In postmenopausal women with symptoms suggestive of overactive bladder (OAB) (urge or stress incontinence), does oestrogen 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, gynaecology, gerontology, and primary care medicine journals.

Study selection and assessment: studies in any language were selected if they were randomised 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 oestrogen 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 oestrogen used were estradiol (5 RCTs), estradiol valerate (1 RCT), and both estradiol and estradiol valerate (1 RCT). Oestrogen was administered systemically (orally [5 RCTs], transdermally [1 RCT]), locally (vaginally [3 RCTs], intravesically [1 RCT]), or as an implant [1 RCT]. Patients who received oestrogen therapy had greater improvement in diurnal frequency, nocturnal frequency, urgency, incontinence episodes, first sensation to void, and bladder capacity than those who received placebo. Oestrogen 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 oestrogen (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), oestrogen therapy improves symptoms of diurnal frequency, nocturnal frequency, urgency, incontinence episodes, first sensation to void, and bladder capacity.

Oestrogen therapies administered locally improve all outcomes. Systemically administered oestrogens improve incontinence episodes and first sensation to void, but worsen nocturnal frequency.

Abstract and commentary also appear in ACP Journal Club.

**Commentary**

The Women’s Health Initiative (WHI) findings indicated that systemic hormone therapy should be limited in older, asymptomatic postmenopausal women because of adverse effects. 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 et al found that oestrogen delivered either systemically or locally improved diurnal frequency, urgency, and urge incontinence more than placebo. This is not surprising, because oestrogen therapy restores the integrity of the genitourinary tissue, particularly the highly oestrogen rich tissue of the trigone of the bladder, urethra, and lower one third of the vagina. Interestingly, systemic oestrogen therapy did not improve nocturnal frequency. Another study showed that vaginal administration of micronised estradiol was an effective and safe therapy for older postmenopausal women with urogenital symptoms, and patients who used local oestrogen had a significantly improved cystometric capacity (including the volume in the urinary bladder at which women first felt the urge to urinate).

Although a number of treatments exist that 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. Oestrogen restores a healthy stratified vaginal epithelium rich in glycogen and the vasoactive vaginal response needed for arousal and vaginal lubrication. Local oestrogen therapy should be considered as first line treatment for postmenopausal women with vaginal atrophy and OAB symptoms.

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Oestrogen (estradiol, estradiol valerate, conjugated oestrogens, or combination of estradiol and estradiol) v placebo for overactive bladder

<table>
<thead>
<tr>
<th>Outcomes at 3–26 weeks</th>
<th>Number of trials (n)</th>
<th>z Value*</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diurnal frequency</td>
<td>8 (372)</td>
<td>3.26</td>
<td>0.001</td>
</tr>
<tr>
<td>Nocturnal frequency</td>
<td>7 (337)</td>
<td>2.08</td>
<td>0.037</td>
</tr>
<tr>
<td>Urgency</td>
<td>3 (244)</td>
<td>2.03</td>
<td>0.042</td>
</tr>
<tr>
<td>Incontinence episodes</td>
<td>7 (331)</td>
<td>3.69</td>
<td>0.0002</td>
</tr>
<tr>
<td>First sensation to void</td>
<td>8 (350)</td>
<td>4.63</td>
<td>0.0001</td>
</tr>
<tr>
<td>Bladder capacity</td>
<td>8 (352)</td>
<td>3.12</td>
<td>0.0018</td>
</tr>
</tbody>
</table>

*Positive z value indicates a favourable result for oestrogen over placebo.