

HEALTH SENSE

Hormones: Does timing make a difference?

By Judy Foreman | February 20, 2006

Back in 2002, researchers warned millions of older women that postmenopausal hormone pills were likely doing them more harm than good. That study, the massive Women's Health Initiative, panicked many women into tossing out their hormones.

Now, researchers are poring over that -- and newer -- data to refine their understanding of the risks and benefits of hormones, especially for women who start taking hormones right at menopause, not a decade or so later.

Two studies published over the last few weeks and aimed at better understanding the role hormones play in heart disease are the first salvos in that scientific effort. Both found that starting estrogen therapy at menopause did not increase the risk of heart problems, while starting later in life does increase risk. In fact, there's a chance estrogen may even protect the hearts of those who take it early. Two more studies are now enrolling women close to the age of menopause to further explore the issue.

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.

Why would the timing of hormones make such a difference? Because estrogen plays an important role in preventing some of the age-related buildup of plaque in artery walls.

"Estrogen slows the early stages of arterial disease," said Dr. Jacques Rossouw, project officer for the Women's Health Initiative, the study of 27,000 women aged 50 to 79.

When a woman's arteries are bathed in hormones -- either naturally or with estrogen supplements -- they harden more slowly. Estrogen appears to decrease "bad" (LDL) cholesterol and raise "good" (HDL). It also makes blood vessels more elastic, allowing them to dilate better, which increases blood flow.

But in older women who already have plaque on their artery walls, adding estrogen can increase the likelihood of blood clots or plaque ruptures that can trigger heart attacks and strokes.

In addition, estrogen stimulates production of a protein called MMP9, which can break down the 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 adding estrogen to an older woman's system might trigger the plaque to rupture.

Estrogen also assists in the secretion of nitric oxide -- which helps open arteries -- from the cells that line arteries, said Dr. Alan Altman, a menopause specialist in private practice in Brookline. When there is a lot of plaque, as there is in older women, the output of nitric oxide is reduced and vessels have a harder time opening to allow blood to flow through.

Rossouw said: "We know now . . . 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.

One of the new studies -- a reanalysis of the Women's Health Initiative that looked at women by age group -- found that women aged 50 to 59 had a 45 percent lower rate of cardiac bypass surgery or angioplasty (a technique for opening closed vessels) than women who took a placebo.

The second study looked at women who started hormones within four years of menopause and found that, whether they took estrogen alone or with a second hormone, progesterin, they had 30 percent less risk of heart disease than women who never used hormones.

Of course, defining exactly when menopause is and thus, when to start taking hormones, is "very tricky," said Dr. Rowan Chlebowski, a medical oncologist at LABioMed, a nonprofit research institute at Harbor-UCLA. The time before menopause, called peri-menopause, can last four or five years. A woman is defined as menopausal only when she has not had a period for a year -- which can only be determined after the fact.

A new issue that the emerging research is raising is how long to continue taking estrogen if you do start within a few years of menopause. Should it become a lifetime treatment?

For some women, Altman says: probably. "That's what I say to my patients, but I don't think the data is obviously supportive of that yet."

Others shudder at the mere idea that a woman might be wedded to her estrogen until death do them part, and say women should take hormones only short-term to relieve hot flashes, insomnia, and other symptoms of menopause.

Nobody knows, said Rossouw of the WHI, "if estrogen will prevent heart disease into the future" as a woman ages. "At some point, the benefit will flip into harm, and we'll never know when that is."

In addition to sorting out the heart disease questions, of course, women still need to consider other factors, such as breast cancer and stroke. The two new studies did not address those issues. The original WHI study showed a slight increase in breast cancer on combined hormones after four years of use, but no increase on estrogen alone after seven years of treatment. For stroke, the WHI data showed a slight increased risk for both oral estrogen alone and with progesterin. There's less data on estrogen delivered via creams and patches.

So, until the new hormone therapy research is completed, women, like the doctors they turn to, will be left making educated guesses about what's best for them. Hormone therapy is still very much a moving target.

If you are interested in joining a trial of hormone therapy for newly menopausal women, you may contact the KEEPS study by the Kronos Longevity Research Institute at www.keepstudy.org or call 617-732-9870. You can also contact the ELITE -- Early versus Late Intervention with Estradiol -- trial, sponsored by the National Institute on Aging: 1-866-240-1489. Both studies will look at women around the age of menopause and use scanning technology to study the effects of hormones on artery walls.

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