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Hormone therapy after menopause might increase risk of kidney stones, UT Southwestern findings suggest

DALLAS – Oct. 11, 2010 – The use of estrogen therapy by postmenopausal women might increase the risk of developing kidney stones, according to findings by UT Southwestern Medical Center researchers.

In a study available online and in today's issue of the *Archives of Internal Medicine*, investigators found that estrogen therapy after menopause increased a woman's chances of developing kidney stones by approximately 20 percent. This discovery calls into question the long-held belief that estrogen might actually protect women from the disease, and clinicians need to keep these results in mind when considering the risks and benefits of hormone therapy protocols in postmenopausal women, said Dr. Naim Maalouf, assistant professor of internal medicine at UT Southwestern and lead author of the paper.

Kidney stones (nephrolithiasis) in women are not uncommon, affecting an estimated 5 percent to 7 percent of postmenopausal women in the U.S., but are still less common than in men. Because women are less likely to develop the painful stones, some researchers have speculated that the estrogen might offer a protection that men don't have.

"This research suggests that the opposite might be true, and it offers new information that might be considered when prescribing estrogen-replacement therapies to postmenopausal women," said Dr. Maalouf, who is affiliated with the Charles and Jane Pak Center for Mineral Metabolism and Clinical Research at UT Southwestern. "Because the process of kidney-stone formation is influenced by a variety of lifestyle and other health-related factors, the true impact of estrogen therapy on the risk of nephrolithiasis is difficult to infer from observational studies."

Study results were drawn from trials conducted at 40 U.S. clinical centers. A total of 10,739 postmenopausal women who had had hysterectomies were randomized to receive an estrogen supplement or a placebo, and 16,608 postmenopausal women who hadn't had hysterectomies were randomized to receive estrogen plus progesterone (another female hormone) or placebo. The rate of nephrolithiasis was determined for an average follow-up of 7.1 years for the estrogen-only group, and 5.6 years for the second group.

In women receiving hormones, 335 cases of kidney stones were reported, while 284 cases
(MORE)

Female kidney-stone risk – 2

occurred in the placebo groups. The baseline demographic characteristics and risk factors for kidney stones were similar in the two groups.

Development of kidney stones during the study was five times more common in women who had a history of kidney stones prior to the trial. Additionally, estrogen therapy increased the risk of kidney stone formation irrespective of age, ethnicity, body mass index, prior hormone therapy use or use of coffee or thiazide diuretics.

“Although these results indicate that estrogen therapy increases the risk of kidney stones in healthy postmenopausal women, the mechanisms underlying this higher propensity remain undetermined and mechanistic studies are needed to carefully explore this relationship,” Dr. Maalouf said. “In view of the sizable prevalence of nephrolithiasis in postmenopausal women, these findings need to be considered in the decision-making process regarding postmenopausal estrogen use.”

An acute kidney-stone event not only can cause physical suffering, Dr. Maalouf said, but also can progress to long-term complications such as renal failure.

“Treatment of nephrolithiasis also incurs substantial costs, estimated at \$2 billion annually in the United States alone. Getting to the bottom of what causes kidney stones and how to prevent them is an important issue in women’s health,” he said.

Dr. Khashayar Sakhaee, chief of mineral metabolism and professor of internal medicine at UT Southwestern, participated in the research. Investigators from the MedStar Research Institute and Georgetown University School of Medicine; the University of Washington School of Nursing; the University of California, Davis; Baylor University Medical Center; and the Women’s Health Initiative Clinical Coordinating Center at the Fred Hutchinson Cancer Research Center also contributed to the study.

The study was conducted as part of the Women’s Health Initiative, a program funded by the National Institutes of Health.

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