

Oestrogen did not prevent death or non-fatal stroke in postmenopausal women with ischaemic stroke or transient ischaemic attack

Viscoli CM, Brass LM, Kernan WN, et al. A clinical trial of estrogen-replacement therapy after ischemic stroke. *N Engl J Med* 2001 Oct 25;345:1243–9.

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Oestradiol-17 β v placebo for postmenopausal women with ischaemic stroke or transient ischaemic attack[†]

QUESTION: In postmenopausal women with ischaemic stroke or transient ischaemic attack (TIA), is oestrogen more effective than placebo for preventing cerebrovascular events?

Design

Randomised [allocation concealed*]†, blinded (patients and clinicians)*, placebo controlled trial with a mean

follow up of 2.8 years (Women's Estrogen for Stroke Trial [WEST]).

Setting

21 hospitals in the USA.

Outcomes at mean 2.8 years	Oestradiol-17 β	Placebo	RRI (95% CI)	NNH
Death or non-fatal stroke	29%	28%	8.3% (–17 to 32)	Not significant
Fatal stroke	3.6%	1.2%	187% (–9.9 to 758)	Not significant
Transient ischaemic attack	8.9%	7.6%	19% (–29 to 92)	Not significant
Non-fatal myocardial infarction	4.2%	3.7%	20% (–50 to 143)	Not significant
			RRR (CI)	NNT
Venous thromboembolic event	0.89%	1.2%	20% (–235 to 80)	Not significant
Breast cancer	1.5%	1.5%	0% (–243 to 70)	Not significant

†Abbreviations defined in glossary; RRI, RRR, NNH, NNT, and CI calculated from Cox proportional hazards data in article.

COMMENTARY

The study by Viscoli *et al* is the first randomised clinical trial to evaluate oestradiol for the secondary prevention of stroke in postmenopausal women. The trial was well designed and leaves no ambiguity: oestradiol does not prevent death or stroke recurrence and might increase fatal stroke risk, although this increase did not differ statistically from placebo.

Interim results from the Women's Health Initiative Hormone Trial ($n > 27\,000$), a primary prevention trial, were that after 3 years of follow up, conjugated equine oestrogen (CEE) alone or with medroxyprogesterone acetate (MPA) was associated with a greater risk for stroke, heart attack, and blood clots than was placebo.¹ An earlier trial for secondary prevention of coronary heart disease (CHD) reported a 52% increased risk for CHD events after 1 year of daily CEE plus MPA, with no benefit after 4 years.² Therefore, neither oestradiol nor CEE alone or with MPA is indicated for the sole purpose of primary or secondary prevention of stroke or CHD.

Hormone replacement therapy (HRT) is indicated for short term (≤ 5 y) treatment of hot flashes and often requires a 6 month taper to avoid rebound symptoms. HRT is no longer approved by the Food and Drug Administration for osteoporosis treatment because other medications have been shown to be effective and oestrogen has never been evaluated for fracture risk reduction in large randomised trials.³ Although HRT is still used for the prevention of osteoporosis, clinicians should use caution and educate patients about the risk for blood clots, gall bladder disease, urinary incontinence, and cardiovascular disease in older women receiving HRT.^{1–4}

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- 1 Women's Health Initiative Hormone Replacement Therapy Update, June 2001. (<http://www.nhlbi.nih.gov/whi/hrt.htm>).
- 2 Hulley SB, Grady D, Bush T, *et al*. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. *JAMA* 1998;280:605–13.
- 3 *Physicians' desk reference*. 55th edition. Montvale, NJ: Medical Economics Company, 2001.
- 4 Grady D, Brown JS, Vittinghoff E, *et al*. Postmenopausal hormones and incontinence: the Heart and Estrogen/Progestin Replacement Study. *Obstet Gynecol* 2001;97:116–20.

Patients

664 postmenopausal women who were > 44 years of age (mean age 71 y, 84% non-Hispanic white) and had had a qualifying ischaemic stroke or TIA within the previous 90 days. Exclusion criteria included ischaemic stroke or TIA that was disabling or had occurred while the patient was taking oestrogen, and a history of breast or endometrial cancer. All patients were included in the analysis.

Intervention

Women were allocated to oestradiol-17 β , 1 mg daily ($n=337$) or placebo ($n=327$). Every 3 months, a nurse contacted each woman to screen for outcomes using a standardised questionnaire. Medical records were reviewed for all reported events.

Main outcome measures

Death or non-fatal stroke. Secondary outcomes included TIA, non-fatal myocardial infarction (MI), and adverse events.

Main results

Analysis was by intention to treat (included 9 women who were censored at their last known date alive without stroke). Groups did not differ for death or non-fatal stroke, TIA, non-fatal MI, venous thromboembolic events, or breast cancer (table). Of those who did not have a hysterectomy before the study, 2 of 189 women (1.1%) in the oestradiol group were diagnosed with endometrial cancer during the study period compared with 0 of 180 women in the placebo group.

Conclusion

In postmenopausal women with ischaemic stroke or transient ischaemic attack, oestrogen was no more effective than placebo for preventing death or non-fatal stroke, transient ischaemic attack, or non-fatal myocardial infarction.

*See glossary.

†Information provided by author.