Menopausal Hormone Therapy Doesn't Increase Mortality In Long-term Followup

By Ruth Kava — September 19, 2017

Ever since the Women’s Health Initiative (WHI) trials of hormone replacement therapy (HRT) for post-menopausal women was halted early because of an observed increased risk of breast cancer, there has been confusion about the positive and negative effects of this treatment, as we discussed here [2]. Early on, it was thought that HRT would reduce a woman’s chance of cardiovascular disease — but the results didn’t show that. Now, HRT is primarily suggested for women who suffer from extreme menopause-related symptoms such as hot flashes. A new analysis of the long-term results of the WHI should provide some additional guidance to women and their physicians.

To review: the WHI was a randomized, double-blind trial with 2 arms. One included women with intact uteri who were given either placebo or a combination of estrogen (CEE) and progestin (MPA). The other arm included women who had undergone hysterectomy and were randomly assigned to receive placebo or CEE alone. The women used the hormones (or the placebos) for from 5 to 7 years.

The current paper reports on the rates of mortality in the different groups at a median 12.5 years later; the cumulative follow-up was 18 years. The study [3] was published in JAMA, and the lead author was Dr. JoAnn E. Manson from Harvard Medical School in Boston.

When they were originally enrolled in the WHI trial, the women were between 50 and 79 years old. There were nearly 17,000 women assigned to receive CEE + MPA or placebo, and about 11,000 were assigned to CEE alone or placebo.

The long term follow-up found that there were no significant differences with respect to either type
of hormone use on all-cause mortality, CVD mortality, or mortality from coronary heart disease (CHD). For these endpoints use of either type of hormone treatment was virtually the same as that of the placebo groups.

In fact, there were few significant findings of effects of the hormones. With respect to breast cancer mortality, however, there was an increased risk in the CEE + MPA group that approached significance, while there was a significant decrease in that risk for the CEE alone group (p<0.02.).

The authors noted “Results for cause-specific mortality should be interpreted cautiously due to multiple comparisons. “ And they also observed

“Hormone therapy has a complex relationship with cancer. Although a significant reduction in breast cancer was seen with CEE, a significant increase in breast cancer incidence with CEE plus MPA has been documented [in other studies]. Divergent findings for CEE alone and CEE plus MPA for breast cancer point to an adverse effect of progestin on the breast epithelium, but progestins have been linked to favorable effects on the endometrium and a decreased risk of endometrial cancer became apparent with long-term follow-up of the CEE plus MPA trial. Moreover, these regimens did not appear to alter mortality outcomes for other cancer sites, including lung cancer, and had no significant effect on total cancer incidence.”

Thus the results of this study are not simple to interpret — while mortality from all causes, cardiovascular and total cancer was reduced 18 years post-treatment, breast cancer mortality was lower in the CEE alone group. Overall, what does this mean? Most likely it means that women and their health care providers will have to carefully assess the individual’s quality of life issues before deciding on HRT to assuage menopausal symptoms. However, it is reassuring to note that several types of long-term mortality risk were not increased after use of HRT.

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