American Family Physician

A peer reviewed journal of the American Academy of Family Physicians

December 1, 2006 Table of Contents

FPIN's Clinical Inquiries

Risks and Benefits of Combination Contraceptives

MARY W. ROEDERER, PHARM.D., Department of Family Medicine, University of North Carolina at Chapel Hill, Chapel Hill, N.C.

JEAN C. BLACKWELL, M.L.S., Health Sciences Library, University of North Carolina at Chapel Hill, Chapel Hill, N.C.

Clinical Commentary by Carol Blenning, M.D., Oregon Health and Science University, Portland, Oregon

Clinical Question

What are the relative risks and benefits of combination contraceptives?

Evidence-Based Answer

The risks of using oral combination contraceptives include: a three- to sixfold increase in the incidence of venous thromboembolism (VTE) apparent by the fourth month of use and highest between six and 12 months of use; a two- to sixfold increase in the risk of ischemic stroke among women with a history of migraine; and an increase in cervical cancer risk after five or more years of use. (Strength of Recommendation [SOR]: B)

For the use of oral combination contraceptives there is no associated increase in risk of weight gain (SOR: A) or breast cancer (SOR: B), and no consistent change in breast milk production (SOR: A), infant growth or weight (SOR: A), or bone mineral density (SOR: B).

The benefits of oral combination contraceptive use include a lower incidence of colorectal cancer without regard to duration of use (SOR: B), a reduction in primary dysmenorrheal pain after one to three months of use (SOR: B), and improvement in acne in trials of six months of use. (SOR: A)

There is little rigorous evidence that combination contraceptive use improves dysfunctional uterine bleeding (SOR: B) or that combination contraceptive use improves heavy menstrual bleeding more than other proposed treatments of low-dose danazol (Danocrine), mefenamic acid (Ponstel), or naproxen (Naprosyn). (SOR: B)

Evidence Summary

The risks and benefits of combination contraceptives have not been consistently studied in all routes of administration. Combination contraceptive use increases a woman's risk for VTE and ischemic stroke.1,2 Observational studies found one to three additional cases of VTE among 10,000 women taking combination contraceptives for one year.1 The risk of ischemic stroke is also higher among combination contraceptive users with a history of migraines with aura.2,3 In absolute terms, measured as ischemic strokes per 10,000 women over 10 years, a woman 25 to 29 years of age has a baseline ischemic stroke risk of 2.7; this risk increases to 4.0 if she uses oral contraceptives, 11.0 if she has migraines with aura, and 23.0 if she both uses oral contraceptives and has migraines with aura.2

Cervical cancer risk increases with duration of combination contraceptive use longer than five years, even after adjusting for infection with human papillomavirus (relative risk [RR], 1.3 to 2.5).4

Regarding the quality or quantity of breast milk, a well-done systematic review found only low-quality trials with conflicting evidence.5 Some found that combination contraceptive use decreases breast milk quality or quantity in women lactating postpartum, whereas other studies did not show a change.5 The yearly risk of pregnancy while using combination contraceptives ranges from 0 to 2.5 percent based on the method selected, for an effectiveness rate of 97.5 to 100 percent with typical use.6

Along with excellent effectiveness rates, combination contraceptives are beneficial in decreasing pain associated with primary dysmenorrhea and the number of acne lesions.7,8 Case-control and cohort studies have found an association between combination contraceptive use and a modest decrease in the risk of colorectal cancer (RR, 0.82 [95% confidence interval, 0.74 to 0.92]). However, these studies were generally of poor quality and did not control for other important factors (e.g., diet) for the development of colorectal cancer.9

The side effects of headache and weight gain are not statistically significantly different between users and nonusers of combination contraceptives.2,10 Insufficient data exist to determine a relationship between combination contraceptive use and heavy menstrual bleeding, dysfunctional uterine bleeding, and bone mineral density.11-13 Data are lacking to prove that combination contraceptive use increases a woman's risk of developing breast cancer, cardiovascular disease, or endometriosis.1,14-16

Recommendations from Others

The World Health Organization (WHO) recommends that women with cardiovascular disease, uncontrolled hypertension, ischemic heart disease, a history of stroke, venous thromboembolic disease, migraine with aura, or a history of breast cancer, or who are smokers older than 35 years who smoke more than 15 cigarettes per day, should avoid combination contraceptive use.17 The WHO discourages combination contraceptives during the six weeks immediately postpartum for women desiring to breastfeed.17

The American College of Obstetricians and Gynecologists recommends using alternate forms of contraception in women with the following conditions: migraine headaches, age older than 35 years who smoke cigarettes, history of thromboembolic disease, coronary artery disease, congestive heart failure, cerebrovascular disease, those who are less than two weeks postpartum, hypertension or diabetes with vascular disease or age older than 35, hypertriglyceridemia, a history of breast cancer, systemic lupus erythematosus with vascular disease, nephritis, or antiphospholipid antibodies.18

Clinical Commentary

This review offers helpful risk values to provide to patients and would help facilitate a patient-specific, targeted discussion of the relative risks and benefits of combination contraceptives. What is particularly helpful in this review is the breakdown of information on combination contraceptives into the categories of risks, nonrisks, and benefits. Fortunately, with the newer combination contraceptives, more options exist to select for the particular combination of hormones that best maximizes benefits and minimizes risks for any given patient. In addition, there is more information about the benefits of combination contraceptives with respect to ovarian cancer rates and treatment of endometriosis and ovarian cysts that may be relevant to select groups of patients.

Address correspondence to Mary W. Roederer, Pharm.D., at mroedere@unch.unc.edu. Reprints are not available from the authors.

Author disclosure: Nothing to disclose.

REFERENCES

1. Gomes MP, Deitcher SR. Risk of venous thromboembolic disease associated with hormonal contraceptives and hormone replacement therapy: a clinical review. Arch Intern Med 2004;164:1965-76.

2. Becker WJ. Use of oral contraceptives in patients with migraine. Neurology 1999;53 (4 suppl 1):S19-25.

3. Curtis KM, Chrisman CE, Peterson HB, for the WHO Programme for Mapping Best Practices in Reproductive Health. Contraception for women with selected circumstances. Obstet Gynecol 2002;99:1100-12.

4. Smith JS, Green J, Berrington de Gonzalez A, Appleby P, Peto J, Plummer M, et al. Cervical cancer and use of hormonal contraceptives: a systematic review. Lancet 2003;361:1159-67.

5. Truitt ST, Fraser AB, Grimes DA, Gallo MF, Schulz KF. Combined hormonal versus nonhormonal versus progestin-only contraception in lactation. Cochrane Database Syst Rev 2003;(2):CD003988.

6. Trussell J. Contraceptive efficacy. In: Hatcher RA, ed. Contraceptive Technology. 18th ed. New York, N.Y.: Ardent Media, 2004:773-845.

7. Proctor ML, Roberts H, Farquhar CM. Combined oral contraceptive pill (OCP) as treatment for primary dysmenorrhoea. Cochrane Database Syst Rev 2001;(2):CD002120.

8. Arowojolu AO, Gallo MF, Grimes DA, Garner SE. Combined oral contraceptive pills for treatment of acne. Cochrane Database Syst Rev 2004;(3):CD004425.

9. Fernandez E, La Vecchia C, Balducci A, Chatenoud L, Franceschi S, Negri E. Oral contraceptives and colorectal cancer risk: a meta-analysis. Br J Cancer 2001;84:722-7.

10. Gallo MF, Grimes DA, Schulz KF, Helmerhorst FM. Combination contraceptives: effects on weight; update. Cochrane Database Syst Rev 2006;(1):CD003988.

11. Hickey M, Higham J, Fraser IS. Progestogens versus oestrogens and progestogens for irregular uterine bleeding associated with anovulation. Cochrane Database Syst Rev 2000;(1):CD001895.

12. Iyer V, Farquhar C, Jepson R. Oral contraceptive pills for heavy menstrual bleeding. Cochrane Database Syst Rev 1997;(2):CD000154.

13. Petitti DB, Piaggio G, Mehta S, Cravioto MC, Meirik O. Steroid hormone contraception and bone mineral density: a cross-sectional study in an international population. The WHO Study of Hormonal Contraception and Bone Health. Obstet Gynecol 2000;95:736-44.

14. Marchbanks PA, McDonald JA, Wilson HG, Folger SG, Mandel MG, Daling JR, et al. Oral contraceptives and the risk of breast cancer. N Engl J Med 2002;346:2025-32.

15. Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Contraception 1998;57:315-24.

16. Moore J, Kennedy S, Prentice A. Modern combined oral contraceptives for pain associated with endometriosis. Cochrane Database Syst Rev 1997;(4):CD001019.

17. World Health Organization. Improving access to quality care in family planning. 3rd ed. Geneva, Switzerland: Reproductive Health and Research, World Health Organization, 2004.

18. ACOG Committee on Practice Bulletins-Gynecology. ACOG Practice Bulletin. The use of hormonal contraception in women with coexisting medical conditions. Number 18, July 2000. Int J Gynaecol Obstet 2001;75:93-106.

Clinical Inquiries provides answers to questions submitted by practicing family physicians to the Family Physicians Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/levels_of_evidence.asp).

 If interested in submitting questions or writing answers for this series, go to http://www.fpin.org or e-mail: questions@fpin.org.