

THERAPEUTICS

Review: Estrogen improves symptoms of overactive bladder in postmenopausal women

Cardozo L, Lose G, McClish D, Versi E. A systematic review of the effects of estrogens for symptoms suggestive of overactive bladder. *Acta Obstet Gynecol Scand.* 2004;83:892-7.

QUESTION

In postmenopausal women with symptoms suggestive of overactive bladder (OAB) (urge or stress incontinence), does estrogen therapy reduce symptoms more than placebo?

METHODS

Data sources: Studies were identified by searching MEDLINE, EMBASE/Excerpta Medica, Science Citation Index (January 1969 to December 1999), and reference lists of articles; and hand-searching urology, gynecology, gerontology, and primary care medicine journals.

Study selection and assessment: Studies in any language were selected if they were randomized controlled trials (RCTs) that were published or presented at a scientific meeting, reported symptoms suggestive of OAB (including frequency, urgency, or urge incontinence), and compared estrogen with placebo.

Outcomes: Diurnal frequency, nocturnal frequency, incontinence episodes, urgency, first sensation to void, and bladder capacity.

MAIN RESULTS

11 RCTs (*n* = 466) met the inclusion criteria. Types of estrogen used were estriol (5 RCTs), estradiol (4 RCTs), conjugated estrogen (1 RCT), and both estradiol and estriol (1 RCT). Estrogen was administered system-

ically (orally [5 RCTs], transdermally [1 RCT], and as an implant [1 RCT] or locally (vaginally [3 RCTs], and intravesically [1 RCT]). Patients who received estrogen therapy had greater improvement in diurnal frequency, nocturnal frequency, urgency, incontinence episodes, first sensation to void, and bladder capacity than those who received placebo (Table). Estrogen improved all outcome variables when it was administered locally (4 RCTs, *Z* value range 2.47 to 4.05). Compared with placebo, patients who received systemically administered estrogen (7 RCTs) improved in incontinence episodes (*Z* value 2.74) and first sensation to void (*Z* value 2.47), but worsened for nocturnal frequency (*Z* value -2.09).

CONCLUSIONS

In postmenopausal women with symptoms suggestive of overactive bladder (urge or stress incontinence), estrogen therapy improves symptoms of diurnal frequency, nocturnal frequency, urgency, incontinent episodes, first sensation to void, and bladder capacity. Estrogen therapies administered locally improve all outcomes. Systemically administered estrogens improve incontinence episodes and first sensation to void, but worsen nocturnal frequency.

Source of funding: Pharmacia Corporation.

For correspondence: Dr. L. Cardozo, King's College Hospital, London, England, UK. E-mail lcardozo@compuserve.com. ■

Estrogen (estriol, estradiol, conjugated estrogens, or combination of estradiol and estriol) vs placebo for overactive bladder at 3 to 26 weeks

Outcomes	Number of trials (n)	Z value*	P value
Diurnal frequency	8 (372)	3.26	0.001
Nocturnal frequency	7 (337)	2.08	0.037
Urgency	3 (244)	2.03	0.042
Incontinence episodes	7 (331)	3.69	0.0002
First sensation to void	8 (350)	4.63	0.0001
Bladder capacity	8 (352)	3.12	0.0018

*Positive Z value indicates a favorable result for estrogen over placebo.

COMMENTARY

The Women's Health Initiative (WHI) findings indicated that systemic hormone replacement therapy should be limited in older, asymptomatic postmenopausal women because of adverse effects (1). However, WHI did not address genitourinary health. Stopping systemic hormone therapy will result in an increase in the incidence of genital atrophy.

In their meta-analysis, Cardozo and colleagues found that estrogen delivered either systemically or locally improved diurnal frequency, urgency, and urge incontinence more than placebo. This is not surprising, because estrogen therapy restores the integrity of the genitourinary tissue, particularly the highly estrogen-rich tissue of the trigone of the bladder, urethra, and lower one third of the vagina. Interestingly, systemic estrogen therapy did not improve nocturnal frequency. Another study showed that vaginal administration of micronized estradiol was an effective and safe therapy for older postmenopausal women with urogenital symptoms, and patients who used local estrogen had a significantly improved cystometric capacity (including the volume in the urinary bladder at which women first felt the urge to urinate) (2).

Although a number of treatments are approved for OAB (including oxybutynin, tolterodine, and trospium), these agents do not restore the integrity of the vaginal mucosa, reduce urinary tract infections, or improve sexual health. Estrogen restores a healthy stratified vaginal epithelium rich in glycogen and the vasoactive vaginal response needed for arousal and vaginal lubrication. Local estrogen therapy should be considered as first-line treatment for postmenopausal women with vaginal atrophy and OAB symptoms.

*Holly L. Thacker, MD
Cleveland Clinic Foundation, Women's Health Center
Cleveland, Ohio, USA*

References

1. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA.* 2002;288:321-33.
2. Simunić V, Banović I, Ciglar S, et al. Local estrogen treatment in patients with urogenital symptoms. *Int J Gynaecol Obstet.* 2003;82:187-97.