Lowest Dose Is Advocated

Hormone Therapy *from page 1*

"Recent data support the initiation of hormone therapy around the time of menopause" to treat menopause-related vasomotor symptoms, sleep disturbance, vaginal atrophy, dyspareunia, or diminished libido and to reduce the risk of osteoporosis and fractures in some women, the authors wrote.

Specifically, findings from the Women's Health Initiative (WHI) trial of estrogen therapy showed that 0.625 mg/day of oral conjugated estrogen effectively treats menopause-related symptoms with low absolute risks. Similarly, in the WHI trial of combined estrogen-progestogen therapy, most risks were deemed rare—except for stroke, which was above the rare category—based on the criteria of the Council for International Organizations of Medical Sciences.

They noted, however, that "there is a growing body of evidence that each type of estrogen and progestogen, route of administration, and timing of therapy has distinct beneficial and adverse effects." As such, more research is needed before the risks and benefits of HT can be generalized, and "it cannot be assumed that benefits and risks of [HT] apply to all age ranges and durations of therapy."

The most notable changes in the NAMS 2010 position statement on postmenopausal HT are the two new sections on ovarian cancer and lung cancer, which were not included in the 2008 position statement, as well as the assertion that HT is not recommended in women with a history of endometrial cancer, Dr. Margery L.S. Gass, executive director of NAMS, commented in an interview.

The new statement also reflects the latest research on the effect of age on the benefit/risk ratio of postmenopausal HT. The current understanding that the benefit/risk ratio is greatest among women who start HT close to the time of menopause and decreases with time since menopause should make clinicians and women more comfortable using HT right at the time of menopause and more cautious about using it later in life for the prevention of osteoporosis. Most of the side effects associated with HT become more common with aging, even without the use of HT. Adding the HT just compounds the problem. Therefore, rather than recommending oral or transdermal estrogen for such problems as vaginal dryness and painful intercourse, we place emphasis on using local/topical estrogen, said Dr. Gass, also a consultant to the Cleveland Clinic Center for Specialized Women's Health, Mayfield Heights, Ohio.

Regarding the association between hormone therapy and cancer, the data are conflicting, according to the NAMS statement authors. "Unopposed systemic estrogen therapy in postmenopausal women with an intact uterus is associated with increased endometrial cancer risk related to the [estrogen therapy] dose and duration," they wrote. Thus, concomitant progestogen is recommended in those who use systemic estrogen therapy, and HT is not recommended for women with a history of endometrial cancer.

With respect to ovarian cancer, most epidemiologic studies show no association or a modest association with HT, but observational trial data suggest an increased ovarian cancer risk, the authors wrote. Based on the available data, "the association between ovarian cancer and hormone therapy beyond 5 years, if any, would fall into the rare or very rare category," they stated, noting that women with a positive family history or other risk factors for ovarian cancer "should be counseled about this rare association."

The link between HT and breast cancer also is uncertain. Studies have demonstrated that diagnosis of breast cancer increases with estrogen-progestogen use beyond 3-5 years. However, a reanalysis of WHI data suggested that women who started estrogen-progestogen shortly after menopause experienced an increased breast cancer risk over the next 5 years, while those with a gap of more than 5 years between menopause and treatment did not, the authors explained.

Among breast cancer survivors, estrogen-progestogen therapy has not been proven safe and may be associated with an increased risk of recurrence, as indicated in a one randomized controlled trial, which "showed a statistically significant 2.4-fold increase in new breast cancer events," they wrote.

The data on lung cancer are particularly contradictory in that, overall, it appears that starting estrogen-progestogen therapy in older women with a history of smoking may promote the growth of existing lung cancers, while "evidence from the WHI and some case-control and cohort studies of hormone therapy in a younger population [less than 60 years] shows some protection against lung cancer," the authors stated. Although confusing, the findings "reinforce the need to encourage prevention or cessation of smoking and possibly to increase surveillance in older smokers who are current or past users of hormone therapy."

The revised statement also addresses the issues of cognitive impairment and coronary heart disease. It recommends against the use of HT at any age "for the sole or primary indication of preventing cognitive aging or dementia," noting that it may increase the incidence of dementia when initiated in women who are 65 years or older.

Additionally, HT is not recommended as a sole or main indication for coronary protection in women of any age. When HT is started in recently menopausal women for the treatment of menopause symptoms, there does not appear to be an increased risk for coronary heart disease, however, women who initiate HT more than 10 years beyond menopause are at increased CHD risk, the authors noted.

In all cases, because each woman is unique with her own risk profile and preferences, "individualization of [hormone] therapy is key to providing health benefits with minimal risks, thereby enhancing quality of life," they wrote. Women should be informed of known risks, with the understanding that "a woman's willingness to accept risks of [HT] will vary depending on her individual situation."

Overall, "NAMS continues to refine our recommendations and approach to hormone therapy as data from the WHI and other studies continue to emerge," NAMS president Cynthia A. Stuenkel said in an interview. "While we support the use of hormone therapy for symptomatic women [younger than age 60 years], close to the time of menopause, we remind our readers that there are some risks, though small, and there are some uncertainties remaining regarding short-term and long-term effects of hormone therapy."

In general, "we strongly advocate for the lowest dose for the shortest time for the individual woman who has been carefully counseled about risks and benefits," said Dr. Stuenkel, clinical professor of medicine at the University of California, San Diego. ■

Disclosures: *The advisory panel members' financial disclosures are listed on the position statement, which can be found on the NAMS Web site at http://www.menopause.org/PSht10.pdf.*

MY TAKE

HT in Clinical Practice

In general, the 2010 NAMS position statement on postmenopausal hormone therapy is in line with clinical practice; however, many doctors are not prescribing hormones, even when supported by the science, because of bad publicity and a lack of interest combined with fear of litigation.

It is pretty clear that hormone therapy should be used for patients with a clear indication, and the statement outlines what the relevant indications are.

The information coming from the Women's Health Initiative seems to reverse itself on the cardiovascular issue. Some of the subanalyses suggest that hormone therapy is associated with a cardiovascular benefit in women close to the age of menopause, while other studies from the same group suggest that this isn't so. Obviously, the science is evolving, and we are only beginning to understand the mechanism of cardiovascular risks and benefits. Overall, however, the statement is pretty clear that we should not use hormones to prevent cardiovascular disease.

In all cases, the decision to initiate hormone therapy has to be individualized to each patient. There is not a one-size-fits-all solution. The main issue is determining what is the safest drug for a woman at a particular time in her life.

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Drug Combination Boosts Rebuilding of Bone Mass

BY SALLY KOCH KUBETIN

PHILADELPHIA — Combining once-a-year zoledronic acid and daily teriparatide significantly increased bone mass in key skeletal sites in postmenopausal women with osteoporosis, according to a study presented at the annual meeting of the American College of Rheumatology.

The trial included 412 postmenopausal women considered to be at high risk for fracture. They were diagnosed with osteoporosis on the strength of having a T score that was 2.5 standard deviations below peak bone mass, or having a slightly better T score but a history of at least one fracture. The women were randomized to one of three treatment groups: treatment with zoledronic acid alone (137), with both zoledronic acid and teriparatide (137), and with teriparatide alone (138). The zoledronic acid dosage was 5 mg intravenously once per year. Teriparatide was given daily in a subcutaneous dose of 20 mcg.

Use of the two drugs in combination increased bone mineral density (BMD) at the spine more than did teriparatide alone, and at the hip more than did zoledronic acid alone, according to study presenter Dr. Kenneth G. Saag, the Jane Knight Lowe Chair of Medicine in Rheumatology at the University of Alabama at Birmingham.

BMD at the spine increased 7.51%, 7.05%, and 4.37% in the combination arm, teriparatide arm, and zoledronic acid arm, respectively. Combination therapy significantly increased lumbar spine BMD at weeks 13 and 26 and total hip BMD at weeks 13, 26, and 52, compared with teriparatide alone.

The incidence of serious adverse events was 9.5%, 14.6%, and 10.9% in the combination, zoledronic acid, and teriparatide arms, respectively. ■

Disclosures: *Dr. Saag disclosed financial relationships with Eli Lilly & Co., maker of teriparatide (Forteo), and Novartis,maker of zoledronic acid (Reclast).*