

TOLTERODINE EXTENDED RELEASE AND SEXUAL QUALITY OF LIFE, ANXIETY, AND DEPRESSION AMONG WOMEN WITH OVERACTIVE BLADDER AND URGENCY URINARY INCONTINENCE

Hypothesis / aims of study

The more women are bothered by overactive bladder (OAB) and urgency urinary incontinence (UUI) symptoms the less likely they are to enjoy sexual activity and the more likely they are to experience sexual dysfunction. Because tolterodine extended release (TER) has proven efficacy for OAB symptoms, we evaluated whether TER would improve sexual function and decrease depression and anxiety, as measured by validated questionnaires, relative to placebo.

Study design, materials and methods

This was a multicenter, 12-week, double-blind, PBO-controlled, randomized trial. Eligible female outpatients (≥ 18 y) had self-reported OAB (≥ 8 voids per 24 h, ≥ 3 urgency-related micturitions per 24 h) and UUI (mean of ≥ 0.6 episodes per 24 h) for ≥ 3 months and rated their bladder condition as causing at least "some moderate problems." Patients described themselves as being sexually active and in a stable relationship with a male partner for ≥ 6 months. Patients were randomized to once-daily TER (4 mg; n=216) or PBO (n=220). At baseline and week 12, patients completed 5-day bladder diaries and 3 validated questionnaires: the Sexual Quality of Life Questionnaire-Female (SQOL-F; higher scores indicate better function, and scores < 75 indicate impaired function), Pelvic Organ Prolapse/Urinary Incontinence Sexual Function (PISQ; higher scores indicate better function), and Hospital Anxiety and Depression scale (HAD; lower scores indicated better function, and scores ≥ 8 are associated with a clinical diagnosis of anxiety and depression). Patients rated the urgency level associated with each micturition on a scale from 1 (no urgency) to 5 (UUI) in their bladder diaries; frequency-urgency sum was defined as the sum of these urgency ratings. The primary endpoint was the change from baseline to week 12 in UUI episodes per 24 hours. Secondary endpoints included other bladder diary variables and sexual, depression, and anxiety quality-of-life measures.

Results

413 patients (mean \pm standard deviation [SD] age, 48 ± 12 y) were randomized; 372 (90%) received ≥ 1 dose of study medication and had ≥ 1 postbaseline efficacy assessment. Of those randomized, 12% were nulliparous and 51% were postmenopausal. At baseline, mean \pm SD SQOL-F scores were 69.2 ± 23.0 and 69.6 ± 23.1 in the PBO and TER groups, respectively, indicating impaired sexual function. Additionally, 59% and 27% of women had HAD Anxiety and Depression scores ≥ 8 , respectively, at baseline. By week 12, TER- vs PBO-treated patients showed reduced least squares (LS) mean \pm standard error (SE) UUI episodes (-1.8 ± 0.1 vs -1.4 ± 0.1 ; $P=0.003$), urinary frequency (-3.3 ± 0.2 vs -2.3 ± 0.2 ; $P=0.0006$), frequency-urgency sum scores (-17.6 ± 0.9 vs -11.5 ± 0.9 ; $P<0.0001$), and pad use per 24 hours (-1.5 ± 0.1 vs -1.0 ± 0.1 ; $P=0.0024$). By week 12, both TER- and PBO-treated patients showed improvement in mean \pm SE change in SQOL-F total scores; however, the change was greater in the TER group (TER, 6.4 ± 1.2 vs PBO, 1.5 ± 1.2 ; $P=0.0042$). PISQ Physical domain and total scores also showed greater change in the TER group (**Figure 1**). At week 12, LS mean HAD Anxiety and Depression scores improved among both TER- and PBO-treated patients; improvement in HAD Anxiety scores was significantly greater in the TER group versus PBO (**Figure 2**).

Figure 1. PISQ Results

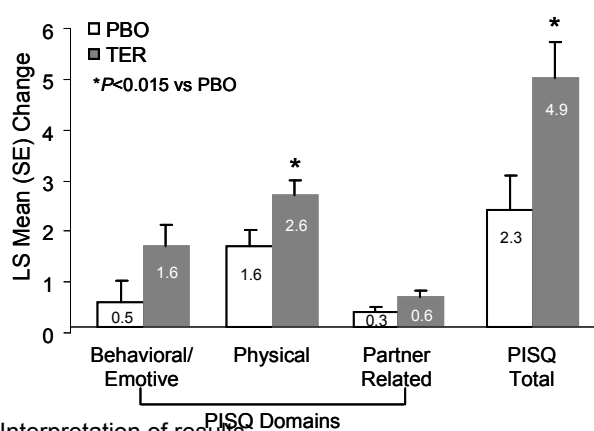
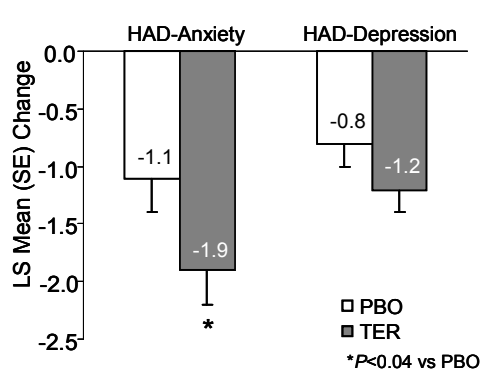


Figure 2. HAD Results



Interpretation of results

As expected, TER (vs PBO) improved the OAB symptoms of UUI, frequency, urgency, and pad use as recorded in bladder diaries. TER-treated patients also had improved sexual function and HAD Anxiety scores but did not show significant improvement in HAD Depression scores vs PBO. This may be because few patients had depression at baseline.

Concluding message

After 12 weeks, TER improved both OAB symptoms and sexual quality of life in women with OAB and UUI. TER also improved measures of anxiety but not depression. It appears that nonurologic aspects of a woman's life, including

sexual quality of life and psychological health, may affect her response to treatment, and these factors should be investigated in larger controlled trials.

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CLINICAL TRIAL REGISTRATION: Clinical Trials Registry - #NCT00143481

HUMAN SUBJECTS: This study was approved by the Schulman Associates and followed the Declaration of Helsinki Informed consent was obtained from the patients.