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WHAT IS URGENCY? EXAMINING THE CLINICAL ADEQUACY OF THE ICS DEFINITION OF URGENCY

Hypothesis / aims of study

ICS currently defines urgency as a "sudden compelling desire to pass urine which is difficult to defer". Urgency has been referred to as one of the most bothersome symptoms of overactive bladder. Researchers, clinicians and patients are struggling to capture the definition and gradation of urgency objectively in scales of sensation and perception, in time around a sensation, in time between sensations or simply in number of events that are meaningful and consistent in overactive bladder patients. Until recently, the experience of urge in overactive bladder has been typically described as 'present' or 'absent'. Further, the ICS definition only allows for a present/absent categorization of urgency. However, use of an urgency severity scale that allows for discrimination in the severity of urgency may allow for more accurate measurement of changes in the urgency felt by patients undergoing antimuscarinic treatment. This study is intended to assess whether the current ICS definition is complete in describing the symptom of urgency, or if the use of an urgency severity scale may be required to allow for more accurate measurement of this symptom.

Study design, materials and methods

The Indevus Urgency Severity Scale (IUSS) was developed, validated and used in two large 12-week placebo-controlled, double-blind U.S. studies of trospium chloride enrolling a total of 1157 patients (581 placebo, 575 trospium). The 7-day voiding diary was collected at baseline, and Weeks 1, 4, and 12, and included collection of the IUSS for each toilet void. This scale asked patients to rate their urgency severity prior to each toilet voiding, where:

0: NONE - no urgency
1: MILD - awareness of urgency, but is easily tolerated and you can continue with your usual activity or tasks
2: MODERATE - enough urgency discomfort that it interferes with or shortens your usual activity or tasks
3: SEVERE - extreme urgency discomfort that abruptly stops all activity or tasks

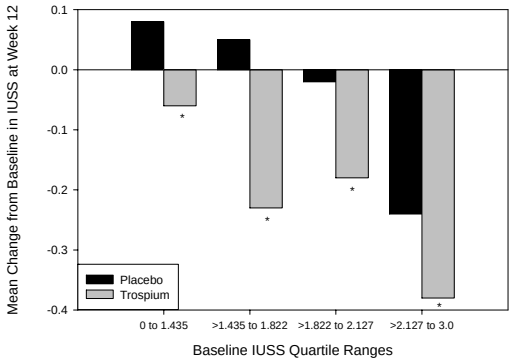
We calculated mean daily urgency severity scores per toilet void within each week for each patient. Using the baseline scores, we determined the average urgency severity quartiles for the total population, and then calculated the change from baseline in urgency severity for each quartile of each treatment group. We also calculated the percent change in the proportion of toilet voids falling into each of the individual IUSS categories (None, Mild, Moderate, Severe). For example, if a patient experienced 10 toilet voids in a given day, and rated the urgency associated with these toilet voids with IUSS values as: 3 mild voids, 4 moderate voids, and 3 severe voids, the proportion of IUSS categories for this patients urgency for that day would be 0% for None, 30% for Mild, 40% for Moderate, and 30% for Severe. These proportions were calculated daily for each patient, and then averaged weekly within each patient. The shift in these weekly proportions (from baseline to Week 12) was expressed as a percent change. Small shifts indicate very little change in the urgency severity experience of patients, while large shifts indicate a distributional change in the urgency severity experience of patients.

Results

The patient population was predominantly female with a mean age of 61 years. Mean daily IUSS scores at baseline were approximately 1.8 (on the scale of 0 to 3) for both treatment groups, indicating a moderate average degree of urgency per toilet void. Baseline quartiles were derived (0 to 1.445, 1.445 to 1.823, 1.823 to 2.134, and 2.134 to 3.00). As expected, patients with a lower severity of urgency at baseline experienced less change from baseline, while patients with a higher severity of urgency at baseline experienced greater change from baseline. However, the treatment effect (the difference between the active and placebo changes within each quartile) was similar across the quartiles (figure 1).

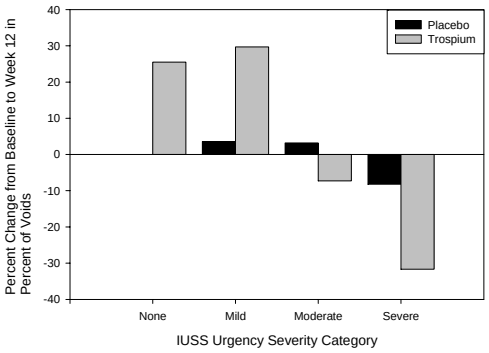
When comparing the proportional distribution of the IUSS severity categories, the trospium group demonstrated a marked shift in the distribution towards lower severity categories from baseline to Week 12, while the placebo group demonstrated no such shift (figure 2).

Figure 1: Mean Change From Baseline to Week 12 in IUSS by Baseline Quartiles (ITT Population, LOCF Data)



Total sample size N=1157, Placebo N=581, Trospium N=575. Thus, baseline quartiles included approximately 145 patients per treatment group per quartile. P-values testing treatment group comparability from an ANOVA.
"*" indicates p-value < 0.05

Figure 2: Percent Change From Baseline to Week 12 in Percent of Voids by IUSS Categories (ITT Population, LOCF Data)



The Placebo group exhibited a 0% percent change from baseline for the 'None' IUSS category, and thus does not have a bar on this graph.

Interpretation of results

Decreases in urgency severity (figure 1) were detected for trospium patients regardless of the level of baseline urgency. This demonstrates that regardless of the baseline location on the scale, an impact of trospium on urgency can be detected. Changes in the distribution of the severity of urgency associated with toilet voids (figure 2) indicated that patients were able to discriminate between severe and less severe urgency episodes, and further, that the IUSS scale was sensitive and detected this distribution shift. Not only did the trospium patients experience a reduction in the number of toilet voids/day (add Delbert and Rudy references), but the trospium patients also experienced a reduction in the proportion of toilet voids that were associated with severe urgency (this reduction was over 30%). In contrast, the placebo patients experienced less than a 10% shift in the proportion of toilet voids that were associated with severe urgency. Further, while the trospium group experienced the reduction in the proportion of toilet voids that were associated with severe urgency, they experienced a corresponding increase in the proportion of toilet voids that were associated with only mild or no urgency.

Concluding message

This study has demonstrated that the current ICS definition may be incomplete in describing the symptom of urgency, and that use of an urgency severity scale with sufficient response gradation may be required to allow for more accurate measurement of this primary symptom. This study supports the argument that a shift in urgency severity from higher to lower severity scores might describe a clinically meaningful change in urgency severity, and may in part explain the improvements in quality of life (as measured by the IIQ) reported by trospium-treated patients. Based on these findings, patient perceptions in urgency are sensitive to severity changes, and the ICS definition may require revision to incorporate this new understanding of patient perception.

References

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FUNDING: Indevus Pharmaceuticals, Inc.