

Study: Vaginal Estrogen Ups Serum Estradiol

BY BRUCE JANCIN

SAN ANTONIO — Vaginal estrogens for the treatment of atrophic vaginitis result in significant systemic absorption, leading to increased serum estradiol levels that are of concern in breast cancer survivors, a study shows.

“All we can say now to patients is that the use of vaginal estrogens does increase the serum estrogen level. There isn’t any information out there to say whether this is going to increase their risk of recurrence or not,” Shannon Wills, Ph.D., said at the San Antonio Breast Cancer Symposium.

But that’s a distinct possibility. It is well established that adjuvant aromatase inhibitors are more effective than tamoxifen at preventing breast cancer recurrences, and they also drive serum estrogen levels lower, noted Dr. Wills of William Beau-



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DR. WILLS

mont Hospital, Royal Oak, Mich.

She reported on the use of a highly accurate radioimmunoassay to measure serum 17-beta-estradiol levels in 24 postmenopausal women who had completed chemotherapy and/or local therapy for breast cancer. All of the women were on an adjuvant aromatase inhibitor or a selective estrogen receptor modulator, and had been using a vaginal estrogen for an average of 20 months to treat severe atrophic vaginitis. Fourteen women were using one vaginal estrogen tablet (Vagifem) inserted twice weekly, and 10 were using the vaginal estradiol ring (Estring), inserted every 3 months. Twenty-four postmenopausal breast cancer patients on adjuvant therapy who were not using vaginal estrogens served as controls.

Preinsertion serum estradiol levels in the patients who were using vaginal estrogen tablets averaged 4.7 pmol/L—not significantly different than controls. Twelve hours post insertion, however, their average serum estradiol level was 76 pmol/L. One patient had a level of 300 pmol/L, and two others were in the 200- to 250-pmol/L range. Preinsertion serum estradiol levels in vaginal ring users averaged 14.2 pmol/L. Eight weeks post insertion, the average serum level was 30 pmol/L, with one patient having a level approaching 180 pmol/L.

Previously, all 24 patients on vaginal estrogens had unsuccessfully tried all the other methods of improving at-

VITALS

Major Finding: Twelve hours post insertion, users of vaginal estradiol tablets had average serum estradiol levels of 76 pmol/L, up from an average of 4.7 pmol/L.

Data Source: A study of 24 postmenopausal breast cancer patients on adjuvant therapy who had been using vaginal estrogen for an average of 20 months to treat severe atrophic vaginitis, and 24 controls.

Disclosures: None reported.

rophic vaginitis. Vaginal estrogens were the only option left, Dr. Wills noted.

The session chair, Dr. Charles L. Loprinzi, asked Dr. Wills which type of product she’d recommend in these desperate situations—tablets or ring?

“I would have to say the vaginal tablets are probably a better option for the patient, based on our results,” she replied. “The Estring had continuous absorption throughout the entire 3-month period. Our pharmacist said it gives a dose of 2 mcg/day for the 3 months of insertion. With the vaginal tablets there appears to be a spike, then the serum level goes back down to baseline.”

Dr. Loprinzi observed that vaginal dryness is a major problem for many postmenopausal women who haven’t had breast cancer and even more of a problem for those who have, “if we ask about it.” Among the old-school potential alternatives to vaginal estrogens for these patients are nonestrogenic vaginal lubricants such as K-Y Jelly and Replens. But the most exciting work in this area involves the use of intravaginal dehydroepiandrosterone (DHEA) capsules (prasterone), according to Dr. Loprinzi, professor of oncology at the Mayo Clinic, Rochester, Minn.

In a series of papers based on a recent phase III randomized, double-blind, placebo-controlled, 12-week clinical trial involving 216 postmenopausal women with vaginal atrophy, Dr. Fernald Labrie and workers at Laval University, Quebec, showed that intravaginal DHEA was highly and rapidly effective for the treatment of vaginal atrophy (Menopause 2009;16:907-22), significantly improved the patients’ libido and sexual function (pp. 923-31 of the same issue of Menopause), and did so with no suggestion of an increase in serum sex steroid levels (pp. 897-906).

“I believe this is something that ideally should be replicated by another group. But it does look quite interesting,” commented Dr. Loprinzi. He and his coworkers recently completed an as-yet unpublished phase III clinical trial of pilocarpine (Salagen) for atrophic vaginitis based on a favorable preliminary report in patients with Sjogren syndrome. “Unfortunately the data do not look promising. There’s some toxicity associated with this, so this will not be a new treatment to utilize,” he said. ■

US: Diagnostic Alternative to Biopsy, Mammography for Some

BY RICHARD HYER

CHICAGO — Women younger than 40 years with focal breast signs or symptoms should be evaluated by targeted ultrasound, and probably not mammography or biopsy, according to findings from two studies of more than 1,800 patients treated at one medical center.

“This is particularly timely with the recent [U.S. Preventive Services Task Force] recommendations that women not perform [breast self-exam],” said Dr. Constance Lehman of the University of Washington in Seattle.

“One of the USPSTF’s concerns was that women will go through unnecessary harms and procedures. We think imaging can better guide us in reducing harms that can be associated with a [breast self-exam].”

The studies’ findings could have broad implications for practice patterns and cost. Reducing biopsies and surgical excision of lumps would lessen trauma and cost, while limiting mammography would reduce cost and unnecessary radiation.

Dr. Lehman described the two studies in a press briefing at the annual meeting of the Radiological Society of North America. Both were retrospective studies of data from the University of Washington.

In the first, investigators reviewed all breast exams performed on women under age 30 from Feb. 1, 2002, to Aug. 30, 2006, and found 1,091 lesions in 830 patients. Three malignancies were found, and all were identified as suspicious by ultrasound. No malignancy was found in any patient with a negative, benign, or probably benign ultrasound.

The rate of biopsy was high, and the yield was low. For example, a third (46/140, 33%) of patients with a Breast Imaging Reporting and Data System (BI-RADS) 3 lesion (probably benign) underwent tissue sampling, and none of these lesions was found to be malignant.

The authors concluded that mammography was not indicated in this setting, and that close surveillance might be a preferred alternative to tissue sampling.

The second study, which included women aged 30-39 years, also found ultrasound to have 100% sensitivity. In this study, investigators reviewed 1,327 lesions in 1,032 patients, finding that 98% (1,301/1,327) were benign and 2% (26/1,327) were malignant.

Ultrasound and mammography had been used to evaluate 91% (1,207/1,327)

VITALS

Major Finding: Targeted ultrasound has 100% sensitivity in evaluating women 30-39 years of age presenting with focal breast signs or symptoms.

Data Source: Two retrospective studies of data involving more than 1,000 breast lesions each.

Disclosures: Both studies were funded by the University of Washington. Dr. Lehman disclosed work as an instructor with General Electric Co. Dr. Portillo said he had nothing to disclose.

of cases, yet all cancers at the site of clinical concern were detected by ultrasound and none by mammography alone.

In a solitary case (1/1,327, 0.08%), mammography resulted in detection of a malignancy in an asymptomatic area.

The authors concluded that ultra-



Coauthors (from left) Dr. Constance Lehman, Dr. Michael Portillo, and Dr. Vilert Loving “don’t recommend ultrasound” as a screen.

sound has 100% sensitivity in evaluating women 30-39 years of age presenting with focal signs or symptoms.

“The added value of mammography in this setting is less apparent,” Dr. Lehman said. “It did help one woman who had an area of cancer identified in another region of the breast, but in all other women, there was no added value of the mammogram.”

In answer to a question from the audience, Dr. Lehman said that ultrasound is recommended as a diagnostic tool and not as a screening tool.

“We strongly recommend women have screening mammography annually, at age 40 and older, and if they are shown to be at high risk, that they add MRI to that. We don’t recommend ultrasound as a screening tool,” she said, because the specificity of ultrasound is low.

At the scientific session, Dr. Michael Portillo, one of Dr. Lehman’s coauthors, was asked whether his institution had changed its practice in the wake of this study. “At this point we’re still following the [American College of Radiology guidelines], but we are currently considering changing our practice,” said Dr. Portillo, who worked on the project while a fellow at the University of Washington. ■