficacy in the treatment of OAB. Night-time dosing with TER was associated with few AEs and AE-related withdrawals. A previous study reported higher rates of dry mouth (23%), constipation (6%), and headache (6%) among patients who took TER during daytime hours [2]. Although the comparative study populations are different, lower AE rates in this study may suggest that, in addition to maintaining 24-hour efficacy, night-time dosing may reduce the AEs associated with TER. It is likely that the AE rates associated with nighttime TER dosing were lower because peak serum concentration was reached while patients were sleeping.

Concluding message

In this predominantly continent population of male patients with OAB and nocturia, night-time dosing with TER significantly reduced urgency-related micturitions without affecting non-OAB micturitions. Efficacy was maintained over 24 hours. TER was associated with few AEs and withdrawals owing to AEs, suggesting that night-time TER dosing may reduce the overall occurrence of AEs.

Table. Summary of Results

	PBO (n=374)			TER (n=371)		
	Mean Micturitions/wk		Median	Mean Micturitions/wk		Median
	Baseline	Δ	% Δ	Baseline	Δ	% Δ
Night-time						
Total	24.4	–4.4	–17.6	24.1	–4.4	–18.8
OAB	15.9	–3.1	–22.2	16.0	–4.2†	–27.3††
Severe OAB	5.8	–1.6	–50.0	5.9	–2.8*	–77.8*
Daytime						
Total	67.1	–3.6	–5.6	66.6	–6.7*	–8.7*
OAB	39.1	–3.1	–8.5	38.2	–5.7††	–12.5*
Severe OAB	13.0	–2.1	–37.5	12.2	–4.9*	–62.9*
24 hour						
Total	91.5	–8.0	–7.9	90.7	–11.0*	–10.8*
OAB	55.0	–6.2	–9.5	54.3	–9.9*	–16.7*
Severe OAB	18.8	–3.7	–41.2	18.1	–7.7*	–68.2*
	Mean Δ in Urgency Rating					
24 hour	–0.03				–0.12*	
Night-time	–0.03				–0.17**	
Daytime	–0.02				–0.09*	

*P<0.05; **P<0.001; †P=0.06; ††P=0.07.

References

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