

A COMPARISON OF THREE APPROACHES TO ANALYZE URINARY URGENCY AS A TREATMENT OUTCOME

Hypothesis / aims of study

Although urinary urgency is a hallmark symptom of overactive bladder (OAB), there is little consensus on how to measure it. We used 3 approaches to analyze urgency ratings obtained using the European Agency for the Evaluation of Medicinal Products' Committee for Proprietary Medicinal Products' (EMA CPMP) suggested diary urgency rating scale.[1] We evaluated which method would be most sensitive to treatment-related change.

Study design, materials and methods

This was a post hoc analysis of data from a 12-week, placebo-controlled trial of patients with OAB and nocturia treated with tolterodine extended release (ER, 4 mg QD). Per EMA CPMP guidelines, a 5-point urgency rating scale was included in the micturition diaries in which patients rated the level of urgency with each micturition. Levels of urinary urgency were: 1 = no urgency, 2 = mild, 3 = moderate, 4 = severe, and 5 = urgency incontinence. Micturition diaries were completed for 7 days before the baseline and week 12 visits.

Treatment may reduce frequency, urgency, or both; however, the ability to detect this change depends upon how the data are analyzed. To meaningfully capture treatment-related changes, we evaluated 3 methods for analyzing the 5-point EMA CPMP diary urgency rating scale:

1. Mean Urgency = sum of urgency ratings/number of total micturitions.
2. Mode Urgency = most frequent urgency rating was used to categorize the patient. For a change in Mode, the patient had to change their most common urgency rating.
3. Sum Urgency = calculated by summing each urgency rating (implicitly reflecting each patient's urinary frequency)

To illustrate the potential advantages and disadvantages of each analytical approach, **Table 1** presents pre- and post-treatment scores for 3 hypothetical OAB patients. Patient 1 reduced frequency, while remaining unchanged in urgency rating; however, this improvement is only reflected in Sum Urgency. Patient 2 improved slightly in urgency rating while frequency increased. Mean and Mode ratings reflected a change in urgency, whereas the slight change in Sum Urgency balanced the urgency improvement with the increased frequency. Patient 3 improved in urgency and frequency, as reflected by Mean and Sum Urgency; Mode failed to detect change.

Table 1. Examples of Pre-and Post-treatment Micturition Diary Values

	Number of micturitions	Urgency ratings	Mean	Mode	Sum
Pt 1: Pre	10	5,3,3,3,3,2,1,4,4,2	3.0	3	30
Pt 1: Post	8	5,3,3,3,3,2,1,4	3.0	3	24
Pt 2: Pre	12	2,2,2,3,3,3,1,3,3,2,3,2	2.4	3	29
Pt 2: Post	14	2,2,2,3,3,3,1,2,2,2,2,2,3	2.2	2	31
Pt 3: Pre	12	2,2,2,3,4,3,1,2,3,2,3,2	2.4	2	29
Pt 3: Post	10	2,2,2,2,3,2,1,1,2,3	2.0	2	20

Pt=patient.

Change scores for all variables were calculated by subtracting the baseline values from the 12-week values. *T*-tests and analyses of variance using general linear models were performed controlling for treatment group, age, and gender.

Results

Data from 596 patients were analyzed (mean age, 58 y; 86% white). When examining Mode Urgency, the most frequent urgency rating was 3 (49.6%) at baseline. At week 12, Mode Urgency remained unchanged in 63.4% of patients. Sum Urgency reflected the change in diary variables among patients who received tolterodine ER (**Table 2**) with significant differences ($p<0.001$) in micturition diary variables among improvement categories. When comparing micturition variables by patient perception of treatment benefit, Sum Urgency appeared to have greater discrimination (**Table 3**).

Table 2. Change in Micturition Diary Variables¹ by Change in Sum Urgency

Variable	Change in Sum Urgency		
	No Improvement (<0) (n=165)	Slight Improvement (0 to 60) (n=187)	Great Improvement (>60) (n=244)
Micturitions/24 h	0.2±0.2	-1.8±0.1	-4.1±0.1*
Urgency rating	0.3±0.0	0.0±0.0	-0.3±0.0*
Nocturia episodes/night	-0.2±0.1	-0.7±0.1	-1.3±0.1*

¹Least squares means ± standard errors.

All post hoc pairwise comparisons adjusted using Scheffe; * $p<0.001$.

Table 3. Change in Micturition Diary Variables¹ by Patient Perception of Treatment Benefit

Variable	Patient Perception of Treatment Benefit		
	No Benefit (n=218)	Little Benefit (n=166)	Much Benefit (n=157)
Mean Urgency	0.06± 0.03	-0.08± 0.04	-0.19±0.04*
Sum Urgency	-12.36 ± 5.26	-47.86± 6.04	-82.10± 6.25**

¹Least squares means ± standard errors.

All post hoc pairwise comparisons adjusted using Scheffe; * $p<0.01$; ** $p<0.001$.

Interpretation of results

Mode Urgency was not a sensitive indicator of treatment-related change. Mean Urgency did not always accurately reflect patient change (see **Table 1**) and thus may have limited sensitivity. Using Sum Urgency accounted for changes in both frequency and urgency; however, the meaningfulness of this rating as an outcome needs further exploration and refinement.

Concluding message

Sum Urgency, a measure incorporating a combined assessment of frequency and urgency appears to be sensitive and accurate to treatment-related changes in OAB. This combined approach to assessing symptoms may provide a useful measure for assessing the multiple outcomes of OAB treatment.

Reference

1. European Agency for the Evaluation of Medicinal Products. Committee for Proprietary Medicinal Products. Note for Guidance on the Clinical Investigation of Medicinal Products for the Treatment of Urinary Incontinence in Women. Nov 2001.

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