

COMMENTARY

Hormone Replacement Therapy for Symptoms but not for Chemoprevention of Chronic Diseases

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Abstract

A little dust has settled since last year's news from the Women's Health Initiative (WHI) randomized trial about the use of combined hormone replacement therapy (HRT) during and after menopause: long-term use may increase a woman's chances of becoming chronically ill (Women's Health Initiative Investigators, 2002). In none of the three age-groups studied (women in their 50s, 60s and 70s) was the presumed cardioprotective effect of HRT confirmed, and in all age groups, the hormone users had more heart attacks, strokes, and blood clots than the control as well as more breast cancer. The placebo arm (women not receiving HRT) had more fractures and more cases of colon cancer than the hormone users, but on balance, the non-users still had fewer serious adverse health effects. The WHI estrogen and progestin arm was prematurely stopped in July 2002 because the overall risks of the intervention outweighed the benefits (Women's Health Initiative Investigators, 2002).

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Given that the hormone therapy was associated with decreased risk of colon cancer and hip fracture, are there women who are at high risk for these conditions who might have a net benefit with hormones? A woman with a family history of colon cancer has a risk of the disease that is approximately twice of women with no such family history. According to the rates of disease and the relative risks found in the WHI, the estimated harm is lower among such women, but the net effect is still about 1.4 serious adverse events per 1000 women per year (Grady, 2003).

The annual increase in risk of serious adverse events associated with postmenopausal hormone therapy is relatively small, but why should women take any risk at all? Until recently, it has been argued that many women feel better when they take hormones. This statement was laid to rest by a recent study by Hays et al (2003) which provided clear evidence that hormone therapy did not result in better quality of life among elderly women without menopausal symptoms.

In a recent issue of JAMA, three further reports from the WHI randomized trial present results on the effect of treatment with 0.625 mg of conjugated estrogen and 2.5 mg

of medroxyprogesterone acetate on central nervous system outcomes (Shumaker et al., 2003; Rapp et al., 2003; Wassertheil-Smoller et al., 2003). All the three papers revealed data which showed that postmenopausal hormone therapy actually increased risk of dementia twofold. These findings provoke a strong "déjà vu" - the same difference between the results of an observational study (estrogen is protective) (Grodstein et al., 2000) and randomized trials (estrogen is harmful) (JAMA 2002) also occurred for coronary disease outcomes. These recent results also suggest that combined hormone therapy is not even protective of Alzheimer disease, in spite of the published beneficial in vitro, animal and observational effects of estrogen on the central nervous system (Yaffe et al., 1998).

Postmenopausal therapy with estrogen and progestin results in increased risk of disease, does not make asymptomatic women feel better (except may be in the perimenopausal period), does not prevent dementia nor improve cognition. All the data published from randomized trials underscore that postmenopausal hormone therapy should be prescribed only for temporary use to treat menopausal symptoms, not for chemopreventive purposes of any kind.

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References

- Grady D (2003). Postmenopausal hormones – Therapy for symptoms only. *N Engl J Med*, **348**, 1835-7.
- Hays J, Ockene JK, Brunner RL, et al (2003). Effects of estrogen plus progestin on health-related quality of life. *N Engl J Med*, **348**, 1839-54.
- Grodstein F, Manson JE, Colditz GA, et al (2000). A prospective, observational study of postmenopausal hormone therapy and primary prevention of cardiovascular disease. *Ann Intern Med*, **133**, 933-41.
- Rapp SR, Espeland MA, Shumaker SA, et al (2003). Effect of estrogen plus progestin on global cognitive function in postmenopausal women: the Women's health Initiative Memory Study, a randomized controlled trial. *JAMA*, **289**, 2663-72.
- Shumaker SA, Legault C, Rapp SR, et al (2003). Estrogen plus progestin and the incidence of dementia and mild cognitive impairment in postmenopausal women: the Women's Health Initiative memory Study, a randomised controlled trial. *JAMA*, **289**, 2651-62.
- Wassertheil-Smoller S, Hendrix S, Limacher M, et al (2003). Effect of estrogen plus progestin on stroke in postmenopausal women: the Women's Health Initiative. *JAMA*, **289**, 2673-84.
- Women's Health Initiative Investigators (2002). Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA*, **288**, 321-33.
- Yaffe K, Sawaya G, Lieberburg I, Grady D (1998). Estrogen therapy in postmenopausal women: effects on cognitive functions and dementia. *JAMA*, **279**, 688-95.