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SIGNIFICANT DECREASES IN PERCEPTION OF URGENCY AND URGE INCONTINENCE EPISODES WITH ONCE-DAILY TOLTERODINE TREATMENT IN PATIENTS WITH OVERACTIVE BLADDER

Aims of Study: Antimuscarinic agents are known to reduce urge incontinence in patients with overactive bladder, but less attention has been paid to the effect on perception of urgency. Tolterodine is a muscarinic receptor antagonist with selectivity for the bladder over other body tissues. The aim of this study was to examine the effect on urgency of a new, once-daily (OD) formulation of tolterodine.

Methods: A total of 1015 overactive bladder patients (81% female), diagnosed exclusively based on symptoms and average volume voided, were randomised into a double-blind, parallel-group, placebo-controlled, multinational, multicentre study comparing tolterodine 4 mg OD (n=507) and placebo (n=508). Patients were treated for 12 weeks after a 7-day washout (for patients currently on other treatments) and a 7 day run-in period (to collect baseline micturition diary information). Efficacy was assessed primarily with micturition diaries but also with patient perception evaluations. Tolerability profiles were determined through adverse event reports.

Results: Overall, 39% of patients treated with tolterodine 4 mg OD reported improvement in their urgency symptoms, and 58% reported improvement in their bladder condition. Both of these results were statistically significant compared to placebo.

As expected, treatment with tolterodine 4 mg OD produced a statistically significant decrease in urge incontinence episodes compared to placebo. Other micturition diary variables were also significantly improved compared to placebo (see Table).

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Percent change from baseline in micturition variables after 12 week's treatment

Variable	Tolterodine 4 mg OD	Placebo	P value
Urge incontinence	-53%	-30%	0.0001
Micturitions	-17%	-11%	0.0047
Volume voided	+24%	+10%	0.0001

Treatment with tolterodine 4 mg OD was well tolerated. More patients on placebo withdrew from treatment due to adverse events than tolterodine-treated patients (6.5% vs 5.3%). Dry mouth was reported by a total of 23% (2% severe) of tolterodine recipients, compared to 8% of placebo-treated patients. The next most common adverse events were headache (6% tolterodine; 5% placebo) and constipation (6% tolterodine; 4% placebo). No safety concerns were noted during the study.

Conclusions: The new OD formulation of tolterodine is highly effective, safe and well tolerated in the treatment of overactive bladder. The effect on urgency and other patient perceptions is interesting and merits further study.

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Title (type in CAPITAL LETTERS, leave one blank line before the text):

EFFECT ON SALIVARY OUTPUT FOLLOWING CONTROLLED-RELEASE OXYBUTYNIN AND TOLTERODINE.

Aims of Study. Both tolterodine (TOL) and controlled-release oxybutynin (OXY-XL) have been separately shown to be effective in the treatment of overactive bladder. Both OXY-XL and TOL have been shown to be associated with less dry mouth than conventional immediate-release oxybutynin (IR-OXY); however, these treatments have not been directly compared in a controlled study. Saliva output studies following all three treatments have been separately reported but differences in study methodology prevent comparison across studies. This is the first study that objectively evaluates dry mouth as measured by saliva output following the three medications and placebo.
Methods. This was a randomized, double-blind, four-treatment, four-period, crossover study. The four treatments were single doses of OXY-XL (10 mg), IR-OXY (5 mg), TOL (2 mg), and placebo, with a 5-7 day washout period between treatments. Saliva output (stimulated by chewing parafilm) was collected in a beaker over a 2-minute period at 1 to 2 hour intervals for 12 hours after dosing. Saliva output integrated as area under the curve (AUC) and the lowest saliva value production (TROUGH) over the 12-h period was estimated.
Results. All three medications resulted in significantly lower saliva AUC compared to placebo. OXY-XL and TOL were similar with respect to saliva AUC but significantly higher than IR-OXY (Table 1 & 2). All three medications also resulted in significantly lower saliva TROUGH compared to placebo. The lowest TROUGH value was observed with TOL followed by IR-OXY, OXY-XL and placebo (Table 1).

Table 1: Mean (SD) Saliva Production Parameters

Saliva Parameter	OXY-XL	TOL	IR-OXY	Placebo
AUC (g.h)	30 (15)	29 (17)	27 (15)	33 (17)
TROUGH (g/2min)	1.7 (1.0)	1.4 (0.9)	1.5 (0.9)	2.0 (1.1)

Table 2: Statistical Comparison (p-values)

Saliva Parameter	Active vs. Placebo	OXY-XL vs. IR-OXY	TOL vs. IR-OXY	OXY-XL vs. TOL
AUC (g.h)	<0.01	0.01	0.005	0.80
TROUGH (g/2min)	<0.001	0.05	0.96	0.06

Conclusion. This study showed that 10 mg controlled-release oxybutynin and 2 mg tolterodine appear to be similar with respect to dry mouth as measured by salivary output and associated with less dry mouth than 5 mg immediate-release oxybutynin.
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Title (type in CAPITAL LETTERS, leave one blank line before the text): RESIDUAL URINE AND URINARY RETENTION DUE TO ANTICHOLINERGIC THERAPY ? - RESULTS WITH PROPIVERINE