

INDIVIDUALIZED DOSING OF EXTENDED-RELEASE OXYBUTYNYN IS ASSOCIATED WITH IMPROVED OUTCOMES IN THE TREATMENT OF URGE INCONTINENCE

Hypothesis / aims of study

To determine whether a flexible dosing regimen that permitted use of the full range of approved doses (5-30 mg daily) of extended-release (ER) oxybutynin was associated with reductions in the frequency of urge urinary incontinence (UUI) episodes, while maintaining treatment tolerability.

Study design, materials and methods

Data were combined from 3 flexible-dosing studies [1-3] in which ER oxybutynin dose adjustments were made to achieve a maximal reduction in UUI episodes with acceptable tolerability. Doses were adjusted in 5 mg increments every 4-7 days, until the patient (1) reached complete continence, (2) experienced more adverse reactions than were tolerable, or (3) reached the maximum dose specified by the protocol (30 mg in two of the studies [1,2] and 20 mg in the third study [3]). If the dose was deemed intolerable by the patient, it was reduced by 5 mg. Efficacy outcomes included mean reduction in UUI episodes and responder rate according to 2 definitions: a reduction of 70% or more in UUI episodes, and the attainment of complete continence. The 70% reduction rate represented a degree of response considered likely to correspond with treatment satisfaction, as gauged by clinical experience.

Results

Data from 368 patients with UUI or mixed incontinence with urge predominating were pooled. For 30% of patients, the preferred dose was 10 mg daily, whereas 47% of patients were maintained at a dose of ER oxybutynin that was greater than 10 mg. Treatment with individualized doses produced an 83% decrease from baseline in UUI episodes, and patients in all dose groups experienced a reduction in UUI episodes greater than 80%, except for those in the 30 mg group, which averaged a 61% reduction. In addition, 82.6% of patients achieved a decrease in UUI episodes of at least 70%. Each dose increment resulted in an increase in the percentage of patients who became completely continent, with nearly 43% of participants overall achieving this goal. The percentage of patients reaching complete continence was similar across the 5-25 mg dosing range (40% to 48.2%); however, the incidence of complete continence was dramatically lower for the group of patients who had selected the 30 mg daily dose (19.2%). Therapy was well tolerated, with 7.6% of patients discontinuing because of adverse events. Rate of discontinuation was very similar for most dose groups (7.7% to 9.9%); only the 5 mg and 25 mg groups fell outside this range (2.4% and 13.0%, respectively). Moderate or severe dry mouth was reported by 85 (23%) patients and was cited as the cause for early withdrawal by 5 (1.4%) patients. Incidence of dry mouth increased with dose (except at 30 mg daily), but no systematic increase in discontinuation rate for adverse events was observed.

Interpretation of results

Almost half of the patients in this study increased their dose of ER oxybutynin beyond 10 mg daily, the dose that has been employed in two fixed dose trials of this agent. The majority of patients in this study experienced a reduction in UUI episodes greater than 70%, thus achieving treatment success by this definition. In addition, over 40% of patients within a similar dose range experienced total continence. The relatively low rate of discontinuation because of adverse events in these studies suggests that tolerability concerns do not reduce treatment compliance in most patients who obtain a satisfactory level of symptom control. Of interest is the fact that rate of complete continence was considerably lower in the 30 mg dose group than in the others, suggesting that perhaps these patients represent a subgroup less responsive to antimuscarinic treatments. This hypothesis is supported by the finding that dry mouth rates in this group were similar to those in the 5 and 10 mg dose groups.

Concluding message

Individualized adjustments in ER oxybutynin dose resulted in effective management of urge incontinence, and were well tolerated.

References

1. Once daily controlled versus immediate release oxybutynin chloride for urge urinary incontinence. *J Urol.* 1999;161:1809.
2. Evaluation of a new once-daily formulation of oxbutynin for the treatment of urinary urge incontinence. *Urology.*1999;54:420.
3. Dry mouth with conventional and controlled-release oxybutynin in urinary incontinence. *Obstet Gynecol.* 2000;95:718.