Do the risks of hormone therapy persist after discontinuation?

Yes, a few. Although the higher cardiovascular, thromboembolic, and stroke risks observed with conjugated equine estrogens (CEE) and medroxyprogesterone acetate (MPA) in the Women's Health Initiative (WHI) disappeared after discontinuation, other risks remained elevated. For example, women who discontinued CEE plus MPA continued to have a greater risk of invasive breast cancer than women who had never taken hormones, although the difference was not statistically significant and risk declined slightly after discontinuation. All-cause mortality also remained higher in women who had taken hormones.

EXPERT COMMENTARY
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In Summer 2002, the WHI randomized trial of CEE plus MPA was stopped after the WHI Writing Group concluded that data showed more risks than benefits from therapy. The risks included venous thromboembolism and stroke, cardiovascular disease, coronary heart disease, and invasive breast cancer, while benefits were reduced risk of fracture and colorectal cancer. In this latest update, WHI investigators report on outcomes 3 years after discontinuation of the study medication.

Risk–benefit ratio improved

In contrast to findings at the time that hormone therapy was discontinued in the WHI, no increased risk of thrombosis, coronary heart disease, or stroke was observed during the subsequent 3 years in women who had taken CEE plus MPA. Furthermore, neither a statistically significant increase in the risk of invasive breast cancer nor a lower risk of fracture or colorectal malignancy was observed after discontinuation.

The global risk index for the entire 8 years of follow-up (hazard ratio [HR], 1.12; 95% confidence interval [CI], 1.03–1.21), which was elevated at the time the trial was stopped, was noted to be 1.11 (95% CI, 0.99–1.27) during the 3 years after discontinuation. All-cause death rate was higher after discontinuation than during overall follow-up, although this difference was not statistically significant (HR, 1.15; 95% CI, 0.95–1.39 and HR, 1.04; 95% CI, 0.91–1.18, respectively).

Three years after the trial was discontinued, risk of any diagnosis of cancer was modestly higher than during active trial in women who had taken hormones (HR, 1.24; 95% CI, 1.04–1.48). An increased incidence of cancer in these women appeared to reflect a higher risk of a diagnosis of cancer other than ones prespecified as outcomes (especially lung).

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The elevated risk of CV disease and invasive breast Ca does not persist after HT ends

What this evidence means for clinical practice

The fact that the increased risk of cardiovascular outcomes and invasive breast cancer, and the reduced risk of fracture and colorectal cancer, did not persist after discontinuation of hormones is the take-home message from this follow-up analysis. At the same time, the overall increase in risk of malignancy justifies continued surveillance after combination hormone therapy is stopped.

Recent WHI reports have suggested that hormone therapy—particularly estrogen-only therapy—may be associated with a lower risk of coronary heart disease in recently menopausal women and menopausal women in their 50s. Accordingly, we look forward to the WHI age-specific follow-up analyses for both combination and estrogen-only therapy.

—Andrew M. Kaunitz, MD

CONTINUED

Does treating asymptomatic bacterial vaginosis reduce preterm delivery?

Sometimes. In a meta-analysis for the US Preventive Services Task Force, screening and treatment for bacterial vaginosis (BV) of pregnant women at low or average risk of preterm delivery did not prolong pregnancy. A slight benefit was seen in women at high risk of preterm birth.

EXPERT COMMENTARY

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BV is one of the most prevalent vaginal disorders, affecting 30% of women of reproductive age.[1] The syndrome is characterized by a relative lack of lactobacillus and increased anaerobes, *Gardnerella vaginalis*, *Mobiluncus* species, and *Mycoplasma hominis*. A strong and consistent association exists between BV during pregnancy and spontaneous preterm birth and amniotic fluid infection.[2,3]

Data were collected with rigor and detail

In this meta-analysis, designed to update 2001 recommendations from the US Preventive Services Task Force, Nygren and colleagues augmented the earlier data with published English-language studies from Ovid Medline (2000 through September 2007) and Cochrane Library databases (through September 2007), reference lists, and expert suggestions. The authors are to be applauded for the rigor and detail with which they collected source data. They used these data to estimate the pooled effect of treatment of BV on preterm delivery (at <37, <34, and <32 weeks' gestation), low birth weight, and preterm, premature rupture of membranes among women at low, average, and high risk of preterm birth.

Heterogeneity of studies was a problem

It usually is difficult to pool studies because of major differences in study design, inclusion and exclusion criteria, diagnostic criteria, assessment of risk status, and treatment. This is particularly true in regard to studies of women at high risk for preterm birth. The authors acknowledge this heterogeneity and considered it in statistical analysis of the data, but the detection of significant benefit or harm for BV screening and treatment remained difficult.

More study is needed

More research certainly is needed to elucidate the relationship between vaginal flora and preterm birth among high-risk women. We currently lack the ability to identify particular subgroups of women with abnormal vaginal flora who are most likely to derive benefit from screening and treatment. ■

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There is no need to treat women at low or average risk of preterm birth for bacterial vaginosis

What this evidence means for clinical practice

Treating pregnant women at low or average risk of preterm birth for asymptomatic BV is not beneficial. This conclusion is well supported by the findings of Nygren and colleagues as well as other studies.

As for high-risk women, screening and treatment are reasonable based on current knowledge, although the data are inconclusive. In this study, three trials demonstrated a reduction in preterm birth with treatment, but one trial demonstrated harm and one trial found no benefit.

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