Diabetes Risk Lower in Women on Hormones

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Women considering the risks and benefits of hormone therapy should be informed of the link between hormones and a decreased risk of diabetes, especially if they are at risk for the disorder, according to Dr. Wulf Utian, executive director of the North American Menopause Society in Cleveland.

"While hormone therapy [HT] is not indicated for the prevention of diabetes, women with diabetes risk factors who are considering it for a valid indication should understand the evidence in this area," Dr. Utian said in an interview. NAMS' newly revised position statement on HT is the group's first to review this evidence.

The paper reviewed three studies on the subject, granting Class I status to the evidence presented in each one: two subanalyses of the Women's Health Initiative (WHI) and one subanalysis of the Heart and Estrogen/Progestin Replacement Study (HERS).

The first of the WHI studies, published in 2004, examined the effect of HT on diabetes development in the 16,600 women included in the estrogen/progestin arm (Diabetologia 2004;47:1175-87). After 5 years of follow-up, women in the active group were 21% less likely to develop diabetes than those in the placebo group (277 cases vs. 324 cases).

The numbers achieved greater significance when the analysis was restricted to the small subgroup of women who remained compliant with therapy throughout the follow-up period. In this group, the decreased risk was 33%. The difference seemed to be driven by steady improvements in fasting glucose and insulin resistance in the active group, the authors wrote. The risk ratios remained unchanged after adjusting for body mass index (BMI) and waist circumference.

Insulin resistance and glucose level were also the driving forces behind the smaller risk reductions seen among women in WHI's estrogen-only arm (Diabetologia 2006;49:459-68). This study included 9,712 women. At year 6, women in the active group were 12% less likely to have developed diabetes than those in the placebo group (a rate of 8.3% vs. a rate of 9.3%). This difference was not significant in the overall group, but became highly so in the smaller group of women who were compliant with therapy through the study's end. These women were 27% less likely to develop diabetes than the placebo group.

Again, adjusting for BMI and waist circumference did not account for the difference, the authors said. Instead, the risk reduction seemed to be related to improvements in fasting glucose and insulin resistance. These were significant within the first year of therapy and then waned in the overall group, but remained significant in the compliant group.

The final study, a subanalysis of the HERS data, confirmed HT's beneficial effect on diabetes development in women with preexisting coronary heart disease. The subanalysis followed 2,029 patients who did not have diabetes at baseline (Ann. Intern. Med. 2003;138:1-9).

At 4 years' follow-up, the incidence of diabetes in the active group was 6.2%, compared with 9.5% in the placebo group—a significant risk reduction of 35%. The risk differential was related to significantly higher fasting glucose levels in the placebo group; these levels remained stable in the active group. There was no association of decreased diabetes with the active group's modest decreases in BMI or waist circumference.

More research is necessary to further define HT's impact on diabetes, Dr. Utian said. ■

Justification Persists to Prescribe Hormones to Preserve Bone Mass

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

The benefits of hormone therapy outweigh its risks in healthy perimenopausal and early-postmenopausal women with menopause-related symptoms and a low baseline risk of stroke, according to the revised position statement released by the North American Menopause Society.

However, the paper cautioned, that HT should not be prescribed for the prevention of any disease, with the exception of postmenopausal osteoporosis.

'There is no cookbook recipe. Each woman has her own potential indications and risk factors.'

DR. UTIAN

HT can be prescribed for the prevention of postmenopausal osteoporosis in women who require drug therapy to maintain bone. "There is strong evidence of the efficacy of [HT] in reducing the risk of postmenopausal osteoporotic bone fracture," the statement read.

For women at risk of a fracture during the next 5-10 years, HT can be an option—but only after a careful risk/benefit analysis.

The statement is based on an expert panel's review of HT studies published subsequent to the group's 2004 position paper, said Dr. Wulf Utian, executive director of the North American Menopause Society (NAMS) in Cleveland. "In this day and age, the life span of any position statement is a maximum of 2 or 3 years," Dr. Utian said in an interview. "In the face of so much new information, we felt an update was due."

The clinical impacts of HT's short- and long-term effects are becoming clearer, especially as additional subanalyses of the Women's Health Initiative (WHI) and the Heart and Estrogen/Progestin Replacement Study (HERS) begin to emerge, he said.

Results of these and other studies enabled more expert consensus in the new paper than was previously possible—most significantly, Dr. Utian said, in the area of cardiovascular disease risk.

"We have modified our stance on level of risk from 2004," he explained.

"Apart from the increased risk of stroke in the older woman [taking HT], the absolute risk of stroke and heart attack is rare, and we agreed that any evidence of an increase in heart attack in the perimenopausal woman was poor. We have concluded that for the symptomatic woman without a contraindication, the benefits of HT outweigh the risks, and that these women have less cause to fear than the popular perception," said Dr. Utian.

Two well-publicized, large studies have precipitated much of the current confusion over the safety of HT, appropriate treatment populations, and timing of therapy, the statement said. "The results of WHI and HERS should not be extrapolated to symptomatic postmenopausal women younger than 50 years of age, who initiate HT at that time, as these women were not studied in those trials."

"We state very clearly there is no cookbook recipe. Each woman has her own potential indications and risk factors, and only a comprehensive evaluation and discussion is going to decide what is most appropriate for that individual," Dr. Utian stressed.

The NAMS statement is available at www.menopause.org/aboutmeno/consensus.htm. ■

Image of the Month

At the first follow-up, the patient's BMD, based on a DXA scan, was up 5.3%. However, at the second follow-up, his BMD had dropped by 5.1%. His primary care physician referred the man to determine why he was no longer responding to therapy.

"What is the first thing to do?" asked Dr. Michael Lewiecki, director of the New Mexico Clinical Research & Osteoporosis Center in Albuquerque. Should you "evaluate for adherence to therapy? Ask about calcium and vitamin D intake? Order lab tests to evaluate for factors contributing to bone loss?"

No, the first step is to actually look at the DXA image, said Dr. Lewiecki. In this case, the vertebral bodies were mislabeled on the second follow-up DXA scan.

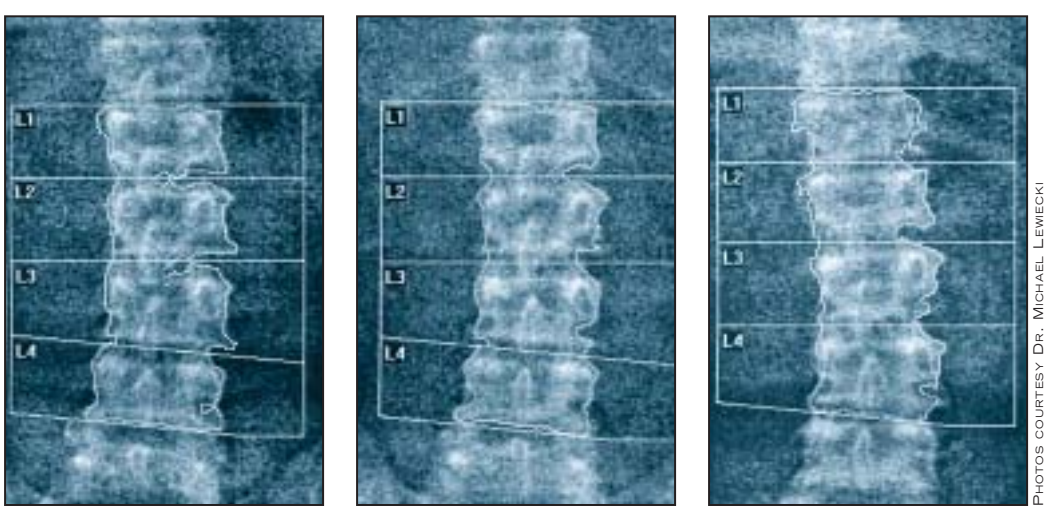
Typically, the DXA computer program selects the labeling for vertebral bodies on DXA scans. It's not uncommon for mislabeling to occur though, said Dr. Lewiecki. A technologist goes over the labeling to double check the computer. Finally, the image should be reviewed by a physician interpreter as an additional check before the report is generated. In this case, the incorrectly labeled scan was not caught and false BMD measurements were reported to the ordering physician.

"When you have a situation in which BMD changes unexpectedly, it is important to verify that it is a valid comparison," said Dr. Lewiecki.

Sometimes a left hip is incorrectly compared with the right hip or vice versa when assessing BMD over time. Other times, the lines used by the computer to delineate the edges of bone are misplaced, which can have a big effect on the amount of bone measured.

"Make sure you're comparing apples to apples," he said. Reanalysis of the image with vertebral bodies correctly labeled showed that the patient's BMD for L1-L4 had been stable since the first follow-up. Response to therapy actually was good, requiring no change in alendronate and hydrochlorothiazide therapy and no laboratory testing for nonresponse to therapy.

—Kerri Wachter



Photos courtesy Dr. Michael Lewiecki

Baseline DXA scan for L1-L4 (left): DXA at 1-year follow-up shows a 5.3% increase in BMD (center). However, a year later, mislabeling of vertebral bodies showed a 5.1% decrease in BMD (right). The erroneous labeling was clear when compared with the previous DXA images.