

Improved inflammation markers during menopausal hormone therapy correlate to ultrasonographic signs of vascular benefit. - a randomized-controlled study

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Context: Menopausal hormone therapy (MHT), initiated soon after menopause, substantially reduces the risk of cardiovascular events during therapy. The atherosclerotic process is basically an inflammatory process and estrogen has anti-inflammatory properties.

Methods: RIA assay for serum E2 and sandwich ELISA for vascular inflammation markers. Intima thickness and intima/media (I/M) ratio of the distal radial artery, assessed by non-invasive ultrasound (Vevo 2100; 50MHz). Increases in intima thickness and the I/M thickness ratio are signs of arterial aging.

Objective: To study whether vascular protective effects of MHT might be mediated via the anti-inflammatory effects of MHT.

Patients: Fifty-one healthy menopausal women (50–59 years and MHT-naïve for ≥3 yrs).

Intervention: Random assignment (1:1) to oral estradiol 0.5mg/norethisterone acetate 0.1mg daily or placebo for 24 months.

Main Outcome Measures: Effects of MHT vs. placebo and changes in serum estradiol (E2) levels vs. changes in serum vascular inflammation markers in relation to changes in signs of arterial aging.

Results: MHT, vs. placebo, significantly reduced serum ICAM, endostatin and osteopontin levels (all $p < 0.02$). In both study groups and follow-up periods combined, higher serum E2 levels were associated with lower serum concentrations of TNF α , ICAM, VCAM and osteopontin (all $p < 0.05$). Over the 2-year, the increase in serum E2 levels were associated with reduced serum endostatin ($p = 0.024$) and ICAM levels ($p = 0.007$). Further, reduced serum endostatin levels associated with reduced radial Intima thickness (0.41; 0.007) and I/M thickness ratio (0.39; 0.010) and osteopontin and ICAM marginally with radial I/M (0.32; 0.05) and Intima thickness (0.28; 0.07), respectively.

Conclusions: Menopausal hormone therapy (MHT) significantly reduced several cardio-vascular risk markers. Further, reduced serum endostatin associated significantly with reduced signs of arterial aging and reduced osteopontin and ICAM marginally so. Findings suggest that at least part of the vascular protective effect of MHT might be mediated through the anti-inflammatory effects of MHT.

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