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Dmochowski, R. [1], Davila, W. [2], Sanders, S. [3]
1. Vanderbilt University, 2. Cleveland Clinic Florida, 3. Watson Laboratories, Inc.

TRANSDERMAL OXYBUTYNIN AND CONTROLLED-RELEASE ORAL TOLTERODINE IN PATIENTS WITH POSITIVE TREATMENT EFFECT TO ANTICHOLINERGIC THERAPY FOR OVERACTIVE BLADDER

Aims of Study

Treatment choice for overactive bladder (OAB) includes transdermal and oral controlled-release products. Comparative studies are required to guide treatment selection for individual patients. The objective of this investigation was to compare the safety and efficacy of oxybutynin (OXY) transdermal delivery system (TDS) versus active (tolterodine controlled release) and placebo in the treatment of OAB patients who had previously achieved a positive treatment effect from anticholinergic agents for up to 1 year of therapy.

Methods

Adult OAB patients with prior beneficial response to pharmacological treatment of OAB (>1 year) were enrolled at 48 US centers. Following treatment withdrawal, a baseline (BL) evaluation was conducted using a 3-day urinary diary. Inclusion criteria were ≥ 4 daily incontinent episodes (UI), ≥ 24 daily voids, and < 350 mL average voided volume. Patients (361) were 92% female, 95% Caucasian, aged 63±13 years, >60% had mixed incontinence. Randomized, blinded treatment included oral controlled-release tolterodine (TOL-CR 4 mg QD), OXY-TDS (3.9 mg/d twice weekly), or matched placebo (PL) for 12 weeks. Changes from baseline for diary parameters and QoL (IIQ) were determined. Statistical analysis was performed using ANCOVA (QoL), confidence intervals (active treatments) and chi-square (adverse events (AE)).

Results

Of the 361 patients, 41 withdrew, 23 due to AEs. UI episodes, frequency, volume, and QoL improved significantly for active treatments compared to PL (Table). Complete continence was achieved in 38% of TOL-CR and 40% of OXY-TDS patients (cf 22% of PL). Dry mouth was reported more frequently for TOL-CR (7.3%, p=0.04 vs placebo 1.7%) than OXY-TDS (4.1%, p=0.27 vs placebo). Most common treatment-related AE was application site pruritus for OXY-TDS (14.0%) and dry mouth for TOL-CR (7.3%). Additional anticholinergic adverse events included: constipation (PL = 1.7%, TOL-CR = 5.7%, & OXY-TDS = 4.1%), abnormal vision (PL = 0.9%, TOL-CR = 0.8%, & OXY-TDS = 2.5%), nausea (PL = 0.9%, TOL-CR = 1.6%, & OXY-TDS = 0.8%), and dizziness (PL = 0.9%, TOL-CR = 2.4%, & OXY-TDS = 0.8%).

Change from Baseline*[1]	**PL**	**TOL-CR*[2]**	**OXY-TDS*[3]**
Daily UI Episodes	-2 (2.1±2.9)	-3 (-3.2±2.8)	-3 (-2.9±3.0)
- p vs placebo		p=0.0027	p=0.0329
		90% CI (median): -1.0 – 0.0	
Daily Frequency	-1 (-1.2±2.7)	-2 (-2.2±2.6)	-2 (-2.0±2.7)
- p vs placebo		p=0.0005	p=0.0405
Average Void Volume	5 (9±63)	29 (29±57)	23 (31±55)
- p vs placebo		p = 0.0021	p=0.002
IIQ*[4] Total Score	-29 (-43±92)	-57 (-72±86)	-55 (-68±85)
- p vs placebo		p=0.0193	p=0.0271

*[1] median (mean ± SD), *[2] Detrol LA 4 mg QD, *[3] TDS Oxybutynin 3.9 mg/d twice weekly,
*[4] Incontinence Impact Questionnaire

Conclusions

In the treatment of OAB patients having shown previous treatment benefit from anticholinergic agents, both OXY-TDS and TOL-CR were directly comparable, with no statistical difference in efficacy between treatments for OAB. However the incidence of dry mouth was significantly greater in the TOL-CR treated patients when compared to placebo (P = 0.04). OXY-TDS was also associated with fewer incidences of constipation, nausea, and dizziness when compared to TOL-CR, although this difference was not statistically significant. The greater incidence and relative risk of systemic anticholinergic side effects must be weighed against local application site reactions to reach the appropriate treatment choice for individual patients.