395

Abrams P [1], Kaplan S[2], Wang J [3], Guan Z[3]
1. Southmead Hospital, 2. Columbia University, 3. Pfizer Inc

EFFICACY, SAFETY, AND TOLERABILITY OF TOLTERODINE FOR OVERACTIVE BLADDER: COMPARABLE PROFILES BETWEEN MALE AND FEMALE PATIENTS

Hypothesis / aims of study

Clinical trials designed to evaluate the clinical effectiveness of antimuscarinics, including tolterodine tartrate, for overactive bladder (OAB) have demonstrated favorable results in predominantly female study populations; male patients typically represent ≤25% of those enrolled. Still, a large number of men in the general population experience lower urinary tract symptoms consistent with OAB [1,2] and would likely benefit from treatment. Because few prospective trials have directly evaluated the potential influence of gender on treatment outcomes, we conducted exploratory subanalyses of data collected during 4 pivotal clinical trials of tolterodine to obtain a better understanding of the relative efficacy, safety, and tolerability profiles of this antimuscarinic in male and female patients with OAB.

Study design, materials and methods

This was a retrospective subanalysis of data collected from: (1) three 12-week randomized placebo-controlled trials of tolterodine immediate release (IR; 2 mg twice daily) in patients with symptoms of urgency, frequency (≥8 micturitions/24 h), and/or incontinence, and (2) a 12-week trial of tolterodine extended release (ER; 4 mg once daily) in patients with symptoms of urgency, frequency (as above), *and* incontinence ≥5 incontinence/wk). Changes from baseline to week 12 in the number of micturitions/24 h, mean voided volume (mL)/micturition, and the number of incontinence episodes/wk were efficacy endpoints. Adverse events (AEs) were recorded for the duration of all studies.

Results

For the 3 tolterodine IR trials involving patients with or without incontinence, efficacy data from 125 male (mean age, 63 years) and 408 female patients (mean age, 59 years) were analyzed. By week 12, both male (n=78) and female patients (n=278) who received tolterodine IR showed statistically significant decreases in the number of micturitions/24 h and significant increases in voided volume/micturition compared with those who received placebo (n=47 and n=130, respectively). For the tolterodine ER trial involving patients with incontinence, male and female patients who received tolterodine ER (n=77 and n=369, respectively) showed a statistically significant decrease in the number of incontinence episodes/week compared with incontinent patients who received placebo (Table 1). Commonly reported AEs are summarized in Table 2. The tolerability profiles of male and female patients were comparable. Although the sample size of male patients was relatively small, numerically, men appeared to tolerate tolterodine ER slightly better that women did. Importantly, few patients of either gender reported urinary retention or urinary tract infection.

Interpretation of results

Although this was a retrospective analysis, the results suggest that tolterodine is equally effective and well tolerated in male and female patients with OAB. Patients with or without incontinence who received 12 weeks of tolterodine IR showed significant improvements in their OAB symptoms relating to frequency and volume per void compared with those who received placebo. Tolterodine ER effectively reduced the number of incontinence episodes in both male and female patients with urge incontinence. Both formulations of tolterodine appeared to be safe and well tolerated in both men and women.

Concluding message

The results of these exploratory analyses suggest that tolterodine has comparable efficacy in men and women. Men appeared to tolerate tolterodine ER slightly better than did women. Both formulations improve the symptoms of OAB with minimal adverse effects.

Table 1. Summary of Pooled Efficacy Results for Male and Female Patients

	Men				Women			
	Median % change				Median % change			
Measure of efficacy	**PBO**	**T–IR**	**T–ER**	***P* value***	**PBO**	**T–IR**	**T–ER**	***P* value***
Micturitions/24 h	–5.1	–15.9		0.006	–12.4	–18.5		<0.001
Voided volume/M (mL)	4.8	15.4		0.008	6.0	21.4		<0.0001
Incontinence episodes/wk	–39.9		–71.4	0.046	–31.0		–71.4	<0.0001

ER=extended release; IR=immediate release; M=micturition; PBO=placebo; T=tolterodine.
*Tolterodine versus placebo.

Table 2. Commonly Reported Adverse Events in Male and Female Patients

	Men			Women		
Adverse event	**PBO (n=133)**	**T–IR (n=78)**	**T–ER (n=77)**	**PBO (n=501)**	**T–IR (n=278)**	**T–ER (n=369)**
Dry mouth, %	11	38	16	10	40	25
Constipation, %	8	8	4	4	6	7
Somnolence, %	2	3	3	2	3	3
Dyspepsia, %	<1	5	4	1	7	3
Abnormal accommodation, %	2	3	0	1	4	0
Urinary retention, %	0	0	1	<1	1	0
Urinary tract infection, %	2	5	1	5	6	4

*Placebo results combined from tolterodine IR and ER studies.
PBO=placebo; T–ER=tolterodine extended release; T–IR=tolterodine immediate release.

References

1. Prevalence and burden of overactive bladder in the United States. World J Urol 2003;20:327-336.
2. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. BJU Int 2001;87:760-766.

FUNDING: Pfizer Inc