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Promising therapies: TOT, duloxetine, botulinum A

Ob/Gyns are being called on more than ever to initiate treatment for urinary incontinence, and new treatment options are enabling us to play a more active role than ever before in treating one of the most common and distressing of chronic diseases in women. Urinary incontinence affects women after

menopause, primarily. Prevalence increases (though not in a linear fashion)—from 20% to 30% in reproductive-aged women, to 30% to 40% in postmenopausal women. Approximately 16 million Americans are affected, and the number of women affected is more than double that of men.

20% cancel surgery after duloxetine therapy

Cardozo L, Drutz HP, Baygani SK, Bump RC for the Duloxetine Severe UI Study Group. Pharmacological treatment of women awaiting surgery for stress urinary incontinence. Obstet Gynecol. 2004;104:511-519.

Efforts to treat stress incontinence with drugs have not succeeded well in the past, but the development of duloxetine may change that.

Duloxetine (*Cymbalta*; *Eli Lilly, Indianapolis, Ind*) is a balanced serotonin-norepinephrine reuptake inhibitor that may act by stimulating pudendal nerve output and improving urethral closure. The FDA approved duloxetine for treatment of major depression for adults in August 2004, and for management of diabetic peripheral neuropathic pain in September 2004. However, duloxetine is not yet FDA-approved for the treatment of stress incontinence.

A randomized, placebo-controlled, double-blinded study involving 14 centers

in Australia, Canada, the Netherlands, and the United Kingdom enrolled women aged 18 to 75 years, all of whom had severe stress incontinence, and had already scheduled surgery. All patients had at least 14 episodes of stress incontinence per week. The dose of duloxetine started at 40 mg twice daily for 4 weeks, then increased to 60 mg twice daily for another 4 weeks.

The study randomized 109 women and included 98 in the intention-to-treat analyses, 46 of whom took duloxetine, and 52, placebo.

Response was defined as at least a 50% reduction in incontinence episode frequency. Of the women taking duloxetine, 63% were responders, compared with 13.5% of the placebo group.

Using the Patient Global Impression of Improvement (PGI-I), one third of women taking duloxetine described themselves as “very much better” or “much better,” compared with 8% of women taking placebo.

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Ten of 49 women (20%) indicated they were not interested in surgery while taking duloxetine, compared with 0 of 45 women taking placebo. Drug discontinuation occurred more frequently in the duloxetine group: 18 of 55 (33%), compared with 3 of 54 (6%) in the placebo group.

■ Cure rate low, but so is risk

Even if the “cure” rate is relatively low, duloxetine offers a low-risk form of

treatment for women who might otherwise be considered surgical candidates.

In addition, pharmacological treatment may be indicated for women whose incontinence is not severe enough to warrant surgery.

While there are no studies that report long-term results of duloxetine use, it seems appropriate that duloxetine be included in the discussion of nonsurgical options, along with pelvic muscle exercises and behavioral treatment, before surgery is considered.

Botulinum A toxin for refractory detrusor overactivity

Kuo H-C. Urodynamic evidence of effectiveness of botulinum A toxin injection in treatment of detrusor overactivity refractory to anticholinergic agents. Urology. 2004;63:868-872.

Cystoscopic detrusor injection of botulinum toxin A appears to be a promising alternative to more invasive treatments for refractory detrusor overactivity.

Urinary incontinence due to detrusor overactivity can be especially difficult to treat when first-line treatment with anticholinergic drugs is unsuccessful. Although newer slow-release or long-acting formulations are tolerated better than the original formulations, many patients still have bothersome symptoms or intolerable side effects.

Previously, such women might have been treated with electrical stimulation.

This less invasive treatment might be an effective option, although further study is needed to identify patients most likely to benefit.

Effectiveness has been observed in patients with detrusor overactivity due to spinal cord injury and, in the study cited above, in patients with neurogenic, idiopathic, and postobstructive detrusor overactivity. Botulinum toxin A is not FDA-approved for incontinence indications.

In the Kuo study, 30 patients (12

women and 18 men) with detrusor overactivity refractory to anticholinergic agents were treated with cystoscopic detrusor injection of 200 units botulinum toxin A at 40 sites in the posterior and lateral bladder (sparing the anterior bladder). Eight patients (27%) regained urinary continence; 14 (46%) had improvement in frequency, urgency, and incontinence; and treatment failed in 8 (27%).

Excellent results were most likely in patients with previous bladder outlet obstruction, and least likely in patients with neurogenic detrusor overactivity. Men were more often successfully treated (83%) than women (58%). Maximal effect was noted at 10 to 14 days after treatment, and the effect lasted 3 to 9 months (average, 5.3 months).

Side effects were not serious: urinary tract infection in 3 patients and transient urinary retention in 4. Six patients with detrusor overactivity and impaired contractility were treated with intermittent self-catheterization for 1 month, after treatment resulted in increased postvoid residual urine volumes.

Patients with impaired bladder emptying before treatment may be at higher risk of posttreatment retention, although even when retention occurs, it seems to be transient and responds well to time-limited management with intermittent self-catheterization.

Botulinum A toxin is a promising alternative to first-line drug therapy.

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