UROGYNECOLOGY

Pharmacologic treatment for urgency-predominant urinary incontinence in women diagnosed using a simplified algorithm: a randomized trial

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OBJECTIVE: The purpose of this study was to evaluate clinical outcomes associated with the initiation of treatment for urgency-predominant incontinence in women diagnosed by a simple 3-item questionnaire.

STUDY DESIGN: We conducted a multicenter, double-blinded, 12-week randomized trial of pharmacologic therapy for urgency-predominant incontinence in ambulatory women diagnosed by the simple 3-item questionnaire. Participants (N = 645) were assigned randomly to fesoterodine therapy (4-8 mg daily) or placebo. Urinary incontinence was assessed with the use of voiding diaries; postvoid residual volume was measured after treatment.

RESULTS: After 12 weeks, women who had been assigned randomly to fesoterodine therapy reported 0.9 fewer urgency and 1.0 fewer total incontinence episodes/day, compared with placebo ($P \leq .001$). Four serious adverse events occurred in each group, none of which was related to treatment. No participant had postvoid residual volume of ≥250 mL after treatment.

CONCLUSION: Among ambulatory women with urgency-predominant incontinence diagnosed with a simple 3-item questionnaire, pharmacologic therapy resulted in a moderate decrease in incontinence frequency without increasing significant urinary retention or serious adverse events, which provides support for a streamlined algorithm for diagnosis and treatment of female urgency-predominant incontinence.

Key words: antimuscarinic therapy, diagnostic algorithm, fesoterodine, urgency incontinence

Cite this article as: Huang AJ, Hess R, Arya LA, et al. Pharmacologic treatment for urgency-predominant urinary incontinence in women diagnosed using a simplified algorithm: a randomized trial. Am J Obstet Gynecol 2012;206:444.e1-11.

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Received Nov. 17, 2011; revised Feb. 6, 2012; accepted March 5, 2012.

Pfizer, Inc, provided funding for the study and the study medication but did not provide other input into the design of the study; collection, analysis, or interpretation of data; writing of the report; or the decision to submit the paper for publication. A.J.H. was additionally supported by grants RR024130 and 1K23AG038335-01A1 from the US National Institutes of Health; however, the views expressed in this article do not necessarily represent those of the National Institutes of Health. A.J.H. and J.S.B. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. No manuscript preparation assistance was provided by the study funders.

A.J.H. has received a University of California San Francisco research grant from Pfizer, Inc, to conduct research related to urinary incontinence. L.A.A. has received a research grant from Pfizer, Inc. H.E.R. has received a research grant and participated in a speaker's bureau for Pfizer, Inc, received a research grant and participated in an advisory board for Astellas, and served as a consultant for Uromedica and GlaxoSmithKline. C.S.B. has served as a consultant for Astellas and for GlaxoSmithKline. S.R.K. has served as a consultant for Pfizer, Inc, and Allergan and has been a course director and teaching faculty member for Laborie. J.S.B. has received research grants related to incontinence through University of California San Francisco from Pfizer, Inc, and Mytrus, Inc. No other authors report any potential conflict of interest.

Presented in abstract form at the 34th annual meeting of the Society of General Internal Medicine, Phoenix, AZ, May 4-7, 2011.

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0002-9378/$36.00 • • doi: 10.1016/j.ajog.2012.03.002

Urinary incontinence affects up to one-third of adult women and is associated with depression, social isolation, physical inactivity, and institutionalization.[1-4] Despite recommendations that nonspecialist clinicians assume a greater role in diagnosing and treating incontinence,[5,6] rates of diagnosis and treatment outside of urology or urogynecology remain low.[7-11]

One obstacle to the diagnosis and treatment of female incontinence is that professional organizations traditionally have recommended an extended evaluation to distinguish between the 2 most common types of incontinence in women: urgency and stress.[12,13] In addition to a clinical history and urinalysis test, this evaluation includes a voiding diary, neurologic examination, pelvic examination, measurement of postvoid residual (PVR) volume, and cough stress test.[12,13] Because there are approved medications to treat urgency but not stress incontinence,[14,15] classification of incontinence has implications for treatment. However, the traditional extended evaluation to classify incontinence in women is not performed easily in primary care or general gynecology settings, which creates a barrier to treatment.[16]

To address this problem, a simple 3-item, self-administered questionnaire (the 3 Incontinence Questions [3IQ]) was developed to identify and classify female incontinence (Appendix, Supplementary Figure). In a sample of 301 generally healthy women with ongoing incontinence symptoms, the 3IQ demonstrated good sensitivity and specificity in distinguishing between urgency and stress incontinence, compared with an extended evaluation.[16] To examine the clinical consequences of using the 3IQ to guide treatment, we sought to examine the efficacy and safety of initiating pharmacologic therapy for urgency incontinence in women using a streamlined algorithm that was based on the 3IQ.

MATERIALS AND METHODS

Study population

Participants were ambulatory women who were ≥18 years old who were recruited from the general community surrounding 13 clinical sites in the United States (Supplementary Table 1). Women who reported clinically frequent incontinence during preliminary telephone screening (ie, ≥7 incontinence episodes per week in the past 3 months) were invited to come to an in-person visit to complete the 3IQ on paper to self-diagnose incontinence. Those who self-diagnosed as having urgency-predominant incontinence on the 3IQ (ie, those who indicated that they had incontinence that occurred most often when they "had the urge or the feeling that [they] needed to empty your bladder but could not get to the toilet fast enough") were eligible to continue. Therefore, the study population consisted of women who indicated that they had either isolated urgency incontinence or mixed incontinence that was associated predominantly with urgency. Women completed the 3IQ on their own and did not receive assistance from research staff in diagnosing or classifying their incontinence. Consistent with the proposed use of the 3IQ in clinical practice,[16] women subsequently underwent dipstick urinalysis testing to rule out urinary-tract infection or hematuria before enrollment; those who tested positive could return after completing treatment. Self-report bladder diaries were used to document baseline frequency of incontinence; those women whose diaries confirmed that they had at least 3 incontinence episodes in 3 days were eligible to continue.

Other eligibility criteria were selected to define a community-dwelling sample of women who would be considered appropriate for evaluation and treatment in primary care. Specifically, women were excluded if they self-reported complex medical histories that automatically would require a specialist evaluation for incontinence, such as anti-incontinence surgery in the past 5 years, other pelvic surgery in the past 6 months, >3 urinary tract infections in the past year, lower urinary tract or rectal fistula, interstitial cystitis, symptomatic pelvic organ prolapse, urogenital cancer or radiation, congenital abnormality that leads to incontinence, or major neurologic disorder.

Because of the pharmacologic intervention that was used in this study, participants could not have specific contraindications to fesoterodine therapy (such as urinary or gastric retention, uncontrolled narrow-angle glaucoma, myasthenia gravis, severe ulcerative colitis, clinically significant hepatic or renal disease, toxic megacolon, potent CYP3A4 inhibitor treatment in the last 2 weeks, or pregnancy or nursing).

Randomization, masking, and treatments

Eligible women were allocated randomly in a 1:1 ratio to receive 12 weeks of pharmacologic treatment with flexible-dose fesoterodine therapy (Toviaz; Pfizer, Inc, New York, NY) 4-8 mg (fesoterodine group) or an identical placebo pill (placebo group) daily. Randomization was performed by computer in permuted blocks of 2-4 without stratification for clinical site. Active and placebo tablets were prepared by the University of California San Francisco pharmacy, where they were labeled by a pharmacist with randomization numbers and then distributed to clinical sites. Participants, clinical personnel, and statistical staff were masked to treatment assignment, and no unmasking occurred during the trial. All participants were asked to forgo other pharmacologic incontinence treatments and pelvic floor or bladder physical therapy for the 12-week trial period to avoid contamination of treatment effects.

According to previously established protocols for participant-directed dosing,[17] participants were started initially on either fesoterodine 4 mg or an identical placebo pill daily. At their 2-week telephone call and their 4-week follow-up visit, women were offered the option of increasing their dose to fesoterodine 8 mg or an identical placebo daily. At their 8-week telephone call, they were invited to readjust their dose to a maximum of 8 or minimum of 4 mg daily.

Clinical efficacy outcomes

All clinical efficacy outcomes were assessed at baseline, 4 weeks, and 12 weeks. The primary efficacy outcome was a 12-week change in the average number of self-reported urgency incontinence episodes per day that were documented by a validated 3-day voiding diary in which women recorded all incontinence and voiding episodes and indicated which