

## EFFECT OF A FIXED DOSE OF EXTENDED-RELEASE OXYBUTYNYN ON URGE AND NON-URGE URINARY INCONTINENCE

### Hypothesis / aims of study

One of the key symptoms of overactive bladder (OAB) is urge urinary incontinence (UUI). However, many OAB patients additionally present with incontinence episodes that are not associated with urgency. This is reflected in the protocols of several recent trials of OAB medications that permit the enrollment of patients with urge-dominant mixed incontinence. These patients are likely to experience greater symptom severity than are patients with UUI alone. Results of these trials support the use of an antimuscarinic agent in treating the dominant urge component in such patients. We investigated whether there were differential effects of treatment with a fixed dose of extended-release (ER) oxybutynin between OAB patients reporting only urge incontinence episodes and those reporting both urge and non-urge episodes.

### Study design, materials and methods

Data were pooled from the OBJECT [1] and OPERA [2] trials, two 12-week, multicenter, randomized, double-blind studies that compared ER oxybutynin 10 mg daily with either immediate-release tolterodine 2 mg bid (OBJECT) or ER tolterodine 4 mg once daily (OPERA) in patients with OAB and UUI, or mixed incontinence with a predominant urge component. This post hoc analysis focused specifically on outcomes for patients treated with ER oxybutynin. Overall reduction in incontinence episodes for patients reporting only urge episodes was compared with that for patients with both urge and non-urge episodes. In addition, the effect of treatment on urge versus non-urge episodes was examined in the latter group.

### Results

Final on-therapy assessments were available for 559 of 576 patients treated with ER oxybutynin in the 2 studies. Of these, 265 (47.4%) reported only urge episodes at baseline (Group 1), and 294 (52.6%) reported a mix of urge and non-urge episodes (Group 2). Overall, the mean weekly number of incontinence episodes at baseline was significantly greater in Group 2 than Group 1 (44.9 vs 31.5,  $P < 0.001$ ). Group 2 also reported more weekly UUI episodes at baseline than Group 1 (35.1 vs 31.5,  $P = 0.008$ ). In Group 1, the weekly mean number of UUI episodes decreased by 72% following treatment, from 31.5 ( $\pm 15.92$ ) at baseline to 8.9 ( $\pm 15.31$ ) at last observation. In Group 2, UUI episodes also decreased by 72%, from 35.1 ( $\pm 15.81$ ) at baseline to 9.9 ( $\pm 13.67$ ) at last observation. These responses to treatment were not significantly different. Among patients in Group 2, non-urge episodes decreased by 76%, from 9.8 to 2.4. At last observation, the difference in the proportion of patients in each group who had achieved total dryness (27% of Group 1 and 21% of Group 2 patients) was not significant ( $P = 0.093$ ). A surprising percentage of patients (64%) in Group 2 achieved complete freedom from non-urge episodes at last observation, compared with 27% who achieved freedom from urge episodes.

### Interpretation of results

These results are in agreement with previous evidence that patients with mixed symptoms suffer from more frequent incontinence episodes, than do patients with UUI only. Treatment with ER oxybutynin resulted in similar reductions in urge incontinence episodes in both groups, as well as an unexpected reduction in non-urge episodes. Nearly two-thirds of patients reporting non-urge episodes were free of them following treatment. It has been generally presumed that the non-urge episodes experienced by many OAB patients represent stress incontinence; however, the assumption may not be well founded, as there is considerable variability across trials with respect to the criteria used to establish the diagnosis of stress. The present results further undermine this assumption by demonstrating a class of non-urge episode that is amenable to antimuscarinic therapy. These findings suggest that the

absence of urge sensation per se may be an inadequate basis for categorizing patients or predicting response to treatment; they also have implications for a taxonomy of incontinence subtypes. Patients exhibit symptoms that cannot be described under the existing classification system [3]. The pathophysiology of non-urge incontinence episodes in this population remains to be established.

#### Concluding message

Pharmacotherapy with ER oxybutynin was similarly effective in reducing urge incontinence episodes in OAB patients with pure UI and those reporting both urge and non-urge episodes. In addition, there was an effect of treatment on non-urge episodes in the latter group. The results suggest the existence of a previously uncharacterized type of incontinence episode.

#### References

1. Prospective randomized controlled trial of extended-release oxybutynin chloride and tolterodine tartrate in the treatment of overactive bladder: results of the OBJECT study. *Mayo Clin Proc.* 2001;76:358-363.
2. Prospective, randomized, double-blind study of the efficacy and tolerability of the extended-release formulations of oxybutynin and tolterodine for overactive bladder: results of the OPERA trial. *Mayo Clin Proc.* 2003;78:687-695.
3. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Urology.* 2003;61:37-49.