

**Mallory McClester, MD;**  
**Anne Mounsey, MD**  
University of North  
Carolina, Chapel Hill

**Leslie Mackler, MSLS**  
Director, Moses Cone  
Health System Library,  
Greensboro, NC

**ASSISTANT EDITOR**  
**E. Chris Vincent, MD**  
Swedish Family Medicine  
Residency—First Hill,  
Seattle, Wash

## Q / Do oral contraceptives carry a significant risk of stroke for women with migraines?

### EVIDENCE-BASED ANSWER

**A / PERHAPS.** Estrogen-containing oral contraceptives may raise the risk of ischemic stroke in women with migraine, particularly migraine with aura (strength of recommendation [SOR]: C, small case-control studies with methodological flaws and conflicting results).

#### Evidence summary

Women with probable migraine with visual aura (PMVA) have an increased risk for ischemic stroke (odds ratio [OR]=2.1) but not hemorrhagic stroke.<sup>1</sup> Women with >12 PMVA episodes per year are at greatest risk (OR=2.2, compared with <12 PMVA episodes per year, OR=1.1).<sup>2</sup> Women taking oral contraceptive pills (OCPs) also have an increased risk for stroke, depending on the estrogen dose (OR=4.8 for 50 mcg; OR=2.7 for 30-40 mcg; OR=1.7 for 20 mcg; and OR=1.0 for progestin-only pills).<sup>3</sup>

#### Women with migraines who smoke and take OCPs have the highest risk

Four case-control studies evaluated the risk of ischemic stroke in women with migraines who take OCPs. The first study compared the OR among 135 women 15 to 49 years of age with PMVA and a first ischemic stroke with 614 controls (no history of stroke, matched for age and ethnicity).<sup>2</sup> Although women with PMVA overall had an increased risk of ischemic stroke (OR=1.5; 95% confidence interval [CI], 1.1-2.0), a subgroup of women with PMVA who also were taking OCPs didn't have a significantly greater stroke risk than women with PMVA who were not taking OCPs (OR=1.6; 95% CI, not given but reported as not significant; *P*=.87). Investigators didn't specify the type of OCPs.

Women with PMVA who smoked had

a greater risk of ischemic stroke (OR=1.5; 95% CI, 1.1-2.3), and women with PMVA who both smoked and took OCPs had the highest risk of ischemic stroke (OR =7.0; 95% CI, 1.4-22.8).

#### In women younger than 45 years, OCPs are associated with higher stroke risk

The second study compared the odds ratio for ischemic stroke among 47 women younger than 45 years with PMVA who were taking combined OCPs with 63 controls.<sup>3</sup> Most OCPs contained 30 to 40 mcg estrogen. Women with PMVA taking a combined OCP had a higher risk of ischemic stroke (OR=13.9; 95% CI, 5.5-35.1) than women with PMVA who didn't take OCPs (OR=3.7; 95% CI, 1.5-9.1). Investigators didn't report the number of PMVA episodes per year among the women.

The third study compared the odds ratio for ischemic stroke among 10 women 20 to 44 years of age with migraines who were taking combined OCPs with 23 controls.<sup>4</sup> Investigators didn't specify the type of migraine, although classic migraine was approximately twice as common as simple migraine among the women in the larger study population. Women with migraine taking OCPs were more likely to have an ischemic stroke overall (OR=16.9; 95% CI, 2.7-106), with the exception of those taking OCPs with <50 mcg estrogen (4 patients) (OR=0.59; 95% CI, 0.79-54.8).

CONTINUED ON PAGE 675

CONTINUED FROM PAGE 662

The fourth study compared the OR for ischemic stroke among 4 women 18 to 44 years old who had a history of migraine (type not specified) and used low-dose OCPs with 14 controls. Women with migraines taking OCPs had a higher risk of ischemic stroke (OR=2.08; 95% CI, 1.19-3.65).<sup>5</sup>

**Recommendations**

The American College of Obstetricians and Gynecologists says that combined OCPs are contraindicated for women with migraine with focal neurologic symptoms such as aura.<sup>6</sup> Although strokes are rare in women with migraine taking OCPs, the impact of a stroke is so devastating that clinicians should consider progestin-only, intrauterine, or barrier con-

traceptives for these women. However, physicians may consider combined OCPs for women younger than 35 years with migraine if they don't have focal neurologic signs, don't smoke, and are otherwise healthy.

The World Health Organization and Centers for Disease Control and Prevention state that women with a history of migraine who use combined OCPs are 2 to 4 times more likely to have an ischemic stroke than nonusers and conclude that combined OCP use in women older than 35 years with migraine, or migraine with aura at any age, represents an unacceptable health risk. However, the advantages of using combined OCPs in women younger than 35 years with migraine generally outweigh the theoretical or proven risks.<sup>7,8</sup>

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