COMMENTARY

The Safest Option for Menopausal Hormone Therapy

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June 20, 2022

This transcript has been edited for clarity.

In the four decades that I've been in practice, the main safety concern patients have expressed regarding menopausal hormone therapy (HT) is that it might increase risk for breast cancer. Given how common breast cancer is, and that most breast malignancies have hormone receptors, angst regarding HT use and breast cancer is understandable.

The Women's Health Initiative (WHI), which represents the largest placebo-controlled trial of HT, assessed oral conjugated equine estrogen (CEE) combined with the synthetic progestin medroxyprogesterone acetate (MPA) in participants with an intact uterus.

A WHI report with more than 20 years of follow-up found that the incidence of breast cancer remained modestly higher among participants with an intact uterus randomized to CEE plus MPA, with a relative risk of 1.28.

Since the initial WHI findings were published in 2002, there has been much interest in assessing whether the type of progestogen (a term that refers to bioidentical progesterone as well as synthetic progestins) makes a difference with respect to risk for breast cancer.

Similar to the earlier WHI findings, among participants with an intact uterus in a 2005 French prospective cohort study who used estrogen along with progestins, mainly MPA, the risk for breast cancer was significantly elevated.

However, no elevated risk for breast cancer was noted among women who used estrogen plus bioidentical progesterone. One limitation of the French study was that the overall number of women with breast cancer was less than 1000.

In the June issue of American College of Obstetricians and Gynecologists' (ACOG's) Green Journal (*Obstetrics & Gynecology*), a landmark case-control study using a UK database derived from British family medicine practices representing more than 7% of the total UK population examined how different types of HT formulations were associated with risk for invasive breast cancer. In this report, which included over 43,000 cases of breast cancer, investigators found that among women who used estrogen plus synthetic progestin, almost all of which was MPA, the odds ratio was 1.28, identical to the long-term follow-up of WHI participants who were randomized to CEE plus MPA.

However, among women who used estrogen plus bioidentical progesterone, no elevated risk for breast cancer was found, consistent with the French study's findings.

A few practical issues when prescribing progesterone as part of menopausal HT: Progesterone capsules, which are available as a generic and formulated with peanut oil, should be taken at bedtime.

When combined with standard dose estrogen, including oral estradiol 1.0 mg, transdermal estradiol 0.05 mg, or oral CEE 0.625 mg, the appropriate dose of progesterone is 100 mg.

An oral formulation which combines estradiol 1 mg and progesterone 100 mg does not contain peanut oil, and accordingly can be safely used by those with peanut allergies. This combination product is marketed under the name Bijuva.

This new report will change how I counsel my patients with an intact uterus who are considering initiating or continuing combination HT. Going forward, I'll counsel patients that from the perspective of breast cancer risk, the safest progestogen appears to be micronized progesterone.

I am Andrew Kaunitz. Please take care of yourself and each other.

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Cite this: Andrew M. Kaunitz. The Safest Option for Menopausal Hormone Therapy - *Medscape* - Jun 20, 2022.