Timing Key in Balancing HT's Risks, Benefits

BY DOUG BRUNK

FROM THE ANNUAL MEETING OF THE ENDOCRINE SOCIETY

SAN DIEGO — The scale that weighs risks and benefits tips more favorably for newly menopausal women who begin hormone therapy at age 50-59 years and who use it for 5 years, compared with women who start the therapy in their 60s, according to a systematic review of several studies and position statements.

Younger women who are newly menopausal and who use hormone therapy have a 30%-40% reduction in total mortality, a phenomenon "that's not seen in older women," said Dr. Richard J. Santen, professor of medicine at the University of Virginia, Charlottesville, who called the findings "very surprising."

"Physicians and their patients need to rethink the use of menopausal hormonal therapy" on the basis of these findings, said Dr. Santen, who chaired the 12-member task force that wrote a scientific statement on behalf of the Endocrine Society suggesting that menopausal hormone therapy may benefit women who start it in their 50s rather than in their 60s.

Importantly, the new analysis points to the need to look beyond data from the Women's Health Initiative, in which the average age was 63 years, in order to advise younger women. "The therapy clearly needs to be individualized, primarily based on symptoms. But if a woman has an underlying risk of breast cancer … you're going to be very cautious about this," Dr. Santen said.

He said that the new analysis is more applicable to the typical menopausal patient whom physicians see in practice: the 53-year-old who had her last period a year ago, and is now trying to make a decision about whether to start menopausal hormonal therapy.

Dr. Santen and his associates used the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) system to evaluate the benefits and risks associated with menopausal hormone therapy based on published randomized controlled trials, cohort studies, and case-control studies, as well as position statements related to the topic.

Overall, the researchers found that women who start menopausal hormone therapy at age 50-59 years experienced a 30%-40% decrease in mortality, no increased risk of heart disease, and a 90% reduction of menopausal symptom such as hot flashes or overactive bladder.

"Relief of symptoms is really the key issue," Dr. Santen said.

Compared with women who did not take hormone therapy, newly menopausal women experienced 10 fewer diagnoses of diabetes per 1,000 women, 4 fewer cases of heart disease (among those on estrogen only), 5 fewer bone fractures, and 2 fewer cases of colon cancer per 1,000 women (among those on estrogen plus progestin only).

Risks associated with menopausal hormone therapy included gallbladder disease (10 more per 1,000 women), blood clots in the legs and lungs (5 more women), and stroke (2 more women).

Women who were on estrogen therapy alone had no increased risk of developing breast cancer, but there were 7 more cases of breast cancer per 1,000 women among those who took estrogen and progestin for 5 years, compared with non-HT users.

"Our tentative conclusion is that estrogen plus progesterone actually didn't cause tumors; it caused preexisting tumors to grow to a size where they became detectable," Dr. Santen said.

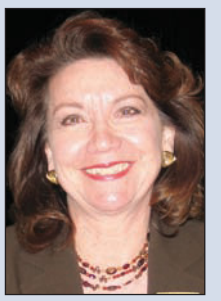
The statement is published in the July 2010 issue of the Journal of Clinical Endocrinology and Metabolism. ■

Disclosures: *Dr. Santen reported having no conflicts of interest.*

MY TAKE

Statement Shores Up NAMS Advice

This has been a banner season for statements regarding postmenopausal hormone therapy (HT). Recently, the North American Menopause Society (NAMS) and the Endocrine Society (ES) issued complementary statements; five senior authors contributed to both documents.



Philosophically, the two societies agree on the fundamentals. While NAMS limits their discussion to estrogen and estrogen combined with progestogen therapy, the ES touches on the use of alternative forms of HT such as tibolone and raloxifene, as well as bioidentical forms of HT, such as testosterone and dehydroepiandrosterone. The NAMS statement, at 14 pages, presents concise, bottom-line risk/benefit assessment and practical clinical recommendations. The ES scientific statement, at 66 pages, presents a tour de force analysis of the literature, carefully weighed according to level of evidence.

The 12 pages dedicated to breast cancer in the ES document clearly illustrate why the relationship between HT and the breast is so complex, and why generalizations regarding risks are so challenging.

Both groups acknowledge the important influences of age and time since menopause on benefits and risks of HT. Both agree that more research is necessary to accurately assess benefits and risks in recently menopausal women most likely to request HT. And both conclude with the familiar mantra to individualize therapy, and use the lowest effective dose for symptom relief for the shortest duration possible.

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Menopause Before Age 46 Doubles CVD Risk Later in Life

VITALS

Major Finding: Women who had menopause before the age of 46 were 2.1 times more likely to have a cardiovascular disease event later in life, compared with those who did not have early menopause.

Data Source: A cohort analysis of 2,509 women in MESA followed for an average of 7 years.

Disclosures: The study was funded by the National Heart, Lung, and Blood Institute.

BY DOUG BRUNK

FROM THE ANNUAL MEETING OF THE ENDOCRINE SOCIETY

SAN DIEGO — Women who go through menopause before the age of 46 are twice as likely to have a heart attack, stroke, or other cardiovascular event later in life as are women who do not go through early menopause, results from a large, multiethnic study showed.

"Our study is observational, so we cannot conclude that early menopause somehow causes these cardiovascular disease events, but our findings support using early menopause as a marker of increased cardiovascular disease risk," Dr. Melissa F. Wellons said during a press briefing at the meeting. "Therefore, getting clinicians to ask women about menopause and about when they went through menopause is an important part of potentially determining what their risk of CVD is in the future. Doing that can give them information on placing these women with early menopause into a higher risk group and counseling them appropriately, such as encouraging them to stop smoking, exercise, and lose weight."

Dr. Wellons, a fellow in the department of medicine at the University of Alabama, Birmingham, and her associates evaluated data from 2,509 women enrolled in the observational Multi-Ethnic Study of Atherosclerosis (MESA), funded by the National Institutes of Health. It included more than 6,000 women, from six communities in the United States, who were recruited in 2000 and followed for an average of 7 years. Most (40%) were white, 25% were black, 22% were Hispanic, and 13% were Chinese American.

"Our work is important because previous studies that have found a relationship between early menopause and cardiovascular disease events have taken place in primarily European and white cohorts," Dr. Wellons noted.

The researchers defined early menopause as occurring before age 46, either naturally or surgically through removal of both ovaries, and they tracked the incidence of CVD among all study participants. This included heart attack, nonfatal cardiac arrest, a definite angina, probable angina (if followed by revascularization), a stroke, or death due to stroke, heart attack, or other cardiovascular disease.

At baseline, the women ranged in age from 45 to 84 years. Of the 2,509 women, 693 (28%) reported early menopause. Of these, 446 (64%) had natural menopause and 247 (36%) had surgical menopause.

In the early menopause group, 41 women (5.9%) had CVD events during the study period. Among those who did not have early menopause, 47 women (2.6%), had CVD events. The difference was statistically significant.

'Our findings support using early menopause as a marker of increased cardiovascular disease risk.'

DR. WELLONS

No woman in either group had a CVD event before the age of 55.

After adjusting for race/ethnicity, level of education, smoking history, hypertension, total cholesterol, HDL cholesterol, diabetes, and whether the menopause was natural or surgical, Dr. Wellons and her associates found that women in the early menopause group were 2.1 times more likely to experience a CVD event, compared with women who did not have early menopause. Further adjustment for current or previous use of hormone replacement therapy and body mass index produced identical results.

"The risk of having a heart attack, stroke, or other cardiovascular disease event later in life doubles in women with early menopause," Dr. Wellons concluded. "We found [this] in a large, U.S., multiethnic cohort, so our findings are generalizable to the U.S. population."

Dr. Wellons was the recipient of an NHLBI Career Development Award. ■

Pages 36a—36b