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EFFECTS OF EXTENDED-RELEASE FORMULATIONS OF OXYBUTYNIN AND TOLTERODINE ON NOCTURNAL VOIDING FREQUENCY IN WOMEN WITH OVERACTIVE BLADDER

Hypothesis / aims of study

Increased micturition frequency is a prominent symptom of overactive bladder (OAB). Waking to void two or more times is one of the most disruptive aspects of increased urinary frequency. This subanalysis compared the effects of extended-release (ER) formulations of oxybutynin and tolterodine on the frequency of nocturnal voiding in women with OAB.

Study design, materials and methods

Data were examined from the OPERA trial [1], a 12-week, multicenter, randomized, double-blind study comparing ER oxybutynin 10 mg daily with ER tolterodine 4 mg daily in women who documented 21 to 60 urge urinary incontinence episodes weekly and ≥10 micturitions daily. The primary endpoint in the OPERA trial was reduction in urge incontinence episodes. The present work reports an analysis of the nocturnal component of micturition frequency, an important secondary outcome. Change from baseline in the number of voids occurring between 12 midnight and 8 AM (a period which may include the first morning void) was compared for the 2 treatments at study weeks 2, 4, 8, 12, and at last observation. In addition, the data were stratified by patient age to examine treatment effects in younger (<65 yrs) and older (≥65 yrs) patients, and by baseline severity.

Results

In the OPERA study, the two treatments did not separate on the primary endpoint of frequency of urge incontinence episodes. However, there was a significantly greater reduction in micturition frequency with ER oxybutynin (P=0.003). Analysis of the nocturnal micturition frequency data revealed a pattern similar to that observed with overall frequency. The mean number of nocturnal voids decreased from 2.92 (±1.2) to 2.04 (±0.92) at last observation for patients treated with ER oxybutynin (n=382, P<0.001). The decrease for patients treated with ER tolterodine (n=393) was also significant, from 2.87 (±1.04) to 2.15 (±0.94), P<0.001, although the reduction was significantly greater for ER oxybutynin at last observation, as well as at each assessment point (P<0.05). In another efficacy comparison, a greater proportion of patients who completed 12 weeks of treatment with ER oxybutynin therapy achieved the goal of 1 or fewer nocturnal voids, compared with patients taking ER tolterodine (13.4% vs. 9.0%, respectively, P=0.05 by McNemar's test). Stratification by age also revealed a significantly greater reduction with ER oxybutynin among patients <65 yrs (n=474) at all assessment points and at last observation (P=0.003). The two treatments did not separate in the older patient group (n=301), and treatment effects were smaller in magnitude compared with patients <65 yrs. Patients were also stratified by severity of symptoms at baseline, using the median frequency (2.75) to split the sample into more and less severe groups. Both severity groups improved significantly compared with baseline (P<0.001). No treatment group differences emerged from this analysis.

Interpretation of results

Both treatments were effective in decreasing nocturnal voiding episodes, but the difference was significantly greater with ER oxybutynin in the sample as a whole and in patients <65 yrs. Significant improvements compared with baseline were also observed in the older subgroup for both ER oxybutynin and ER tolterodine (P<0.001 for both treatment groups), suggesting that detrusor overactivity may be a contributing factor to nighttime voiding symptoms in older patients. The smaller benefit of antimuscarinic treatment in this group is not surprising, given the variety of conditions among the elderly that may contribute to nocturnal polyuria [2].

Concluding message

Given that incremental increases in the frequency of nocturnal voids have a measurable impact on patients' quality of life [3], even a small reduction in the number of these episodes may result in meaningful improvements. ER oxybutynin may provide greater benefits for patients who present with this symptom of OAB.

References

1. 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.
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3. The prevalence of nocturia and its effect on health-related quality of life and sleep in a community sample in the USA. *BJU Int.* 2003;92:948-954.