Obesity, Estrogen Status Sway Breast Ca Outcomes

BY AMY ROTHMAN SCHONFELD

FROM THE ANNUAL MEETING OF THE ENDOCRINE SOCIETY

BOSTON – Obesity increases the odds of a woman with breast cancer dying from her disease, according to a retrospective data analysis.

Further, this link between obesity and breast cancer death is strongest among those obese women who have estrogen receptor (ER)–positive cancer, according to the analysis of data on nearly 4,000 participants in the California Teachers Study.

"This is another reason why the public should be aware of the importance of maintaining a healthy body weight, particularly how it pertains to cancer and especially breast cancer," according to Christina M. Dieli-Conwright, Ph.D., an assistant research professor at City of Hope National Medical Center, Duarte, Calif., who presented the findings at the meeting.

The study looked at a cohort of women who had taken a self-administered baseline questionnaire in 1995-1996 and who were diagnosed with their first primary invasive breast cancer during 1995-2006. Of the 3,995 women studied through 2007, 262 died of breast cancer and 321 died of non-breast cancer causes.

There was a significant link between breast cancer mortality and body mass index. Women who were obese (BMI of at least 30 kg/m^2) had a 69% higher risk of dying of their breast cancer than did women with a BMI of less than 25. A similar increased risk in breast cancer mortality was seen in women who were overweight at age 18 (BMI 25-29) compared with those with a lower BMI. No significant ties were noted between weight and deaths due to non–breast cancer causes or from all causes.

When the data were stratified according to ER status, weight and breast cancer mortality were significantly related in women who were ER positive, but not in ER-negative women. Obese women who were ER positive had a 64% increased risk of death due to breast cancer compared with those who had a BMI of less than 25. No significant associations were seen between weight and death due to all causes according to ER receptor status. Interestingly, there was more than a threefold increase in death from breast cancer in women who were ER negative if they were overweight at age 18 years.

Dr. Dieli-Conwright reported having no conflicts of interest. ■

Obesity May Curb LNG-IUS Efficacy in Menorrhagia

BY NASEEM S. MILLER

FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS

WASHINGTON – In very obese women, treatment of menorrhagia with levonorgestrel intrauterine system may be slightly less effective, but the treatment's success rate justifies its use, according to a study conducted by researchers at the University of Michigan.

In addition, levonorgestrel intrauterine system (LNG-IUS) "may be an especially important treatment choice for women at high surgical risk," the authors reported.

Although studies have shown the effectiveness of LNG-IUS in treatment of menorrhagia, most have not considered the role of body mass index (BMI), said Ms. Paige C. Fairchild, a medical student at the university who presented the study at the meeting.

The team conducted a retrospective chart review of 398 women with menorrhagia who were treated with LNG-IUS between 1999 and 2009 within the University of Michigan Health System, Ann Arbor. Nearly 50% had BMI of 30 kg/m^2 or greater; 25% had BMI of 35 or greater. Treatment failure was defined as removal of LNG-IUS for continued menorrhagia, need for additional treatment, or expulsion. Continued menorrhagia was uncommon in all BMI groups, but it was most common in women with BMI greater than 34 kg/m^2, compared with those in all BMI groups (6.9% vs. 3.3%).

Also, removal of LNG-IUS because of continued menorrhagia was more common among women who had BMI greater than 34, compared with those in all BMI groups (6.9% vs. 4.1%).

The odds of surgery within 2 years of LNG-IUS removal also was higher in obese patients (2.6 times), compared with other groups.

Some factors that might contribute to the reduced effectiveness of LNG-IUS in obese women are a larger uterus, persistent unopposed estrogen endometrial stimulation, and poor placement/difficulty in achieving fundal placement, Dr. Vanessa Dalton of the departments of obstetrics and gynecology at the university and one of the study authors, said in an interview.

Despite the findings, the authors concluded that the high continuation rates of LNG-IUS and low surgery rates indicate that the treatment is still a good option for women with a high BMI.

Ms. Fairchild and Dr. Dalton had no relevant financial disclosures. ■

Triptorelin Cuts Early Menopause in Breast Cancer

BY MARY ANN MOON

FROM JAMA

Taking the GnRH analogue triptorelin during chemotherapy led to a 17% absolute reduction in the occurrence of early menopause in young women with early-stage breast cancer, investigators have reported.

"Our results suggest that temporarily suppressing ovarian function by administering triptorelin reduces the incidence of chemotherapy-induced early menopause. This treatment can therefore be offered to premenopausal patients with breast cancer who wish to decrease the risk of permanent ovarian failure associated with chemotherapy," wrote Dr. Lucia Del Mastro of Istituto Nazionale per la Ricerca sul Cancro, Genoa, Italy, and her associates.

In what they described as the largest phase III study to examine this issue, the investigators assessed 281 women aged 18-45 years who were treated for stage I, II, or III breast cancer at 16 Italian medical centers. The patients were randomized to receive adjuvant or neoadjuvant chemotherapy alone or chemotherapy plus intramuscular triptorelin, and were followed for 1 year to compare the incidence of early menopause. For this open-label trial, early menopause was defined as no resumption of menstrual activity and postmenopausal levels of FSH.

Women with hormone-sensitive tumors were also given tamoxifen for 5 years following the end of chemotherapy. Those whose ovarian function returned during the follow-up year also received triptorelin every 4 weeks until ovarian function had been suppressed for at least 2 years, to optimize their chance of eradicating the breast cancer.

The rate of early menopause was 26% for chemotherapy alone, compared with 9% for the addition of triptorelin, an absolute decrease of 17%. The number of patients who needed to take triptorelin to prevent one case of early menopause was just six, Dr. Del Mastro and her colleagues wrote (JAMA 2011;306:269-76).

Moreover, in a multivariate analysis the only factor found to significantly reduce the development of premature menopause was the use of triptorelin.

In a secondary analysis of a subgroup of 260 patients, menses resumed in 50% of the chemotherapy-only group, compared with 63% of the chemotherapy-plus-triptorelin group. The median time to resumption of menses was 6.7 months with the addition of triptorelin, but was not reached in the women who received chemotherapy alone.

"There was no difference in the incidence of selected toxicities that may have been partly related to the use of triptorelin," they added.

Longer follow-up is needed to assess the long-term maintenance of ovarian function and preservation of fertility in these patients. However, "at the time of the last annual follow-up, 1 full-term pregnancy in the chemotherapy-alone group and 3 pregnancies (1 full-term, 1 premature delivery, and 1 voluntary abortion) in the chemotherapy plus triptorelin group were reported," the researchers said.

In addition, longer follow-up is necessary to assess the effectiveness of the breast cancer therapy. So far, it doesn't appear that adding triptorelin interferes with chemotherapy's effects. There have been 27 breast cancer recurrences (13 with chemotherapy alone and 14 with the addition of triptorelin) and 11 deaths (3 in the chemotherapy-alone group, 8 in the chemotherapy plus triptorelin group), the researchers said. ■

VIEW ON THE NEWS

Approach With Caution

The findings of Del Mastro and associates are "intriguing, and represent an important and encouraging addition to the study of ovarian preservation for women in this difficult situation," wrote Dr. Hope S. Rugo and Dr. Mitchell P. Rosen.

However, it would be premature to advocate the routine use of GnRH analogues for these patients of childbearing age who are facing early menopause.

"Given that patients with hormone receptor–positive disease in the current study who had evidence of ovarian recovery were immediately suppressed without data on long-term recovery and that breast cancer outcome data are not available, and given as well the potential adverse effects on disease outcome, the use of GnRH agonists concomitant with chemotherapy cannot be recommended as a standard treatment and should be approached with caution in women with hormone-sensitive disease," they said.

HOPE S. RUGO, M.D., *and* MITCHELL P. ROSEN, M.D., *are at the University of California, San Francisco. The university has received research funding from Pfizer, Novartis, Roche/Genentech, Abbott, Celgene, Merck, and Bristol-Meyers Squibb. Dr. Rugo reported receiving honoraria from Genomic Health. Dr. Rosen reported having no disclosures. These remarks were taken from their editorial accompanying Dr. Del Mastro's report (JAMA 2011;306: 312-4).*