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Gittelman M[1], Swift S[2], Forero-Schwanhaeuser S[3]
1. South Florida Medical Research, 2. Medical University of South Carolina, 3. GlaxoSmithKline

SOLIFENACIN TREATMENT IN PATIENTS REPORTING SEVERE SYMPTOM BOTHER WHILE TAKING TOLTERODINE: EFFECTS ON PATIENT-REPORTED OUTCOMES

Hypothesis / aims of study

Overactive bladder (OAB) is a symptom-based syndrome, and its clinical management relies largely on reporting of symptoms by patients.[1] Consequently, the value placed on patient-reported outcome (PRO) measures in the clinical management of OAB is increasing. Several PRO tools have been validated to assess symptom bother and health-related quality of life (HRQL) in patients with OAB. In the VESIcare Efficacy and Research Study US (VERSUS), patients experiencing residual urgency while being treated with tolterodine were transitioned to solifenacin to determine any changes in symptoms and PROs. Here we report outcomes specifically in a cohort of patients on tolterodine and experiencing severe symptom bother.

Study design, materials and methods

VERSUS was a 12-week, open-label study of flexibly-dosed solifenacin in patients who had OAB for at least 3 months and who had received tolterodine ER 4 mg for 4 weeks or longer without satisfactory improvement in episodes of urgency. Residual urgency was defined as a mean of 3 or more urgency episodes per 24 hours, while taking tolterodine. After a 14-day "washout" period, patients began taking solifenacin 5 mg/day. At Week 4, in consultation with the physician, they could maintain or increase their dose to 10 mg/day, and at Week 8, they could maintain or decrease their dose to 5 mg/day. Episodes of OAB symptoms were recorded in 3-day diaries immediately before washout, after washout, and at weeks 4, 8, and 12. PRO measures included the Patient Perception of Bladder Condition (PPBC) and the Overactive Bladder Questionnaire (OAB-q), which have been validated for the assessment of symptom bother and HRQL[2] and test-retest reliability.[3] This post hoc analysis included data from patients with severe OAB, defined at baseline by a score of 5 or greater on the PPBC scale. We compared PRO values while patients were taking tolterodine (pre-washout baseline) to results at end of study (12 weeks).

Results

In the full-analysis set population, patients in this cohort with severe symptom bother (n=165) had a mean age of 61.8 years (40.6% age 65 or older) and were mostly female (90.3%), demographics comparable to the full VERSUS population (n=440). At Week 4 of solifenacin treatment, 100 patients (about 60%) in this severe-symptom cohort increased their dose to 10 mg/day. At Week 8, a majority of these patients (83 out of 100) remained on the 10-mg dose of solifenacin, while 9 returned to the 5-mg dose; 54 patients remained on their original 5-mg dose.

Overall, 80% of patients with severe OAB symptom bother reported PPBC score improvements relative to pre-washout baseline (BL). For this cohort, the mean PPBC score was 5.3 at BL, which corresponds to a designation of "severe to many severe problems." After 12 weeks of treatment with solifenacin, the PPBC score was 3.5 (a mean change of –1.8; 95% CI –2.0 to –1.5), corresponding to a designation of "minor to moderate problems." On the OAB-q, score improvements from BL are shown in the Table.

OAB-q Domains	Baseline Score (Pre-washout)	Change from Baseline	95% Confidence Interval
Symptom bother*	66.7	–33.2	–37.3, –29.0
Coping	44.1	29.9	25.3, 34.6
Concern	41.0	32.2	28.0, 36.4
Sleep	40.8	28.0	23.8, 32.2
Social Interaction	72.4	16.3	12.9 to 19.7
Overall HRQL	48.3	27.5	23.8 to 31.2

*Negative score change indicates improvement in the symptom bother domain. (Improvements in all other domains are indicated by positive score changes.)

The PRO improvements for this cohort coincided with reductions in diary-recorded OAB symptoms. Before starting solifenacin, the severe cohort had a mean of 6.8 urgency episodes/day, 11.5 micturitions/day, and 4.0 incontinence episodes/day. By end of study, daily episodes of urgency decreased by a mean of 3.6 episodes/day, micturition by a mean of 1.9 episodes/day, and incontinence by a mean of 2.3 episodes/day.

Interpretation of results

After 12 weeks of treatment with solifenacin, patients with severe symptom bother and residual urgency while taking tolterodine experienced decreases in OAB symptoms (recorded by 3-day diaries). These patients also reported statistically significant improvements from baseline in symptom bother and HRQL, as measured by the PPBC and OAB-q. In particular, for the OAB-q, patients reported reduced symptom bother and improvement in 4 HRQL domains (coping, concern, sleep, and social interaction) as well as the overall HRQL score. In addition, approximately one third of patients in this cohort were able to achieve improved outcomes using the 5-mg dose, thus indicating that 10 mg of solifenacin may not be requisite for treating patients with more severe OAB as defined here.

Concluding message

In patients with severe symptom bother who experienced insufficient symptom relief with tolterodine ER 4 mg, solifenacin at either 5-mg or 10-mg doses reduced OAB symptoms and improved symptom bother and health-related quality of life.

References

1. Urology (2006) 68; 17-28.
2. Eur Urol (2006) 49; 1079-1086.
3. Neurourol Urodyn (2005) 24; 215-225.

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CLINICAL TRIAL REGISTRATION: www.clinicaltrials.gov (currently in process)
HUMAN SUBJECTS: This study was approved by the The protocol and amendments were reviewed and approved by the Institutional Review Boards at each study center or the Copernicus Institutional Review Board. and followed the Declaration of Helsinki Informed consent was obtained from the patients.