Oral Contraceptive Use Increases Risk for Premenopausal Breast Cancer

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Oral contraceptive (OC) use is associated with increased risk for pre-menopausal breast cancer, according to the results of a meta-analysis reported in the October issue of the Mayo Clinic Proceedings.

"Although the medical research community has long recognized breast cancer risk factors such as a positive family history of breast cancer, early menarche, late menopause, nulliparity, and lack of breastfeeding, concordance is lacking regarding the carcinogenic potential of female hormones," write Chris Kahlenborn, MD, from Altoona Hospital in Pennsylvania, and colleagues. "The Women's Health Initiative Clinical Trial reported that prolonged exposure to exogenous estrogens andprogestins in hormone therapy increases a woman's risk of developing breast cancer. In addition, the World Health Organization recently classified both postmenopausal hormone replacement and oral contraceptives (OCs) as group 1 carcinogens."

The investigators searched the MEDLINE and PubMed databases and bibliography reviews for case-control studies of OCs and premenopausal breast cancer published during or after 1980, and they identified 34 studies meeting inclusion criteria. Two reviewers extracted data from the original research articles or from additional data provided by study authors.

Use of OCs was associated with increased risk of premenopausal breast cancer in general (odds ratio [OR], 1.19; 95% confidence interval [CI], 1.09 - 1.29) and across various patterns of OC use. In studies providing separate data for nulliparous and parous women, OC use was associated with breast cancer risk both in parous women (OR, 1.29; 95% CI, 1.20 - 1.40) and in nulliparous women (OR, 1.24; 95% CI, 0.92 - 1.67).

In nulliparous women, longer duration of use did not substantially affect risk (OR, 1.29; 95% CI, 0.85 - 1.96). In parous women, increased risk was more pronounced when OCs were used before the first full-term pregnancy (OR, 1.44; 95% CI, 1.28 - 1.62) than after first full-term pregnancy (OR, 1.15; 95% CI, 1.06 - 1.26). The association between OC use and breast cancer risk was highest in parous women who used OCs 4 or more years before first full-term pregnancy (OR, 1.52; 95% CI, 1.26 - 1.82).

“Use of OCs is associated with an increased risk of premenopausal breast cancer, especially with use before [first full-term pregnancy] in parous women,” the authors write.

Study limitations include use of populations differing substantially in race and culture, reliance on assumptions underlying the random-effects model, relatively rapid change in the age of first use of OCs during the past few decades, possible survivor bias, possible recall bias, use of crude ORs instead of adjusted ORs, and lack of specific data regarding timing since last use for premenopausal parous women who used OCs before first full-term pregnancy.

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In an accompanying editorial, James R. Cerhan, MD, PhD, from the Mayo Clinic College of Medicine in Rochester, Minnesota, discusses changes in OC formulations, breast cancer epidemiology, and patterns of use of OCs over time. He suggests that risk-benefit analysis should be applied to individual patient decisions regarding OC use.

the perspective of epidemiology and public health, we must continue to closely follow the epidemiology of OC use and health outcomes, given the widespread use of these agents and their high potential to impact women’s health in both a beneficial and a deleterious manner,” Dr. Cerhan writes.

“The current study highlights the need for a close evaluation of OC use before first full-term pregnancy since this is an important biologic issue with clear clinical and public health implications,” according to Dr. Cerhan. “Any association would also add additional support for identifying other exposures during the time before first full-term pregnancy associated with breast cancer risk in later life because identification of modifiable factors in this period would support expanding the window for breast cancer prevention to earlier in life.”

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Clinical Context

Approximately 1 in 5 cases of breast cancer is diagnosed in women younger than 50 years in the United States, according to the authors of the current study. Breast cancer is the most common cause of cancer death among US women between the ages of 20 and 59 years. While the overall prevalence of breast cancer has increased in the last 4 decades, the increased frequency of breast cancer diagnosis has been particularly marked among women younger than 50 years.

It remains largely unclear whether the use of OCs has contributed to the higher prevalence of breast cancer. The current meta-analysis examines case-control data to determine whether OCs promote breast cancer in women younger than 50 years.

Study Highlights

Researchers examined MEDLINE and PubMed databases for case-control studies examining the risk for breast cancer among women who were either younger than 50 years or defined to be premenopausal. The authors included studies in which breast cancer was diagnosed during or after 1980. They could not adjust for possible confounders of breast cancer risk, and therefore the main study outcome was the crude odds ratio between the use of OCs and the risk for breast cancer.

39 studies were available for analysis. There was significant heterogeneity among the individual research studies. Overall, the use of OCs was associated with a significant OR of 1.19 for the development of breast cancer. Of studies that provided data on any use of OCs vs no previous OC use, 29 demonstrated an increased risk for breast cancer with OCs, while 8 trials demonstrated a protective effect of OCs against breast cancer. The duration of OC use did not significantly affect the risk of developing breast cancer (OR among nulliparous women who ever-used OCs and nulliparous women with at least 4 years of OC use: 1.24 and 1.29, respectively).

OC use raised the risk for breast cancer to a similar degree among parous and nulliparous women. OC use prior to a first full-term pregnancy increased the risk for breast cancer to a larger degree than OC use after a term pregnancy (OR, 1.44 and 1.15, respectively).

Pearls for Practice

Breast cancer is growing more prevalent, particularly among younger women, and it is the most common cause of cancer death for women between the ages of 20 and 59 years.
The current meta-analysis suggests that the use of OCs increases the risk for breast cancer diagnosed prior to the age of 50 years. While parity and the duration of OC use did not significantly affect this risk, women who used OCs prior to a first full-term pregnancy appeared to be at higher risk for breast cancer.

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