The Other Shoe Drops: New WHI Analysis

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Unfavorable balance of risks and benefits also applies to women who initiated HT within 5 years after menopause.

Results of the Women's Health Initiative (WHI) showed that postmenopausal hormone therapy with conjugated equine estrogens alone or plus medroxyprogesterone acetate did not lower risk for coronary heart disease (CHD) and, overall, had an adverse risk-benefit profile (*JW Womens Health* Aug 2008, p. 59, and *JAMA* 2002; 288:321). However, most WHI participants were >5 years past menopause, which might be too late to benefit from HT's potentially cardioprotective properties. Now, WHI researchers have reexamined the data to determine the effects of initiating HT within the first 5 years after menopause. Participants were from the estrogen clinical trial, an observational subcohort that had undergone hysterectomy prior to enrollment, the estrogen/progestin clinical trial, and an observational subcohort with intact uteri at enrollment. Ages at menopause and first HT use were known for all women; none had histories of breast cancer.

Most women who began HT <5 years after menopause did so before WHI enrollment. Both estrogen-alone HT and estrogen/progestin HT adversely affected risk for CHD, stroke, and venous thromboembolism, regardless of whether they were initiated <5 years or ≥5 years after menopause. Women who initiated either regimen within 5 years after menopause had substantially higher risk for invasive breast cancer than did those who initiated HT later. The authors caution that the results might have been influenced by the nature and duration of HT use prior to WHI study entry but, overall, concluded that the unfavorable risk-benefit balance for combined HT users and the lack of benefit for estrogen-only users apply to participants who started HT within 5 years after menopause.

Comment

Clinicians who have been awaiting guidance about risks and benefits of initiating postmenopausal HT early now have an answer: The latest WHI analysis provides little support for the hypothesis that such timing could have favorable effects. Why do these findings differ from those of previous reports (*JW Womens Health* Jun 2007, p. 43, and *JAMA* 2007; 297:1465)? One important difference is that this analysis centers around time between menopause and first use of HT, whereas earlier studies focused on time between menopause and study entry; therefore, prior HT use now assumes a more important role in driving the conclusions. Editorialists note that these new results constitute the best available evidence and that further data will be difficult to obtain; thus, these findings must guide clinical practice with respect to use of oral conjugated equine estrogens and medroxyprogesterone acetate in menopausal women. The current guidelines of professional organizations (*JW Womens Health* Aug 2008, p. 61, and *Menopause* 2008; 15:584), the FDA, and similar international organizations seem the most prudent: HT generally should be used by well-informed and well-monitored patients for menopausal symptoms only, in the lowest possible doses, and for the shortest amount of time that results in symptomatic relief.

Dr. Hanes' Comments:

This well titled report "The Other Shoe Drops…" is the final nail in the coffin for any doctors that still insist that hormone replacement therapy (aka HT or HRT) is of any benefit for anything other than alleviating symptoms. The truth is that it should have never been called hormone replacement therapy in the first place, because the drugs used only vaguely resembled true bioidentical hormones. Premarin®, literally stood for Pregnant Mares Urine, which was collected from mares that were constantly impregnated to gather the hormone and then it was modified so that it could be patented. Then it was given in doses several hundred to thousands of times what is necessary for biological activity; and given unopposed by the balancing of Progesterone which furthered the imbalance in millions of women. **Balancing hormones (male of female) can effectively eliminate symptoms, improve longevity and vitality, but only if you first get an accurate picture of what the current state of the patient's hormones are (i.e. with saliva testing) and use real, bioidentical hormones in tiny amounts and in the right combination.**