Medical Xpress

Study: Timing matters for hormone therapy

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Ever since a landmark federal clinical trial gave menopausal hormone therapy a black eye almost a generation ago, critics have argued that the results overstated the cardiac dangers for newly postmenopausal women.

Now, a new trial suggests that women who start taking hormones within six years of menopause can slow age-related thickening of their heart arteries, an indicator of heart disease.

The therapy had no effect on two other indicators of heart disease, and the trial was not large or long enough to see if estrogen and progesterone actually reduced heart attacks and strokes.

Nonetheless, the study, published this week in the *New England Journal of Medicine*, lends credence to the "timing hypothesis" - the idea that estrogen helps women's hearts, but only if started within several years of the final menstrual period, which usually occurs around age 51.

"This really is the first study to test the timing hypothesis," said lead author Howard N. Hodis, director of atherosclerosis research at the University of Southern California in Los Angeles. "These data clearly show that there is a beneficial effect on the atherosclerotic (heart disease) process according to the time since menopause."

Experts said the findings should reassure women that they can safely take hormones as currently recommended - to relieve hot flashes and other passing menopausal discomforts. However, the findings do not mean hormone therapy use should be expanded.

"Even when doctors recommend hormone therapy for the menopausal transition, the caveat is, take the lowest possible dose for the shortest possible time," said Judy Hannah, a clinical research specialist with the National Institute on Aging, which funded the $13.8 million study. "I don't think this is going to change that."

Current guidelines caution against using hormones to try to prevent heart attacks, "and that's the way it should remain," said John F. Keaney, chief of cardiology at the University of Massachusetts Medical School and author of an editorial accompanying the new study.

For decades, doctors routinely put women of a certain age on hormone therapy - indefinitely - because of vast but circumstantial evidence that it was good for many organs, particularly their hearts. Although therapy slightly increased breast and endometrial cancer risks, in theory it would help most women live longer.

But in 2002, the Women's Health Initiative - which gave hormones or placebo for five years to 16,000 women ages 50 to 79 - provided the real scorecard: increases in heart attacks and strokes, as well as breast cancer, endometrial cancer and dementia. The risks trumped reductions in hip fractures and colon cancer.

Later reanalyses of the surprising, contentious data looked at the timing question. In women under 60, hormones actually had neutral or even slightly favorable cardiac effects.

Since then, studies that tested the timing hypothesis have been "suggestive but inconsistent," Keaney wrote.

The new trial - which used different estrogen and progesterone products than the Women's Health Initiative - enrolled 248 early-postmenopausal women, and 348 women at least 10 years past menopause.

In the younger group, but not the older women, coronary artery thickening was significantly less with hormones than placebo over five years. However, hormones had no effect on fatty plaque buildup or artery hardening in either group.

The anti-thickening effect suggests that estrogen receptors in blood vessels shut down if estrogen dries up, and don't work properly if estrogen suddenly surges years later, the researchers wrote.

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