Oestrogen therapy increased stroke risk and decreased hip fracture risk but did not affect coronary heart disease risk in postmenopausal women with prior hysterectomy


Clinical impact ratings GP/FP/Primary care **************************** IM/Ambulatory care **************************** Endocrine ****************************

Gynaecology ****************************

MAIN RESULTS

Women who received CEE had a greater incidence of stroke (number needed to harm 120) and a decreased incidence of hip fracture (number needed to treat 219) than did those who received placebo; no differences were seen for incidences of CHD, venous thromboembolic disease, invasive breast cancer, or colorectal cancer (table).

CONCLUSION

In postmenopausal women with prior hysterectomy, oestrogen increased the risk of stroke and decreased the risk of hip fracture but did not affect the risks of coronary heart disease, venous thromboembolic disease, breast cancer, or colorectal cancer.

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Oestrogen v placebo for incidences of major diseases in postmenopausal women with prior hysterectomy at mean 6.8 years

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of cases</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease</td>
<td>177</td>
<td>0.91 (0.75 to 1.12)</td>
</tr>
<tr>
<td>Stroke</td>
<td>158</td>
<td>1.39 (1.10 to 1.77)</td>
</tr>
<tr>
<td>Venous thromboembolic</td>
<td>101</td>
<td>1.33 (0.99 to 1.79)</td>
</tr>
<tr>
<td>disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invasive breast cancer</td>
<td>94</td>
<td>0.77 (0.59 to 1.01)</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>61</td>
<td>1.08 (0.75 to 1.55)</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>38</td>
<td>0.61 (0.41 to 0.91)</td>
</tr>
</tbody>
</table>

*See glossary.*

*Information provided by author.

Commentary

Results of the oestrogen CEE only arm of the WHI contrasts with those of the oestrogen progestin (CEE medroxypregesterone acetate [MPA]) arm in that no increased risk of breast cancer was seen in 6.8 years. This is reassuring for the women who have had hysterectomy and whose main concern has been the risk of breast cancer. The lack of benefit for CHD is disappointing but not surprising. The only risk seen with 0.625 mg CEE was an increased risk of stroke. The WHI was a preventive trial in older postmenopausal women, and thus the intent was not therapeutic. Hormone therapy (HT) remains the only US Food and Drug Administration approved treatment for menopausal symptoms. Many questions remain unanswered. Is the increased risk of breast cancer related to all progestins or just MPA? Is the neutral breast effect related to equine oestrogens or is this translatable to all oestrogens? Is the risk of stroke (and deep vein thrombosis) more of a risk with oral than with transdermal oestrogen? Further information about the characteristics of women sustaining stroke while on CEE and CEE MPA will be important, and studying lower doses of oestrogen will also be useful.

We can now reassure women who have had a hysterectomy and take CEE that no increased risk of breast cancer exists in 6.8 years of use. Extrapolation of risks of the oestrogen and CEE MPA preventive arm of the WHI with respect to early and late cardiovascular effects and to cerebral aging in younger women remains to be studied. The International Menopause Society’s recent statement was that, in addition to lifestyle management, HT remains a principal tool in preventing bone wasting, fractures, and atrophy of connective tissue and in influencing the quality of life in women who are symptomatic. 3

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