Cochrane for Clinicians

Putting Evidence into Practice

These are summaries of reviews from the Cochrane Library.

This series is coordinated by Corey D. Fogleman, MD, Assistant Medical Editor.

A collection of Cochrane for Clinicians published in *AFP* is available at http://www.aafp.org/afp/cochrane.

CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz Questions on page 351.

Author disclosure: No relevant financial affiliations.

The Impact of Contraception on Lactation

DREW C. BAIRD, MAJ, MC, USA, *Carl R. Darnall Army Medical Center, Fort Hood, Texas*

Clinical Question

Does use of hormonal contraception impact lactation and infant growth?

Evidence-Based Answer

Use of hormonal contraception does not appear to shorten breastfeeding duration or negatively impact infant growth, based on inconsistent evidence of moderate quality. It is unclear if hormonal contraception negatively impacts breast milk volume or composition. Overall, there was limited evidence regarding any particular hormonal contraceptive method. (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Contraception is an important health topic for breastfeeding women, because unintended pregnancy is associated with late entry into prenatal care, lower birth weight, and decreased breastfeeding rates. Similarly, a shortened interpregnancy interval is associated with low birth weight and preterm births.[1] This review sought to determine whether contraceptives adversely affect infant growth or breast milk supply and breastfeeding duration.

The authors identified 11 randomized trials with 1,482 women that examined the effects of combined oral contraceptives, the levonorgestrel-releasing intrauterine system (Mirena), progestin-only pills, or an etonogestrel-releasing implant vs. another method or placebo. Five studies were published before 1985, whereas six were published within the past 11 years. No studies examined the vaginal ring or transdermal patch. Inclusion and exclusion criteria varied across trials, although most included healthy women who delivered at 37 weeks' gestation or later and planned to breastfeed, had previous success with breastfeeding, or were actively breastfeeding. Follow-up ranged from 10 days to one year. The overall quality of the evidence was moderate, with several studies lacking information about randomization and allocation concealment; limited reporting of results; or many patients being lost to follow-up. Data could not be meta-analyzed because of differing protocols and outcomes.

Eight trials examined the effect of contraception on breastfeeding duration. One suggested a negative effect of combined oral contraceptives compared with placebo, but no adequate data were reported. Another trial showed fewer women were breastfeeding 75 days after insertion of the levonorgestrel-releasing intrauterine system compared with a nonhormonal intrauterine device (IUD; 56% vs. 79%; $P < .05$), but there was no significant difference between the groups at one year. Other head-to-head comparison trials showed no difference in breastfeeding duration between combined oral contraceptives and progestin-only pills, and between a levonorgestrel-releasing intrauterine system and nonhormonal IUD. In two trials that compared different insertion times for levonorgestrel-releasing intrauterine system and etonogestrel-releasing implant, there was no significant difference in breastfeeding duration between early postpartum insertion (within 48 hours in the levonorgestrel-releasing intrauterine system trial, and at one to three days postpartum in the etonogestrel-releasing implant trial) and standard insertion at four to eight weeks postpartum.

Milk volume or composition was assessed in six trials. One older trial reported decreased milk volume in participants using combined oral contraceptives compared with placebo, whereas another reported no difference. Neither trial provided data. Another trial (n = 171) conducted more than 30 years ago found diminished average milk volumes in patients using combined

oral contraceptives vs. progestin-only pills after nine weeks (mean difference [MD] = –17.8 mL; 95% confidence interval [CI], –28.8 to –6.8), 16 weeks (MD = –24.0 mL; 95% CI, –34.5 to –13.5), and 24 weeks (MD = –24.9 mL; 95% CI, –36.0 to –13.8). Milk volumes decreased in both groups after study initiation, but average volumes decreased by a greater amount among combined oral contraceptive users compared with progestin-only pill users (42% vs. 12% reduction in volume, respectively) from weeks 6 to 24. Two studies showed no significant difference in milk volume or composition between progestin-only pills vs. placebo. Another trial showed no difference between etonogestrel-releasing implant insertion times.

Seven trials looked at infant growth. Six found no significant difference between progestin-only pills and placebo, combined oral contraceptives and progestin-only pills, or levonorgestrel-releasing intrauterine system and nonhormonal IUD. One study showed that use of an etonogestrel-releasing implant led to greater infant weight gain than no method at six weeks (MD = 426 g; 95% CI, 59 to 793), but less infant weight gain than depomedroxyprogesterone (Depo-Provera) from six to 12 weeks (MD = –271 g; 95% CI, –355 to –188).

The Centers for Disease Control and Prevention has medical eligibility criteria categories for contraceptives in breastfeeding women. Combined oral contraceptives, the combined hormonal patch, and ring are considered category 4 (i.e., unacceptable health risk) when the patient is less than 21 days postpartum because of the risk of venous thromboembolism. They are considered category 3 (i.e., theoretic or proven risks usually outweigh the advantages of the method) from 21 to 30 days, and category 2 (i.e., advantages generally outweigh the risks) after 30 days in women with no risk factors. Progestin-only pills, depomedroxyprogesterone, and the etonogestrel-releasing implant are category 2 during the first 30 days postpartum and category 1 (i.e., no restrictions for use) thereafter. The levonorgestrel-releasing intrauterine system is category 2 before four weeks postpartum, whereas the copper IUD is category 1 within 10 minutes of delivery of the placenta and category 2 up to four weeks postpartum. Both IUDs are considered category 1 after four weeks.[1]

SOURCE: Lopez LM, Grey TW, Stuebe AM, Chen M, Truitt ST, Gallo MF. Combined hormonal versus nonhormonal versus progestin-only contraception in lactation. *Cochrane Database Syst Rev.* 2015;(3):CD003988.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD003988.

The opinions and assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the Department of Defense, the U.S. Army Medical Corps, or the U.S. Army at large.

REFERENCE

1. Centers for Disease Control and Prevention. Update to CDC's U.S. Medical Eligibility Criteria for Contraceptive Use, 2010: revised recommendations for the use of contraceptive methods during the postpartum period. *MMWR Morb Mortal Wkly Rep.* 2011;60(26):878-883.

Influenza Vaccination for the Prevention of Cardiovascular Disease

MELANIE RAFFOUL, MD, and KENNETH W. LIN, MD, MPH, *Georgetown University School of Medicine, Washington, District of Columbia*

▶ **See related article at http://www.aafp.org/afp/2014/0201/p224a.html.**

Clinical Question

Does influenza vaccination have any benefit for primary or secondary prevention of cardiovascular disease?

Evidence-Based Answer

Influenza vaccination may reduce cardiovascular mortality in patients with established cardiovascular disease. The effect of vaccination is unclear among patients in the general population without known cardiovascular disease. (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

Globally, cardiovascular disease remains the number one cause of death.[1] By 2030, it is estimated that the number of annual deaths from cardiovascular disease will increase to 23.3 million.[1] Innovative strategies for

primary and secondary prevention of cardiovascular disease are important. Observational studies have shown an association between receipt of the influenza vaccine and lower cardiovascular morbidity and mortality, especially among older and vulnerable populations.[2,3] Another study found that influenza infection, but not influenza vaccination, was associated with an increased risk of cardiovascular events.[4]

This Cochrane review included eight randomized controlled trials with 12,029 participants 18 years or older. Interventions included influenza vaccine administered by any route at any dosage vs. a saline infusion or no intervention. Four trials (n = 10,347) focused on influenza prevention in the general and older populations and reported cardiovascular outcomes in their safety analyses. Two of these studies (n = 5,267) included adults 18 to 60 years of age, whereas the other two studies (n = 5,080) included participants 60 to 98 years of age. A minority of these patients had diabetes mellitus or undefined cardiac disease, and one-half of the patients in one of the studies had hypertension. Four trials (n = 1,682) focused on prevention of cardiovascular events in patients of varying ages with established coronary heart disease, including participants with acute myocardial infarction. These populations were analyzed separately. Primary outcomes included myocardial infarction, unstable angina, and death from cardiovascular causes. Follow-up durations ranged from 42 days to one year.

Overall, study quality was high. Three primary prevention trials and two secondary prevention trials were deficient in three or more risk of bias criteria. The four secondary prevention trials reported significant reductions in cardiovascular mortality with influenza vaccination (relative risk = 0.45; 95% confidence interval, 0.26 to 0.76). Although three of the four primary prevention studies reported cardiovascular mortality, cardiovascular events were too scarce to allow the authors to draw conclusions.

Another systematic review that examined the effect of influenza vaccination on cardiovascular outcomes found no effect on cardiovascular mortality, but it did find a reduction in a composite outcome of cardiovascular events among those receiving influenza vaccination. This effect was greatest in those with established cardiovascular disease.[2] Although data regarding the benefit of influenza vaccination for primary prevention of cardiovascular disease are inconclusive, current U.S. guidelines recommend routine vaccination for all adults without contraindications,[5] and international guidelines recommend annual vaccination for patients with chronic heart disease.[6]

SOURCE: Clar C, Oseni Z, Flowers N, Keshtkar-Jahromi M, Rees K. Influenza vaccines for preventing cardiovascular disease. *Cochrane Database Syst Rev.* 2015;(5):CD005050.

The practice recommendations in this activity are available at http://summaries.cochrane.org/CD005050.

REFERENCES

1. Global Status Report on Noncommunicable Diseases 2010. Geneva, Switzerland: World Health Organization; 2011.
2. Udell JA, Zawi R, Bhatt DL, et al. Association between influenza vaccination and cardiovascular outcomes in high-risk patients: a meta-analysis. *JAMA*. 2013;310(16):1711-1720.
3. Nichol KL, Nordin JD, Nelson DB, Mullooly JP, Hak E. Effectiveness of influenza vaccine in the community-dwelling elderly. *N Engl J Med*. 2007;357(14):1373-1381.
4. Smeeth L, Thomas SL, Hall AJ, Hubbard R, Farrington P, Vallance P. Risk of myocardial infarction and stroke after acute infection or vaccination. *N Engl J Med*. 2004;351(25):2611-2618.
5. Grohskopf LA, Sokolow LZ, Olsen SJ, Bresee JS, Broder KR, Karron RA. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices, United States, 2015-16 influenza season. *MMWR Morb Mortal Weekly Rep*. 2015;64(30):818-825.
6. UK Department of Health. Influenza: the Green Book. Chapter 19. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/456568/2904394_Green_Book_Chapter_19_v10_0.pdf. Accessed February 3, 2016. ■