Hip Fractures Rose as the Use of HT Declined

BY RICHARD HYER

FROM THE ANNUAL MEETING OF THE NORTH AMERICAN MENOPAUSE SOCIETY

CHICAGO – Prescriptions for hormone therapy for elderly postmenopausal women declined significantly after the results of the Women's Health Initiative were reported in May 2002, and it now appears that there has been a correspondingly steep rise in hip fracture rates, said Roksana Karim, Ph.D., of the University of Southern California, Los Angeles.

"The rise in hip fracture rates in elderly postmenopausal women may be partially attributed to the continued decline in hormone therapy use," she said at the meeting. "Hormone therapy–related benefits on hip fracture do not carry over after cessation."

This was the conclusion of a longitudinal observational study of 80,995 postmenopausal women aged 60 years or older using data from 11 Kaiser Permanente medical centers in southern California. The study was designed to assess the risk of hip fracture for women who stopped taking hormone therapy (HT), compared with those who continued the therapy. It was also designed to evaluate the risk of hip fracture over time after stopping HT, and to measure bone mineral density (BMD) over time after stopping HT.

Data was collected on hip fracture, HT use, and the use of antiosteoporotic medication from June 2002 through December 2008. All hip fractures were verified by chart review by an orthopedic surgeon who was blinded to patients' HT status. Exclusion criteria included fractures secondary to tumors or high-energy trauma, and periprosthetic fractures. Patients were considered to be HT users if they had filled at least two prescriptions in a given year, as each prescription provides a 3-month supply of medication. HT was defined as estrogen alone or estrogen plus progesterone.

BMD data of the hip and lumbar regions were available for 54,209 women (67%). The 80,955 women had a mean age of 68.8 years and a mean body mass index of 26.9 kg/m^2; the study's mean follow-up was 5.6 years. There were 1,419 hip fractures (2%) and 6,928 deaths (9%). In all, 15% of the 80,955 patients (12,486) were terminated from Kaiser.

Between July 2002 and December 2008, HT use in this population decreased from 85% to 18%. After adjustments for age and race, women who did not use HT in the previous year had a 55% increased risk of hip fracture (hazard ratio, 1.55), said Dr. Karim. She also said that hip fracture risk significantly increased with 2 or more years of HT cessation. Mean BMD was significantly and inversely associated with cumulative years of HT nonuse, she said.

Dr. Karim acknowledged that the study was limited by lack of body mass index data in 47% of the population, or information on history of past HT use or on previous fractures.

The estimated annual cost for osteoporotic fractures in the United States is $18 billion, and hip fractures result in a greater cost and disability than do all other osteoporotic fractures combined, said Dr. Karim.

"Women at risk of hip fracture should consider carefully before making a decision of stopping using hormone therapy," she said.

During a question-and-answer session, Andrea LaCroix, Ph.D., professor of epidemiology at the University of Washington, Seattle, said, "It certainly comes as no surprise that women discontinue hormone therapy. There's some loss of bone density and an increase in hip fracture rates. I agree with the conclusion that women coming off hormone therapy should be counseled about their potential for losing bone and having an increased fracture risk, but they've never enjoyed more alternatives for the prevention of hip fracture than they do today, including many agents besides hormone therapy." ■

VITALS

Major Finding: The Women's Health Initiative reported in May 2002 that risks of coronary heart disease and cancer were associated with HT. Between July 2002 and December 2008, HT use in this population decreased from 85% to 18%. After adjustment for age and race, women who did not use HT in the previous year had a 55% increased risk of hip fracture.

Data Source: A study of 80,995 patients in the Kaiser Permanente Southern California database.

Disclosures: Dr. Karim said she had no financial conflicts of interest. The study was supported by the University of Southern California.

Novel Oral Drug for Menorrhagia Boosts Quality of Life Measures

BY BRUCE JANCIN

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE

DENVER – A novel oral formulation of tranexamic acid provided immediate and enduring improvement in two quality of life measures among women with menorrhagia in a large open-label study.

The improvements were noted during the first menstrual cycle after initiation of treatment. The benefits were maintained throughout the 15-cycle study, Dr. Ken Muse reported at the meeting.

Tranexamic acid is a lysine analogue that acts as a competitive plasmin inhibitor and an antifibrinolytic agent. The oral formulation was approved by the Food and Drug Administration late last year for the treatment of cyclic heavy menstrual bleeding and is marketed under the trade name Lysteda. It's a valuable alternative to surgical or hormonal treatments for this disorder, which affects up to 22 million Americans, said Dr. Muse of the University of Kentucky, Lexington.

Oral tranexamic acid won marketing approval on the strength of studies showing it reduced menstrual flow by nearly 40%.

The quality of life study involved 723 women who took oral tranexamic acid at 1.3 g three times per day for a maximum of 5 days per menstrual cycle, starting with the onset of heavy menstrual bleeding. General quality of life was assessed using the 36-Item Short Form Health Survey. The Aberdeen Menorrhagia Clinical Outcome Questionnaire was used as a disease-specific measure of the impact of treatment.

Significant improvements were noted in six of eight SF-36 categories and domains at cycle 15 compared with baseline. The greatest improvements were in vitality, with a 13.5% gain, and social functioning, with an 8.3% gain. Patients also showed significant long-term improvements in bodily pain, mental health, role-physical, and role-emotional items. Only physical functioning and general health weren't significantly different at cycle 15 compared with baseline.

Women on oral tranexamic acid had a mean 5.4% long-term improvement in the mental health component of the SF-36, and a less robust but nonetheless significant 1.7% gain in the physical functioning component, Dr. Muse said.

Treatment-related adverse events occurred in 7.3% of subjects, the researchers noted. These were mild to moderate in nature and usually consisted of headache, menstrual discomfort, or back pain. There were few gastrointestinal side effects, and no thrombotic or thromboembolic events.

Scores on the AMCOQ indicated patients had a consistent improvement in daily activities that are affected by cyclic heavy menstrual bleeding.

The study was funded by Xanodyne Pharmaceuticals Inc. and Ferring Pharmaceuticals, which acquired global marketing rights to Lysteda last May. Dr. Muse disclosed that he has received research grants from, and served as an adviser to, Xanodyne. ■

Metabolic Syndrome Plus HT Ups Coronary Risk

BY RICHARD HYER

FROM THE ANNUAL MEETING OF THE NORTH AMERICAN MENOPAUSE SOCIETY

CHICAGO – The results of the Women's Health Initiative randomized clinical trial suggest that postmenopausal women who begin hormone therapy may be at risk for coronary heart disease, but a new study from the University of Oklahoma Health Sciences Center suggests that the presence or absence of the metabolic syndrome at baseline is a key determining factor.

"If the metabolic syndrome was present, indeed there was a greater risk, greater odds of event, and this was statistically significant," said principal investigator Dr. Robert Wild, professor of ob.gyn. and adjunct professor of medicine–cardiology at the center.

The nested case-control study examined the Women's Health Initiative cohort for an effect modification between elevated baseline risk and hormone therapy (HT). It found 359 incident cases of coronary heart disease (CHD), and matched these to 817 controls without CHD. Controls were matched with a variety of criteria, including prevalent cardiovascular disease at baseline. Trials of estrogen plus progesterone and estrogen alone were studied separately and in a pooled analysis. Metabolic syndrome was defined by ATP III criteria, at least three of the following: elevated waist circumference, triglycerides, HDL cholesterol, blood pressure, and fasting glucose.

In the pooled trial analysis of estrogen plus progesterone and estrogen alone, the metabolic syndrome was found to be an effect modifier. The odds ratio for treatment effect was 0.98 for women without the metabolic syndrome and 1.72 for those with the metabolic syndrome.

The individual trials had limited power, said Dr. Wild, but the findings were similar.

"Women without metabolic syndrome had no increase in risk of coronary heart disease vs. placebo, whereas women with metabolic syndrome had elevated risk," said Dr. Wild. The reasons for this heightened risk might be more advanced stages of atherosclerosis and a heightened thrombogenic state among women with the metabolic syndrome, he said.

"Baseline CHD risk assessment may be helpful to identify women at increased risk for CHD when taking hormone therapy," said Dr. Wild.

He disclosed no relevant financial relationships. This study was sponsored by the University of Oklahoma Health Sciences Center, Oklahoma City. ■