Rates of Changes in Brain Volumes and Ischemic Lesion Volumes Following Exposure to Conjugated Equine Estrogen Therapies: Results From the WHIMS Magnetic Resonance Imaging Studies

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Abstract

Background: The WHI Memory Study (WHIMS) reported women 65 and older treated an- average 5.6 years with conjugated equine estrogen (CEE)-based hormone therapy (HT), with-and-without medroxyprogesterone acetate (MPA), compared to placebo, increased dementia risk (HR 1.76 [95% CI: 1.19-2.60] P=0.0005). WHIMS MRI reported treated women, relative to placebo, had smaller hippocampal (p=0.05), frontal p=0.004), and total (p=0.07) brain volumes 1.4 to 3 years on average following trial termination. We extend these cross-sectional MRI findings to evaluate 4.7-year change in brain and lesion volumes.

Methods: Of 1403 WHIMS MRI participants, 1345 were potential enrollees for WHIMS MRI2. 1230 (91.4%) were contacted; 797 (64.8%) consented; 791 (64.3%) were scanned and 699 (57%) analyzed. Mixed model repeated measures analysis of covariance assessed differences between treatment groups in brain volumes and changes in brain volumes, with adjustment for baseline hysterectomy status, clinical site, age, intracranial volume, and timing of scans.

Results: Treatment groups were balanced with respect to demographic and risk factors for cognitive decline. Mean (SD) age was 82.8 (3.5) years. Overall, women experienced a decline in total brain volume of approximately 13.3 cc (p=0.02) and an increase in gray matter lesion volume (p=0.01) over the 4.7-year interval. Rates of change in total brain, gray matter lesion, and total ischemic lesion volumes were similar, regardless of prior treatment assignment.

Conclusions: CEE-based postmenopausal HT, with-and-without MPA, compared to placebo was associated with persisting decrements in brain volumes, but no long-term acceleration in brain atrophy or lesion accumulation during the 4.7 years between initial and follow-up MRI scans.

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