Low-dose aspirin and preeclampsia prevention: Ready for prime time, but as a "re-run" or as a "new series"?

Guidelines from ACOG and the USPSTF support use of low-dose aspirin to minimize complications of preeclampsia in pregnancy, but more studies are needed. What should we advise our patients?

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In November 2013, The American College of Obstetricians and Gynecologists (ACOG) published the results of its Task Force on Hypertension in Pregnancy.[1] The Task Force aimed to help clinicians become familiar with the state of research in hypertension during pregnancy as well as to assist us in standardizing management approaches to such patients.

The Task Force reported that, worldwide, hypertensive disorders complicate approximately 10% of pregnancies. In addition, in the United States, the past 20 years have brought a 25% increase in the incidence of preeclampsia. According to past ACOG President James N. Martin, Jr, MD, in the last 10 years, the pathophysiology of preeclampsia has become better understood, but the etiology remains unclear and evidence that has emerged to guide therapy has not translated into clinical practice.[1]

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The Task Force document contained 60 recommendations for the prevention, prediction, and management of hypertensive disorders of pregnancy, including preeclampsia, gestational hypertension, chronic hypertension, HELLP syndrome, and preeclampsia superimposed on an underlying hypertensive disorder (see box on page 8). One recommendation was that women at high risk for preeclampsia, particularly those with a history of preeclampsia that required delivery before 34 weeks, could possibly benefit from taking aspirin (60–81 mg) daily starting at the end of the first trimester. They further noted that this benefit could include prevention of recurrent severe preeclampsia, or at least a reduction in recurrence risk.

The ACOG Task Force made its recommendation based on results of a meta-analysis of low-dose aspirin trials, involving more than 30,000 patients,[2] suggesting a small decrease in the risk of preeclampsia and associated morbidity. More precise risk reduction estimates were difficult to make due to the heterogeneity of the studies reviewed. And the Task Force further stated that this (low-dose aspirin) approach had no demonstrable acute adverse fetal effects, although long-term adverse effects could not be entirely excluded based on the current data.

Unfortunately, according to the ACOG document, the strength of the evidence supporting their recommendation was "moderate" and the strength of the recommendation was "qualified" so, not exactly a resounding endorsement of this approach, but a recommendation nonetheless.

Data suggest aspirin for high-risk women could be reasonable

A recent study by Henderson and colleagues presented a systematic review for the US Preventive Services Task Force (USPSTF) on the potential for low-dose aspirin to prevent morbidity and mortality from preeclampsia.[3] The design was a meta-analysis of

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Obstetric practice changers 2014

Hypertension and pregnancy and preventing the first cesarean delivery

A peer-to-peer audiocast

Dr. Repke recently sat down with Dr. Errol R. Norwitz, fellow OBG MANAGEMENT Board of Editors Member and author of this month's Update on Operative Vaginal Delivery (page 38). Their discussion focused on individual takeaways from ACOG's Hypertension in Pregnancy guidelines and the recent joint ACOG–Society of Maternal-Fetal Medicine report on emerging clinical and scientific advances in safe prevention of the primary cesarean delivery.

From their conversation:

Dr. Repke: *About 60 recommendations came out of ACOG's Hypertension in Pregnancy document; only six had high-quality supporting evidence, and I think most practitioners already did them. Many really were based on either moderate- or low-quality evidence, with qualified recommendations. I think this has led to confusion.*

Dr. Norwitz, how do you answer when a clinician asks you, "Is this gestational hypertension or is this preeclampsia?"

Find Dr. Norwitz's response, and the full peer-to-peer transcripted discussion, in the Audio Library at **obgmanagement.com**

28 studies: two large, multisite, randomized clinical trials (RCTs); 13 smaller RCTs of high-risk women, of which eight were deemed "good quality"; and six RCTs and two observational studies of average-risk women, of which seven were deemed to be good quality.

The results essentially supported the notion that low-dose aspirin had a beneficial effect with respect to prevention of preeclampsia and perinatal morbidity in women at high risk for preeclampsia. Additionally, no harmful effects were identified, although the authors acknowledged potential rare or long-term harm could not be excluded.

Questions remain

While somewhat gratifying, the results of the USPSTF systematic review still leave many questions. First, the dose of aspirin used in the studies analyzed ranged from 50 mg/d to 150 mg/d. In the United States, "low-dose" aspirin is usually prescribed at 81 mg/d, so the applicability of this review's findings to US clinical practice is not exact. Second, the authors acknowledged that the putative positive effects observed could be secondary to so-called "small study effects," and that when only the larger studies were analyzed the effects were less impressive.

In my opinion, both the USPSTF study and the recommendations from the ACOG Task Force provide some reassurance for clinicians that the use of daily, low-dose aspirin by women at high risk for preeclampsia probably does afford some benefit, and seems to be a safe approach—as we have known from the initial Maternal-Fetal Medicine Units (MFMU) trial published in 1993 on low-risk women[4] and the follow-up MFMU study on high-risk women.[5]

The need for additional studies is clear, however. The idea that preeclampsia is the same in every patient would seem to make no more sense than thinking all cancer is the same, with the same risk factors, the same epidemiology and pathophysiology, and the same response to similar treatments. Fundamentally, we need to further explore the different pathways through which preeclampsia develops in women and then apply the strategy best suited to treating (or preventing) their form of the disease—a personalized medicine approach.

In the meantime, most patients who have delivered at 34 weeks or less because of preeclampsia and who are contemplating another pregnancy are really not interested in hearing us tell them that we cannot do anything to prevent recurrent preeclampsia because we are awaiting further studies. At least the ACOG recommendations and the results of the USPSTF's systematic review provide us with a reasonable, although perhaps not yet optimal, therapeutic option.

The bottom line

In my own practice, I discuss the option of initiating low-dose aspirin (81 mg/d) as early as 12 weeks' gestation for patients who had either prior early-onset preeclampsia requiring delivery before 34 weeks' gestation or preeclampsia during more than one pregnancy.

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