Drug Monitor

ONLINE EDITION

Hormone Therapy and Incontinence in Younger Postmenopausal Women

Results from large, randomized clinical trials have indicated that postmenopausal women aged 60 years and older who use hormone therapy (HT) have a higher risk of urinary incontinence (UI) compared with similarly aged women who don't use HT after menopause. Whether UI is associated with HT in younger postmenopausal women, however, is unknown. Researchers from Brigham and Women's Hospital, Harvard Medical School, and Harvard School of Public Health, all in Boston, MA, and University of Pittsburgh, Pittsburgh, PA prospectively analyzed the association between incident UI and HT use in postmenopausal women aged 37 to 54 years between 2001 and 2003.

The researchers analyzed data from the Nurses' Health Study II—an observational cohort study of women who responded to biennial questionnaires beginning in 1989. After identifying 17,193 women who reported menopause on a questionnaire mailed in 2001, they excluded questionnaires in which data regarding HT use, UI frequency, and key UI risk factors were missing. In addition, they excluded women who reported UI at least once per month (or less than once per month if it was enough to wet their underwear) at baseline and those who had major health conditions or functional limitations. In all, there were 7,341 women who were at risk for incident UI in 2001.

Of the 1,868 women who reported never using postmenopausal HT, 211 reported incident UI in 2003. Of the 1,033 women who reported past HT use, 140 reported incident UI, and of the 4,440 who reported current HT use, 675 reported incident UI. The multivariable adjusted odds of incident UI in current HT users was 1.39 times that in women who had never used HT. These odds did not seem to vary according to the type of HT used or the estrogen dose.

In all, 14% of the 7,341 postmenopausal women reported having at least monthly episodes of UI; 4% reported having incontinent episodes at least weekly. Among the women with at least one episode per week, 55% of the episodes were classified as stress incontinence and 18% were classified as urge incontinence, with the rest identified as another or a mixed type.

The researchers conclude that there is a moderate risk of UI with HT use across all age groups. The similarities in the relationship between UI and HT across age suggest that multiple mechanisms may be at work, they say. Estrogen therapy, for instance, may increase collagen turnover and weaken the structure of the connective tissues supporting the urethra. Moreover, they note, HT is associated with neurovascular disease, which could affect bladder innervation and increase the risk of urge UI.

Source: *Am J Obstet Gynecol.* 2009;200(1):86.e1–86.e5. doi:10.1016/j.ajog.2008.08.009.

Effects of Adding Ezetimibe to Statin Therapy for Patients with Diabetes

Since its FDA approval in 2002, ezetimibe has become the main add-on agent to statin therapy for reducing elevated low-density lipoprotein cholesterol (LDL-C) levels. Research into whether adding ezetimibe to statin therapy positively affects subclinical atherosclerosis is limited, however. So far, the only data on this question was from the Effect of Combination Ezetimibe and High-Dose Simvastatin Versus Simvastatin Alone on the Atherosclerotic Process in Subjects With Heterozygous Familial Hypercholesterolemia (ENHANCE) trial. In this study, researchers found that adding ezetimibe to simvastatin boosted reductions in LDL-C by a further 17%, but over two years, the average increase in common carotid artery intima-media thickness (CIMT) didn't differ significantly from that in the statin-only group.

To gain a better understanding of this issue, investigators from the Stop Atherosclerosis in Native Diabetics Study (SANDS) performed a secondary analysis of data from their trial. In SANDS, the effects of achieving aggressive goals for LDL-C (70 mg/dL or less), non–high-density lipoprotein cholesterol (100 mg/dL or less), and blood pressure (115/75 mm Hg or less) were compared with the effects of achieving the standard goals of 100 mg/dL or less, 130 mg/dL or less, and 130/80 mm Hg or less, respectively, in 499 Native American patients aged 40 years or older with type 2 diabetes and no prior cardiovascular (CV) events.

In the secondary analysis, the researchers compared CIMT changes in patients in the aggressive group treated with statin monotherapy (n = 154), patients in the aggressive group treated with a statin plus ezetimibe (n = 69), and patients in the standard group treated with statin monotherapy (n = 204). They found that, for the aggressive group, mean CIMT at 36 months regressed 0.025 mm from baseline in the patients receiving a

statin plus ezetimibe, which was similar to the mean regression from baseline in the patients receiving a statin only (0.012 mm). Among patients in the standard group receiving statin monotherapy, however, the mean CIMT progressed by 0.039 mm.

The researchers point out that their study was not a randomized comparison and that their sample size was not powered to detect clinical event differences between the groups. They say results from ongoing trials should shed light on whether the use of ezetimibe plus statin therapy to achieve aggressive lipid and blood pressure goals will lower the rate of CV events in patients without prior CV events.

Source: *J Am Coll Cardiol.* 2008;52(25):2198–2205. doi:10.1016/j.jacc.2008.10.031.