FPIN's Clinical Inquiries

Cardiovascular Risks of Combined Oral Contraceptive Use

ADRIENNE D. FEHR, DO, *New Hanover Regional Medical Center Family Medicine Residency, Wilmington, North Carolina*
ANNE MOUNSEY, MD, *University of North Carolina Family Medicine Residency, Chapel Hill, North Carolina*
JENNIFER E. YATES, MD, *Womack Army Medical Center, Fort Bragg, North Carolina*
DONNA FLAKE, MSLS, MSAS, *Southeast Area Health Education Center, Wilmington, North Carolina*

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 individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/?o=1025).

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Clinical Question

What are the risks of combined oral contraceptive use in patients with cardiovascular risk factors?

Evidence-Based Answer

Because of an increased risk of cardiovascular disease, the use of combined oral contraceptives (OCs) should be considered carefully in women who smoke and in those with hypertension or hyperlipidemia. (Strength of Recommendation: B, based on systematic reviews of case-control and cohort studies.) Combined OC use in patients with hypertension may increase the risk of peripheral arterial disease.

Evidence Summary

Many studies report wide confidence intervals because of the heterogeneity among the studies in systematic reviews and the low event rates in single studies. The increase in cardiovascular risk is small and must be weighed against the benefits of contraception.

HYPERTENSION

A meta-analysis of five case-control studies involving more than 1,200 women evaluated the effect of hypertension on stroke in those who used OCs.[1] When comparing women with hypertension who used OCs with those who did not, the pooled odds ratio (OR) for stroke was 9.82 (95% confidence interval [CI], 6.97 to 13.84). In normotensive OC users, the pooled OR was 2.06 (95% CI, 1.46 to 2.92).

A systematic review with three case-control studies found mixed outcomes for women with hypertension who are using OCs and the risk of acute myocardial infarction (MI).[2] Two studies with a total of 363 women reported little difference in the risk of acute MI between those who used OCs and those who did not. The third, a multicenter case-control study that included 368 women, found a 12-fold increased risk of acute MI in those who used OCs compared with those who did not.[3] According to a risk model developed from this study using baseline MI and stroke rates from multiple countries, women with hypertension who are 20 to 24 years of age will have an additional four MIs and ischemic strokes per 100,000 years of OC use; those 30 to 34 years of age will have an additional seven; and those 40 to 44 years of age will have an additional 29.[4]

PERIPHERAL ARTERIAL DISEASE

A case-control study of 152 women with angiographically diagnosed peripheral arterial disease found that women with hypertension who used OCs were more likely to develop peripheral arterial disease (OR = 8.8 [95% CI, 3.9 to 19.8]) compared with those who did not use OCs (OR = 4.9 [95% CI, 2.5 to 9.5]).[5]

HYPERLIPIDEMIA

A case-control study (103 cases, 347 control patients) found that patients with hyperlipidemia who used OCs were more likely to have an ischemic stroke than those with hyperlipidemia who did not (OR = 10.8 [95% CI, 2.3 to 49.9]).[6] Women with hyperlipidemia who previously used OCs (104 cases, 567 controls) did not have more ischemic strokes (OR = 1.1 [95% CI, 0.4 to 3.3]). Another case-control study (245 cases, 914 control patients) found that patients with hyperlipidemia who used OCs had an increased risk of MI (OR = 24.7

[95% CI, 5.6 to 108.5]) compared with women with hyperlipidemia who did not use OCs (OR = 3.3 [95% CI, 1.6 to 6.8]).[7] Both studies compared outcomes in cases against baseline outcome rates in women without hyperlipidemia who did not use OCs.

SMOKING

A cohort study of 17,032 women 25 to 39 years of age who took OCs found that those who smoked were more likely to die than nonsmokers.[8] Women who smoked fewer than 15 cigarettes per day had a relative risk (RR) of 1.24 (95% CI, 1.03 to 1.49) compared with nonsmokers; for those who smoked 15 cigarettes or more per day, the RR was 2.14 (95% CI, 1.81 to 2.53). Women who smoked and used OCs were also more likely to have an ischemic stroke than nonsmokers who used OCs (RR = 2.9 [95% CI, 0.7 to 12.6] for women who smoked 15 or fewer cigarettes per day versus nonsmokers; RR = 4.3 [95% CI, 0.9 to 20.0] for those who smoked more than 15 cigarettes per day versus nonsmokers).[8]

Recommendations from Others

The American College of Obstetricians and Gynecologists states that OC use is safe in healthy, nonsmoking women older than 35 years. However, OCs should be prescribed with caution, if at all, to women older than 35 years who smoke. Women with well-controlled hypertension may use OCs if they are 35 years or younger, nonsmokers, and healthy (without evidence of end-organ vascular disease). Women with dyslipidemia may use OCs if they have a low-density lipoprotein level of 160 mg per dL (4.14 mmol per L) or less and a triglyceride level of 250 mg per dL (2.82 mmol per L) or less, and do not have additional risk factors for coronary artery disease.[9]

Address correspondence to Adrienne D. Fehr, DO, at adfehrfp@gmail.com. Reprints are not available from the authors.

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