Overactive bladder

(FEBRUARY 2005)

TO THE EDITOR: The review of overactive bladder by Drs. Rosenberg and Dmochowski[1] did not discuss some of the newer treatments such as trospium chloride (Sanctura). And while the authors noted that women with overactive bladder are "far more likely than men to have episodes of incontinence," they made only very cursory remarks that "vaginal atrophy should be noted" and that some practitioners prescribe estrogen therapy, noting that they "lacked any good data to support dosing regimens, route of administration, or treatment duration."

In a recent meta-analysis, Cardozo and colleagues[2] found that estrogen, delivered either systemically or locally, improved diurnal frequency, urgency, and urge incontinence more than placebo. Another study[3] specifically examining vaginal administration of micronized estradiol showed that this was an effective and safe therapy for postmenopausal women with urogenital symptoms and that the women who used it had significantly improved cystomimetric capacity, including the volume in the urinary bladder at which they first felt the urge to urinate.

This is not surprising, as estrogen therapy restores the integrity of the genitourinary tissue, particularly the highly estrogen-rich tissue of the trigone of the bladder and urethra. Estrogen is known to restore healthy stratified vaginal epithelium and furthermore reduces recurrent urinary tract infections in women. The effects of estrogen on the genitourinary system are mixed, however: the recent report of the Women's Health Initiative indicated increased urinary incontinence with oral hormone therapy.[4]

In addition, while the authors touched on stress urinary incontinence, they did not mention duloxetine, a new agent which will probably be approved by the US Food and Drug Administration for treatment of stress urinary incontinence in women. This common debilitating problem of overactive bladder and mixed incontinence deserves a more comprehensive discussion of available therapeutic options.

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IN REPLY: We thank Drs. Thacker and Paraiso for their informative critique. We will attempt to address each of their points in order.

In regard to newer treatments such as trospium chloride, we agree it is now available and quite effective. However, when we submitted our manuscript it was not yet approved for use in the United States and, therefore, was not available.

It is true that we represented the use of estrogen therapy as lacking good data. The recent information from the Women's Health Initiative is pretty clear on that.[1] The data that Drs. Thacker and Paraiso quote from Cardozo et al[2] is quite intriguing; however, it is based on a meta-analysis of 11 randomized trials that are "relatively heterogeneous, using different study designs as well as outcome measures." Cardozo et al state: "The method of analysis employed could not control for this heterogeneity, and this may have accounted for the differences between estrogen and placebo."[2] Further, Thacker and Paraiso interpret the study as finding there was an improvement in several categories; however, review of the paper could lead one to a different conclusion. Whereas the benefit of estrogen vs placebo for diurnal frequency had a *P* value of .0011, its effect on urgency attained a *P* value of .0425, and urge incontinence was not even addressed. Incontinence was addressed and got a wonderfully significant benefit with a *P* value of .0002; however, Cardozo et al admit that this group included an unknown number of patients with stress incontinence.

We argue that although the data are of interest, we must take it at face value as a historical meta-analysis of not necessarily compatible studies. A well-designed study may answer this question in the future.

The study by Simunic et al[3] that looked at the benefit of vaginal estrogen dosing was well designed. We believe that the significance that Thacker and

Paraiso place on the data is appropriate. The information is certainly different than the data in the Women's Health Initiative and again leads one to believe that there is no definitive answer yet.

By no means did we advocate against the use of estrogen in women suffering from overactive bladder. But the use is variable, and we do believe there is need for further study.

The final point made by Thacker and Paraiso is in regard to duloxetine, "a new agent that will *probably* be approved by the US Food and Drug Administration." This medication remains investigational and apparently is undergoing further clinical evaluation. Its release for the indication of stress incontinence remains, as yet, undefined. In addition, the role of duloxetine in bladder overactivity has yet to be established by any clinical data. Our article was meant to be a review of what is now available for overactive bladder, not on the hypothetical future.

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