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THE EFFICACY, EFFECTIVENESS, AND SAFETY OF TRANSDERMAL OXYBUTYNIN IN PATIENTS WITH OVERACTIVE BLADDER

Aims of Study

Oxybutynin (OXY) is a mainstay in the treatment of overactive bladder (OAB). In its oral form, the drug undergoes extensive hepatic and gastrointestinal presystemic metabolism to form a primary active metabolite, *N*-desethyloxybutynin (DEO). This metabolite is present in the circulation at levels 4 to 10 times higher than that of the parent compound and appears to be responsible for many of the drug's anticholinergic adverse events (AEs). Transdermal delivery of OXY, which avoids presystemic metabolism, produces a DEO concentration that is only 1.5 times greater than parent, and subsequently generates fewer anticholinergic AEs comparable to placebo while providing efficacy that is comparable to that of oral formulations. The aim of this investigation is to compare the safety and efficacy of OXY transdermal delivery system (OXY-TDS) versus placebo during 12 weeks of treatment.

Methods

Pooled data from 2 placebo-controlled studies:
Study 1 is a double-blind, placebo-controlled study of 249 urge urinary incontinence (UI) patients. Study 2 is a double-blind, active- and placebo-controlled study of 238 urge and mixed UI patients. Symptom requirements recorded in 3-day and 7-day urinary diaries for Studies 1 and 2, respectively, after prestudy treatment washout, included 10 or more urge UI episodes in study 1 and 4 or more episodes in study 2; 56 or more voids in study 1 and 24 or more voids in study 2; and 350 mL or less urinary void volume in both studies. The efficacy end points of this study were the change from baseline to end point in the number of incontinence episodes, comparisons of daily urinary frequency, and urinary void volume. The safety end points were the confirmation of continued efficacy and continued adherence to therapy. As OXY-TDS continuously releases OXY over a 3.5 to 4 day period, OXY-TDS 3.9 mg/day or matching placebo system was applied to the abdomen twice weekly. Patients were 91.9% female, 92.4% Caucasian, and had a mean age of 62.4 years, with 49.8% of patients 65 years and older; 40.6% had no previous anticholinergic experience.

Results

Urinary incontinence episodes, frequency, and void volume improved significantly for active treatment versus placebo (Table 1). The most common AE for OXY-TDS was localized application site pruritus and erythema accompanied by a low incidence of systemic anticholinergic side effects comparable to that of placebo (Table 2). Most patients presented AEs that were mild to moderate in severity. Of the 487 patients, 30 (6.2%) withdrew – OXY, 27 (11.2%); placebo, 3 (1.2%) – due to drug-related AEs.

Combining both the active treatment and placebo arms of the study, most patients (83.9%) experienced no application site reactions during the study. Similarly, most patients in the OXY-TDS arm (93% vs. 94.7% for placebo) experienced no dry mouth.

Table 1: Changes From Baseline in Adult Patients With Overactive Bladder Who Received OXY-TDS or Placebo for up to 12 Weeks

End Points – Change From Baseline*	**OXY-TDS 3.9 mg/d 2x/wk***	**Placebo***	***P* value (vs Placebo)**
Daily UI episodes	-2.9 ± 2.77	-2.4 ± 3.05	.0004
Average daily urinary frequency	-2.1 ± 2.59	-1.56 ± 2.83	.0023
Average urinary void	31.8 mL ± 60.34 mL	9.9 mL± 59.87 mL	<.0001

volume			

* Mean ± SD

Table 2: Treatment-Emergent Adverse Events

Adverse Event	**OXY-TDS 3.9 mg/d (N=242)**	**Placebo (N=245)**
Dry mouth	17 (7.0%)	13 (5.3%)
Constipation	5 (2.1%)	5 (2.0%)
Diarrhea	6 (2.5%)	5 (2.0%)
Application site pruritus	39 (16.1%)	13 (5.3%)
Application site erythema	17 (7.0%)	6 (2.4%)

Conclusions

OXY-TDS 39 mg/day administered in a twice-weekly regimen is an effective, safe, and well-tolerated treatment for patients with symptoms of OAB. The significant mean reductions in the number of incontinence episodes and urinary frequency, along with the increase in void volume, support the efficacy of the transdermal system. OXY-TDS was associated with a low incidence of anticholinergic AEs, comparable to placebo. Local application site reactions were consistent with those observed in the safety profile of other matrix transdermal systems and are generally mild to moderate (pruritus and erythema). These combined efficacy and tolerability data suggest that OXY-TDS confers unique clinical effectiveness in the management of patients with OAB.