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Hormone therapy timing may cut heart risk

Judy Foreman -- Medical Matters

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After years of frightening findings on hormone therapy, there is reassuring news for women who start taking hormones close to menopause.

The new results suggest a window of opportunity near menopause during which estrogen therapy may reduce heart disease risk, not raise it, as starting hormones a decade or so later seems to do. And this makes good biological sense.

"Estrogen slows the early stages of arterial disease," said Dr. Jacques Rossouw, project officer for the Women's Health Initiative, a study of 27,000 women ages 50 to 79 run by the National Heart, Lung and Blood Institute and published in a series of articles beginning in 2002.

But starting hormones later, such as in a woman's mid-60s when arteries become more clogged with plaque, may be dangerous. "We know now from trials and angiographic studies [of blood vessel walls] that women who already have arterial disease, if you give them hormones, you do them no good and may increase the risk" of heart disease, he said.

"We have come full circle on this," said Dr. Hunter Champion, a cardiologist at Johns Hopkins School of Medicine. "It's not one size fits all" with hormone therapy.

It's increasingly clear that "a woman's age, or more specifically, the time since menopause, is an important factor in terms of heart outcomes on hormone therapy," said Dr. JoAnn Manson, chief of the Division of Preventive Medicine at Brigham and Women's Hospital in Boston.

The idea that starting hormones early can be beneficial was bolstered by two studies, one published last week in the Archives of Internal Medicine and the other published several weeks ago in the Journal of Women's Health. Two more studies - one called KEEPS (Kronos Early Estrogen Prevention Study) by the Kronos Longevity Research Institute and the other, ELITE (Early versus Late Intervention Trial with Estradiol) sponsored by the National Institute on Aging - are enrolling women close to the age of menopause to further explore the issue.

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In last week's study, researchers focused on the youngest women (ages 50 to 59) in the part of the WHI involving women with hysterectomies who took estrogen without progestin, the hormone needed to protect the uterus in women who still have one.

Even in the original analysis of this group in 2004, these women had no increased cardiac risk. The study published last week goes further, showing a clear benefit in these women.

In this group, there was a 45 percent lower rate of cardiac bypass surgery or angioplasty (a technique for opening clogged arteries) in those on estrogen versus those on placebo, and a 34 percent lower rate of fatal or nonfatal heart attack, bypass or angioplasty.

For the record, it was in the other part of the 2002 WHI study - on nearly 17,000 women ages 50 to 79 taking both estrogen and progestin - that researchers linked hormone use to a modest increase in heart disease, as well as breast cancer, stroke and blood clots.

That original study panicked millions of women into giving up their hormones, even though the increased cardiac risk was principally in the first year of combined hormone use, and the risk tapered off with time.

The second new study involved a different group of women, those participating in the Nurses' Health Study. This one showed that women who started taking hormones within four years of menopause had a 30 percent lower risk of heart disease than women who never used hormones.

This was true whether a woman took estrogen alone or with progestin, said Manson, an author on both studies. "It all relates to the underlying stage of atherosclerosis," she said.

Estrogen slows development of atherosclerosis in several ways. It decreases "bad" (LDL) cholesterol and raises "good" (HDL). It makes blood vessels more elastic, enabling them to dilate better, which increases blood flow. But in older women who already have plaques on artery walls, estrogen can increase the likelihood of blood clots or plaque ruptures that can trigger heart attacks and strokes.

Estrogen also assists in the secretion of nitric oxide from the cells that line arteries, said Dr. Alan Altman, a menopause specialist in private practice in Brookline, Mass. Nitric oxide helps dilate arteries. But when there is a lot of plaque, as there is in older women, the plaque blocks the access of estrogen to its receptors on artery walls, thus reducing the output of nitric oxide and making it harder for vessels to dilate.

In addition, estrogen stimulates production of a protein called MMP9, an enzyme that breaks down tissue, including plaque on artery walls, said Dr. Howard N. Hodis, chairman of cardiology at the University of Southern California Keck School of Medicine. That means that "estrogen may facilitate the rupture" of plaques in older women.

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Defining the exact onset of menopause - and thus, when to start taking hormones - is very tricky, according to Dr. Rowan Chlebowski, a medical oncologist at LABioMed, a nonprofit research institute at Harbor-UCLA.

The time that elapses around menopause, called peri-menopause, can last four or five years. It is only when a woman has not had a period for a year - which can only be determined retrospectively - that she is defined as menopausal.

Another unresolved issue is how long to continue taking estrogen if you start within a few years of menopause. Should it become a lifetime treatment?

"We don't have good evidence for either taking estrogen therapy forever or for taking for a short time only, when you look at benefits and risks for heart disease," said USC's Hodis.

Others shudder at the idea that a woman might be wedded to estrogen until death do them part. The mainstream party line is still that a woman should start estrogen at menopause - but not for its heart benefits, only to combat symptoms such as hot flashes - and that she should stay on it for a short time.

Nobody knows, said Rossouw of the WHI, "if estrogen will prevent heart disease into the future," as a woman ages.

As for breast cancer, the two new studies did not address that risk. The original WHI study showed a slight increase in risk on combined hormone therapy after four years of use, but no increase on estrogen alone during seven years of treatment. For stroke, WHI data showed a slight increased risk for oral estrogen - alone and with progestin.

And so it goes. The studies pile up. The data get refined. The nuances get clearer. Some questions get answered, but we are still stuck with an ever-growing mass of new ones.

For more information on the ELITE trial: 866-240-1489. For more information on the KEEPS study, visit keepstudy.org.

Send your questions to foreman@baltsun.com.

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