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CLINICAL EFFICACY AND SAFETY OF TOLTERODINE EXTENDED RELEASE IN MALE PATIENTS WITH OVERACTIVE BLADDER AND URGENCY URINARY INCONTINENCE

Hypothesis / aims of study
Overactive bladder (OAB) is characterized by the symptoms of urinary urgency with or without urgency incontinence, usually with frequency and nocturia. In the United States[1] and Europe,[2] OAB affects approximately 16% of men and 17% of women. Based on the results of 1 study,[1] approximately 16% of men with OAB experience urgency urinary incontinence (UUI), and 84% of men with UUI report some degree of symptom bother.[3] Unfortunately, men have been underrepresented in clinical trials of pharmacotherapy for OAB. We evaluated the efficacy and safety of tolterodine extended release (ER) on objective and subjective endpoints in men with OAB and UUI.

Study design, materials and methods
This was a post hoc analysis of data from incontinent men with OAB who were enrolled in a 12-week, randomized, double-blind, placebo-controlled trial of tolterodine ER performed at 167 centers in Australia, Europe, and North America. Eligible patients were ≥18 years of age with symptoms of urinary frequency (≥8 micturitions/24 h) and UUI (≥5 episodes/wk) for ≥6 months. Patients received once-daily treatment with placebo or tolterodine ER (4 mg). Micturition diaries were completed for the 7 days before the baseline visit and again before the last dose of study medication. All micturitions and UUI episodes were recorded at the times they occurred. Patient perception of treatment benefit was evaluated at week 12 using a 2-step assessment and ordered categorical scale. Adverse events (AEs) were recorded throughout the study. Data are reported as medians owing to the non-normal distribution of data. Median percentage change in UUI episodes from baseline to week 12 were analyzed using a rank analysis of covariance model fitted with terms for baseline values and treatment. Patient perception of overall treatment benefit was analyzed using a 2-sided chi-square test.

Results
163 (placebo=86, tolterodine ER=77) incontinent (mean UUI ≥5 episodes/wk at baseline) men with OAB were evaluated. Mean ± SD ages for the placebo and tolterodine ER groups were 66±14 and 64±16 years, respectively. Patients were predominantly white (placebo, 98%; tolterodine ER, 96%). At baseline, men receiving placebo and tolterodine ER reported 21 and 22 mean weekly UUI episodes, respectively. Compared with placebo, tolterodine ER significantly reduced weekly UUI episodes (median % change, –71% vs –40%, $P<0.05$). A significantly larger number of tolterodine ER- (63%) versus placebo-treated patients (46%) reported a benefit of treatment ($P<0.05$). AEs reported by ≥2% of men in the tolterodine ER vs placebo group included dry mouth (16% vs 7%), constipation (4% vs 9%), headache (3% vs 5%), flatulence (3% vs 4%), dizziness (5% vs 1%), dyspepsia (4% vs 1%), somnolence (3% vs 1%), and diarrhoea (0% vs 2%). The occurrence of acute urinary retention was low (1% vs 0%).

Interpretation of results
Compared with placebo, tolterodine ER significantly reduced UUI episodes and improved patient perception of treatment benefit in male patients with OAB and UUI. Tolterodine ER was safe and well tolerated in men with OAB and was not associated with an increased risk of urinary retention. These results negate the clinical concern that the inhibitory effect of muscarinic receptor antagonists on detrusor muscle contraction could theoretically aggravate the voiding difficulties of, or cause urinary retention in men with OAB symptoms.

Concluding message
This analysis suggests that tolterodine ER is a safe and efficacious treatment option for men with OAB and UUI.

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