Therapy appears to reduce rate of chemotherapy-induced early menopause for women with breast cancer

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Temporarily suppressing ovarian function with use of the hormone analogue triptorelin reduced the occurrence of early menopause induced by chemotherapy among women with breast cancer, according to a study in the July 20 issue of *JAMA*.

Approximately 6 percent of women with breast cancer are diagnosed before age 40 years, with the majority of young patients receiving systemic treatment with chemotherapy, hormonal therapy, or both. Chemotherapy regimens are associated with an incidence of long-term amenorrhea (absence of menstruation) of at least 40 percent, according to background information in the article. No standard strategies for preventing chemotherapy-induced ovarian failure are yet available. Preclinical data have suggested that temporary ovarian suppression with a gonadotropin (hormones that are secreted by the pituitary gland)-releasing hormone (GnRH) analogue (chemical compound) during chemotherapy reduces ovarian toxicity.

Lucia Del Mastro, M.D., of the Istituto Nazionale per la Ricerca sul Cancro, Genova, Italy, and colleagues conducted a phase 3 trial designed to assess the efficacy of temporary ovarian suppression induced by the GnRH analogue triptorelin in reducing the incidence of early menopause in young women with breast cancer undergoing supplemental or neoadjuvant (i.e., administered before surgery for breast cancer) chemotherapy. The randomized trial was conducted at 16 sites in Italy

and enrolled 281 patients between October 2003 and January 2008. The patients were premenopausal women with stage I through III breast cancer who were candidates for adjuvant or neoadjuvant chemotherapy. Before beginning chemotherapy, patients were randomly allocated to receive chemotherapy alone or combined with triptorelin, which was administered intramuscularly at least 1 week before the start of chemotherapy and then every 4 weeks for the duration of chemotherapy.

After the patients received treatment as indicated in the trial, the researchers found that the rate of early menopause was 25.9 percent in the chemotherapy-alone group and 8.9 percent in the chemotherapy plus triptorelin group, an absolute difference of 17 percent. The number needed to treat (i.e., the number of patients that need to be treated with triptorelin to prevent early menopause in 1 patient) was 6. Further analysis showed that only treatment with triptorelin was associated with a significant reduction of the risk of developing early menopause. Patient age and the type of chemotherapy did not significantly affect the risk.

Resumption of menses was observed in 60 patients in the chemotherapy-alone group (49.6 percent) and in 88 in the chemotherapy plus triptorelin group (63.3 percent).

"In conclusion, 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," the authors write.

Editorial: Reducing the Long-term Effects of Chemotherapy in Young Women With Early-Stage Breast Cancer

In an accompanying editorial, Hope S. Rugo, M.D., and Mitchell P. Rosen, M.D., of the University of California, San Francisco, write that the data reported in this study represent an important and encouraging addition to the study of ovarian preservation for women in this difficult situation.

"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 [at the same time] with chemotherapy cannot be recommended as a standard treatment and should be approached with caution in women with hormone-sensitive disease."

"International guidelines recommend discussion of fertility options before starting chemotherapy, and when possible before surgery, to allow optimal timing for consultation and oocyte [egg cell] harvesting. When feasible, and for patients with hormone-insensitive disease, GnRH agonist therapy to suppress ovarian function during chemotherapy is an additional treatment that can potentially expand fertility possibilities. Although recovering menses is not the same as fertility preservation, it is one step in the right direction."

More information: Paper: *JAMA*. 2011;306[3]269-276. Editorial: *JAMA*. 2011;306[3]312-314.

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