

▪ Duloxetine for stress incontinence

THE QUESTION: Is duloxetine hydrochloride effective in the treatment of stress urinary incontinence (SUI)?

PAST STUDIES Research has indicated that the neurotransmitters serotonin and norepinephrine are responsible for neural control of the lower urinary tract. Serotogenic agonists generally suppress parasympathetic activity and enhance sympathetic and somatic activity in the lower urinary tract—effects that promote urine storage.

THIS STUDY This double-blind, randomized, placebo-controlled study examined 553 women, ages 18 to 65, with at least a 3-month diagnosis of SUI. Subjects were assigned a 12-week course of either placebo (n=138) or duloxetine treatment at 1 of 3 daily doses: 20 mg (n=138), 40 mg (n=137), or 80 mg (n=140). The women were examined once every 4 weeks and asked to keep a diary documenting voiding episodes.

The diary entries revealed a decrease in incontinence episodes for all subjects. Patients taking placebo recorded a 41% decline, compared to 54% in women taking 20 mg/d of duloxetine, 59% for users on 40 mg of duloxetine, and 64% for women taking 80

mg of duloxetine. Among women taking the 80-mg dose, half experienced at least a 64% reduction in incontinence frequency and 67% noted at least a 50% decrease.

Researchers concluded that duloxetine is a safe and effective agent for treating SUI.

FIND THIS STUDY Norton PA, Zinner NR, Yalcin I, Bump RC. July 2002 issue of *American Journal of Obstetrics and Gynecology*; abstract online at www3.us.elsevierhealth.com/ajog.

WHO MAY BE AFFECTED BY THESE FINDINGS? Women suffering from SUI.

EXPERT COMMENTARY The annual direct cost of female urinary incontinence in the United States is approximately \$12.4 billion,¹ with \$1.3 billion dedicated to treatment. Of that, surgical management accounts for nearly 80% (or \$1 billion), while pharmacologic therapy utilizes only 9% (\$114 million).¹ Thus, even with rising medication costs, medical incontinence management uses fewer health-care dollars than surgery. If more women can be effectively treated pharmacologically, therefore, we can conserve valuable health-care resources while reducing related costs, such as time off from work.

Presently, there are agents available to treat urge incontinence.



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tinence, but no effective, tolerable medical therapies for stress incontinence. Alpha-1 agonists such as pseudoephedrine have been used for SUI, but the side effects of nervousness, dizziness, and insomnia have proved prohibitive.

SUI typically is treated either surgically or with physical therapy designed to strengthen pelvic-floor muscles. Recently, however, advances in the understanding of neuromuscular control of women's "stress continence control system" has spurred the development of new drugs.²

In this study, duloxetine use was associated with significant decreases in incontinent episodes (as measured by diary entries). Quality-of-life measures also improved significantly. In addition, voiding intervals lengthened, indicating that women were not voiding more frequently to avoid incontinent episodes. This result may indicate duloxetine's dual efficacy with the continence system: increasing bladder capacity and increasing striated urethral sphincter activity. A more recent analysis of a subgroup of patients with both stress and urge incontinence showed similar improvements.³

Interestingly, cough stress tests at 400 mL and pad tests failed to demonstrate any significant improvement in the study's treated patients. However, these conflicting results may reflect inherent problems with assessing urinary incontinence treatments: A patient with 400 mL of urine in her bladder may leak with vigorous coughing in the upright position, but if she voids at 300 to 350 mL—a reasonable bladder capacity—she may never leak in "real life."

BOTTOM LINE Duloxetine hydrochloride appears to be a promising new pharmacologic agent to treat stress incontinence. However, clinicians must keep in mind that even when drugs seem efficacious in clinical trials, they may not yield the same results in clinical practice. Patients in this study completed weeklong diaries every 4

weeks, which, by itself, may improve bladder control.

As mentioned by the authors, larger multinational trials are needed to further demonstrate duloxetine's safety and efficacy in more diverse clinical settings.

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3. Exploring new treatment options for stress urinary incontinence. Satellite symposium presented at: American Urogynecological Society Conference; October 17-19, 2002; San Francisco, Calif.



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