Goserelin for ovarian protection in breast cancer chemotherapy

More reasons to offer gonadal protection with long-acting GnRH agonists to young women with ER-negative breast cancer


Summary. The use of gonadotropin-releasing hormone (GnRH) agonists or antagonists to protect reproductive function in women undergoing chemotherapy is not a new concept. It has been long discussed but rarely put to a rigorous scientific test. Moore and colleagues provide encouraging preliminary data to suggest that ovarian function and pregnancy outcomes are better in women with estrogen receptor (ER)-negative breast cancer randomized to a GnRH agonist (goserelin) concurrent with their chemotherapy compared with those who received chemotherapy alone. Moreover, they found a statistically significant improvement in survival among women who were assigned to goserelin (disease-free survival, \( P = .04 \); overall survival, \( P = .05 \)).

Comment. Strengths of this study include the long follow-up (median, 4.1 y) and the unambiguous secondary outcome of pregnancy. The information adds to the body of literature endorsing the use of long-acting GnRH agonists to prevent chemotherapy-induced ovarian toxicity. Unfortunately, there is almost no information on hormone levels to be found within the article. Ovarian failure was defined as amenorrhea plus a follicle-stimulating hormone (FSH) level in the “menopausal range.” Ovarian dysfunction was defined as an FSH, estradiol, or inhibin B level that was “menopausal” at 1 or 2 years. The authors do not communicate the specifics. We also do not know whether outcomes are dependent on the age at diagnosis, which is likely to be the case. The study also suffered from a very large rate of loss to follow-up (almost 50%), but the authors took pains to attempt to account for their missing data.

For clinicians, the data are relevant to everyday practice in that we now have more reasons than ever to offer gonadal protection with long-acting GnRH agonists to young women with ER-negative breast cancer, recognizing that there may not always be enthusiastic uptake on the part of the patient or her family. Every little bit helps.

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Duration of menopausal vasomotor symptoms

Several factors related to longer duration of vasomotor symptoms


Summary. Researchers performed analyses of data from 1,449 women with frequent vasomotor symptoms (VMS) in the Study of Women’s Health Across the Nation (SWAN) to determine total VMS duration in years (hot flashes or night sweats) and VMS persistence after the final menstrual period (FMP). The median total VMS duration was 7.4 years, and median post-FMP persistence was 4.5 years (in 881 women with an observable FMP). Women who were premenopausal or early peri-menopausal at their first report of frequent VMS had the longest duration (median, >11.8 y) and post-FMP persistence (median, 9.4 y). Those who were postmenopausal at onset of VMS had the shortest duration (median, 3.4 y). African American women reported the longest total VMS duration (median, 10.1 y). Other factors also related to longer duration of VMS included younger age, lower educational attainment, greater perceived stress and symptoms sensitivity, and higher depressive symptoms and anxiety at first report of VMS.

Comment. This data from the SWAN study sheds new light on the effect of VMS in various racial or ethnic groups across the United States, including in African American, Chinese, Hispanic, non-Hispanic white, and Japanese women. This article addresses the unique burden of these symptoms in diverse populations.

Moreover, the evidence of the prevalence and persistence of vasomotor symptoms has a major effect on women’s lives. Often considered merely a “quality-of-life” issue and not a priority in the healthcare domain, hot flashes, particularly in the post-Women’s Health Initiative era, may go unmentioned by the patient and untreated by the clinician. Because the average duration of VMS reported in the African American population was 10.1 years, with an overall median of 7.4 years, it is time to strategize new treatment options, redefine hormone therapy, and remember that healthcare for women as they age isn’t just about lengthening life but also about helping women live well.

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Vitamin D, bone mineral density, and fracture risk in menopause

Levels are inversely associated with nontraumatic fracture in midlife women


Summary. Researchers aimed to determine whether higher serum 25 hydroxyvitamin D (25(OH)D) levels are associated with slower loss of bone mineral density (BMD) and lower fracture risk during the menopause transition in this prospective cohort study that found 124 women (mean age, 48.5 ± 2.7 y) with an incident traumatic fracture, 88 women with incident nontraumatic fracture, and 1,532 women without incident fractures (average follow-up time, 9.5 y). The BMD analysis included 922 women who had a documented final menstrual period. The mean 25(OH)D level was 21.8 ng/mL. There was no significant association between 25(OH)D and traumatic fractures. The hazard ratio for nontraumatic fractures was 0.72 (95% confidence interval, 0.54-0.95) for each 10 ng/mL increase in 25(OH)D. Researchers concluded that serum 25(OH)D levels are
inversely associated with nontraumatic fracture in midlife women, and vitamin D supplementing is warranted in those with 25(OH)D levels below 20 ng/mL.

Comment. Several points emerge from these interesting observational data. They are consistent with the knowledge that serum 25(OH)D levels must be interpreted differently in black women because, in part, of differences in serum vitamin D-binding protein levels. Second, the nontraumatic fractures reported here should not be construed as osteoporotic fractures because women who experienced those fractures had none of the important and consistent risk factors for osteoporotic fractures (thinness, low bone mineral density, older age, prior fracture history, smoking). Other than estrogen, no drug has been shown to reduce fracture risk in such women. Finally, the association between nontraumatic fracture and low serum 25(OH)D in perimenopausal women certainly raises the possibility that correction of D deficiency could reduce nonvertebral fracture risk. Although correcting vitamin D deficiency seems reasonable in women of any age, we need more evidence before we can be confident that correcting the D deficiency will prevent those fractures. Perhaps that evidence will emerge from the prospective vitamin D supplement trials in progress, such as VITAL. A major challenge in accomplishing the recommendation resides in the high cost of identifying those women with low serum levels for whom supplements would be appropriate. Because, as shown again in this study, the prevalence of vitamin D deficiency is so high, it may be more cost-effective to provide supplements to all perimenopausal women until the cost of screening becomes lower.

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References


Alternatives to hysterectomy could be pursued more often

Analysis of Michigan data suggests opportunities to reduce hysterectomy use.


Summary. Hysterectomy is the most common major gynecologic operation in the US, yet medical and minor surgical alternatives can be as effective for some patients. Using data from the Michigan Surgical Quality Collaborative, investigators analyzed records of 3400 women undergoing benign hysterectomy for abnormal uterine bleeding, uterine fibroids, chronic pelvic pain, endometriosis, or a combination of these conditions to determine evidence of medical management or minor procedures prior to hysterectomy.

At least one alternative treatment was identified in 62% of cases (among the majority of these, only one therapy was pursued). Women younger than 40 were more likely to have alternative treatment than those aged 40 or older. Overall, only 12% of women were counseled about possible use of a levonorgestrel intrauterine device. Postoperative pathology did not support preoperative diagnosis in 18% of all women and 38% of those younger than 40, suggesting that a significant number of women with abnormal bleeding caused by anovulation underwent hysterectomy.

Comment. These data were abstracted from hospital records and therefore might underestimate the frequency with which alternative treatments were used. Nonetheless, this analysis provides strong evidence
supporting opportunities to decrease the number of hysterectomies performed in the United States. As health insurers search for ways to provide more cost-effective care, we as clinicians should more thoroughly document the necessity of hysterectomy while advocating for safer, less costly alternative treatments.

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Menopause Editor’s picks from March 2015

NAMS spotlights selections from the most recent issue of the Society’s official journal, Menopause, chosen by its editor in chief, Isaac Schiff, MD.

Incremental direct and indirect costs of untreated vasomotor symptoms.
Philip Sarrel, MD, David Portman, MD, Patrick Lefèbvre, MA, Marie-Hélène Lafeuille, MA, Amanda Melina Grittner, MA, Jonathan Fortier, MA, Jonathan Gravel, MSc, Mei Sheng Duh, MPH, ScD, and Peter M. Aupperle, MD, MPH.

Consistent ovulation may not be enough to make women healthy when approaching menopause: an update from the Study of Women’s Health Across the Nation.
Amanda A. Allshouse, MS, Alex Polotsky, MD, MS, Sybil Crawford, PhD, Hsiang-Yu Chen, MS, Samar R. El Khoudary, PhD, MPH, and Nanette Santoro, MD.

Use of hormone therapy in Swedish women aged 80 years or older
Lotta Järvstråt, MSc, Anna-Clara E. Spetz Holm, MD, PhD, Lotta Lindh-Åstrand, RN, PhD, Mikael J. Hoffmann, MD, PhD, Mats G. Fredrikson, PhD, and Mats L. Hammar, MD, PhD.

The level of evidence indicated for each study is based on a grading system that evaluates the scientific rigor of the study design, as developed by the US Preventive Services Task Force. A synopsis of the levels is presented below.

<table>
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<tr>
<th>Level</th>
<th>Description</th>
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<tr>
<td>Level I</td>
<td>Properly randomized, controlled trial.</td>
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<tr>
<td>Level II-1</td>
<td>Well-designed controlled trial but without randomization.</td>
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<tr>
<td>Level II-2</td>
<td>Well-designed cohort or case-control analytic study.</td>
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<td>Level II-3</td>
<td>Multiple time series with or without the intervention (eg, cross-sectional and uncontrolled investigational studies).</td>
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<tr>
<td>Level III</td>
<td>Meta-analyses; reports from expert committees; descriptive studies and case reports.</td>
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