REFERENCES

1. Grünebaum A, McCullough LB, Sapra KJ, et al. Early and total neonatal mortality in relation to birth setting in the United States, 2006-2009. Am J Obstet Gynecol 2014;211:390.e1-7.
2. Grünebaum A, McCullough LB, Brent RL, Arabin B, Levene MI, Chervenak FA. Perinatal risks of planned home births in the United States. Am J Obstet Gynecol 2014 [Epub ahead of press].
3. Chervenak FA, McCullough LB, Brent RL, Levene MI, Arabin B. Planned home birth: the professional responsibility response. Am J Obstet Gynecol 2013;208:31-8.

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Contraception with levonorgestrel system and risks of breast cancer

TO THE EDITORS: Werth et al[1] reported that Hispanic women were more likely to choose a long-acting reversible contraceptive (LARC) method compared with non-Hispanic women and had a high rate of continuation and satisfaction of this method. LARC included levonorgestrel intrauterine system, subdermal implant, and copper intrauterine device. The Contraceptive CHOICE Project promoted the use of LARC methods. In this study, a levonorgestrel intrauterine system was inserted in 3549 women, and a progestogen implant was inserted in 1390 women, for a total of 7403 women.

However, in this study these women were not informed on the potential risks of levonorgestrel on the breast; progestagen as contraception seems to play an important role in the development of breast cancers in vitro and in vivo.

Indeed, in the study of Soini et al,[2] levonorgestrel-releasing intrauterine system use was associated with a higher incidence of breast cancer compared with the general population.

Ruan et al[3] showed that levonorgestrel increased the proliferation in MCF-7 breast cancer cells by overexpressing the progesterone receptor.

Furthermore, women with familial history of breast cancer and carriers of BCRA1 or BCRA2 mutations were not screened and not excluded from hormonal LARC methods.

The continuation of levonorgestrel intrauterine system is not recommended for women with a history of breast cancer. Unfortunately, there was no information concerning cancer history of women who were included in this study. Indeed, the recurrence of breast cancer is increased in women who continue to use the levonorgestrel intrauterine system.[4]

We understand that oral contraceptives do not prevent abortions and unwanted pregnancies sufficiently; however, the enthusiasm around hormonal LARC methods should be moderated by the new studies on the increased risks of breast cancer. The screening of risks factors for breast tumors should be reinforced before these methods are prescribed.

Short-, median-, and long-term follow-up examination and evaluation of side-effects on the breast are necessary when the levonorgestrel contraceptive system is inserted. ■

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REFERENCES

1. Werth SR, Secura GM, Broughton HO, Jones ME, Dickey V, Peipert JF. Contraceptive continuation in Hispanic women. Am J Obstet Gynecol 2014 [Epub ahead of print].
2. Soini T, Hurskainen R, Grénman S, Mäenpää J, Paavonen J, Pukkala E. Cancer risk in women using the levonorgestrel-releasing intrauterine system in Finland. Obstet Gynecol 2014;124:292-9.
3. Ruan X, Neubauer H, Yang Y, et al. Progestogens and membrane-initiated effects on the proliferation of human breast cancer cells. Climacteric 2012;15:467-72.
4. Trinh XB, Tjalma WA, Makar AP, Buytaert G, Weyler J, van Dam PA. Use of the levonorgestrel-releasing intrauterine system in breast cancer patients. Fertil Steril 2008;90:17-22.

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REPLY

We thank Dr Alouini et al for their thoughts on our recent article regarding continuation and satisfaction of long-acting reversible contraception among Hispanic women in the Contraceptive CHOICE Project (CHOICE). They state that “women were not informed on the potential risks of levonorgestrel on the breast where progestagen as contraception seems to play an important role in the development of breast cancers in vitro and in vivo.” However, the references Dr Alouini et al present do not support a causal association between the levonorgestrel intrauterine (LNG-IUS) system and breast cancer.

Despite the claims of Dr Alouini et al, there is no clear association of the LNG-IUS system and breast cancer. In their letter, they fail to mention 2 other large epidemiologic studies that found no increased risk of breast cancer with the use of the LNG-IUS system.[1,2] The one study that found a modest association (odds ratio, 1.19) failed to control for important confounders such as parity, family history, lifestyle factors, and use of exogenous hormones.

In our report, only 1 of the participants had a diagnosis of breast cancer. She received a copper intrauterine device, which may be an ideal, nonhormonal, contraceptive method for women with this medical history. No CHOICE participants who chose the LNG-IUS system had breast cancer. Thus, the point that "recurrence of breast cancer is increased" in women who use the LNG-IUS system is irrelevant.

It is not the standard of care to screen for BRCA1 and BRCA2 before contraceptive use. Family history of breast cancer and positivity for these gene mutations are not contraindications to progestin-containing contraceptive use. In fact, according to the Centers for Disease Control and Prevention's US Medical Eligibility Criteria (MEC) for Contraceptive Use, both the LNG-IUS system and etonogestrel implant received a "1" recommendation (a condition for which there is no restriction for the use of the contraceptive method) for women with family history of breast cancer.[3] In the CHOICE Project, counselors screened participants per MEC guidelines and informed them of the risks that are associated with contraceptive method use.

Readers of the medical literature should examine the totality of the evidence, not just the studies that support their point of view. Intrauterine devices and implants are outstanding methods of contraception. Clinicians and patients should follow the Centers for Disease Control and Prevention's MEC guidelines, and should offer the most effective contraceptive methods to all women. ■

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REFERENCES

1. Dinger J, Bardenheuer K, Minh TD. Levonorgestrel-releasing and copper intrauterine devices and the risk of breast cancer. Contraception 2011;83:211-7.
2. Backman T, Rauramo I, Jaakkola K, et al. Use of the levonorgestrel-releasing intrauterine system and breast cancer. Obstet Gynecol 2005;106:813-7.
3. Centers for Disease Control and Prevention. Progestin-only contraceptives; and intrauterine devices. MMWR Morb Mortal Wkly Rep 2010;59:34-49, 52-63.

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