Cerclage Benefits Subset Of High-Risk Women

BY DOUG BRUNK

SAN DIEGO — Women with prior early spontaneous preterm birth and a midtrimester sonographic cervical length of less than 25 mm may benefit from cerclage, but the benefit is most pronounced when the cervical length is less than 15 mm, results from a large, multicenter, randomized study showed.

"Although clinicians have recommended cerclage for shortened cervical lengths, previous randomized trials have not supported this practice," Dr. John Owen said at the annual meeting of the Society for Maternal-Fetal Medicine.

A recent meta-analysis of four randomized trials of cerclage for shortened cervical length uncovered a relationship between pregnancy history and cerclage effectiveness. Cerclage was helpful only in singletons—it was harmful in multiples—but it was especially helpful in women who'd had a prior preterm birth (Obstet. Gynecol. 2005;106:181-9).

"Our hypothesis was that in women with a prior early spontaneous preterm birth [gestational age less than 34 weeks] and cervical length less than 25 mm, cerclage would reduce the rate of preterm birth before 35 weeks' gestation," said Dr. Owen of the department of obstetrics and gynecology at the University of Alabama at Birmingham.

To test the hypothesis, he and his colleagues at 15 centers in the United States, known as the Vaginal Ultrasound Trial Consortium, studied 1,014 women with a prior spontaneous birth at less than 34 weeks and a current singleton pregnancy who underwent serial ultrasound evaluation in the period beginning at 16 weeks and ending before 23 weeks (that is, no later than 22 weeks and 6 days). Of these, 301 women with a cervical length of less than 25 mm were randomized to either cerclage or no cerclage.

Vaginal ultrasound exams lasted a minimum of 5 minutes to allow the clinician to observe any spontaneous shortening, and included fundal pressure as a provocative measure to induce cervical shortening. The scans were scheduled every 2 weeks as long as the cervical length remained at least 30 mm. They were performed weekly if the cervical length shortened to 25-29 mm. The last scan was scheduled to occur just before the 23 weeks' gestational point.

Dr. Owen reported that the cerclage and no-cerclage groups were similar in terms of race/ethnicity, mean cervical length (18.7 vs. 19.5 mm, respectively), mean gestational age at randomization (19.4 vs. 19.5 weeks), and mean gestational age of earliest prior preterm birth (24.4 vs. 24.9 weeks).

Preterm birth before 35 weeks occurred in 42% of the no-cerclage group, compared with 32% of the cerclage group, a difference that revealed a statistical trend ($P = .09$).

However, further analysis revealed that women in the cerclage group maintained their pregnancies significantly better if their cervical length was less than 15 mm (odds ratio, 0.23), but there was no significantly positive effect if their cervical length was 15-24 mm (OR, 0.84).

Dr. Owen had no conflicts to disclose. ■

Don't Hesitate to Give Women Topical Retinoids, Expert Says

SAN FRANCISCO — There is no reason to be hesitant in prescribing topical retinoids to women with acne, according to Dr. Hilary E. Baldwin.

While the teratogenic potential of oral isotretinoin is well known, topical retinoids appear to be safe for use in women of childbearing potential, said Dr. Baldwin of the State University of New York, Brooklyn.

According to data from Allergan Inc., which makes Tazorac (tazarotene gel), the normal, endogenous plasma level of retinoids is 6.6 ng/mL. These retinoids come from food sources such as carrots, red peppers, sweet potatoes, and fish, she said at a meeting sponsored by Skin Disease Education Foundation. Oral isotretinoin raises this level to 862 ng/mL, according to the Accutane package insert. In contrast, tretinoin 0.1% cream raises the endogenous plasma level by only 2.9 ng/mL, tazarotene 0.1% gel by 0.14 ng/mL, and adapalene 0.1% gel (Differin) by 0.04 ng/mL, she said.

Several studies looking at women who used topical retinoids during pregnancy found no increase in developmental anomalies among offspring, even though the Food and Drug Administration classifies tazarotene as category X. "My soapbox issue is that whether or not you decide to use it in women who are actively pregnant—and that's a completely different medical-legal concern—you can't ignore half of the world population with acne simply because they happen to have a uterus," she said. Dr. Baldwin disclosed serving as a consultant to, and being on the speakers bureau of, Allergan and several other pharmaceutical companies. SDEF and this news organization are owned by Elsevier.

—Robert Finn

DRUGS, PREGNANCY, & LACTATION

SSRIs and PPHN Revisited

The risks associated with selective serotonin reuptake inhibitor use in pregnancy have been addressed in previous columns because of the accumulating data suggesting that depression during pregnancy is common and that many pregnant women use SSRIs. A recent study indicated that as many as 8% of pregnant women are treated with SSRIs, so clearly delineating the spectrum of associated risks is of critical clinical importance.

Although an increasing amount of data suggests that the teratogenic risks associated with fetal exposure to SSRIs are small and the potential for problems with neonatal adaptation symptoms are common (about 30%) but typically self-limited, several recent studies have evaluated the risk for persistent pulmonary hypertension of the newborn (PPHN) associated with late trimester exposure to SSRIs.

BY LEE COHEN, M.D.

I have reviewed several studies suggesting a spectrum of risk, dating back to the case-control study using data from a birth defects database, which ascribed about a sixfold increase in risk for PPHN to late trimester exposure to SSRIs (N. Engl. J. Med. 2006;354:579-87). This was followed by a case-control study published last year from the Swedish Medical Birth Register, which found approximately a twofold increased risk of PPHN associated with SSRI exposure late in pregnancy (Pharmacoepidemiol. Drug Saf. 2008;17:801-6).

Recently, another study using an administrative database from four health plans in an ongoing HMO research network study of birth outcomes provided yet another estimate. The investigators retrospectively identified 1,104 full-term infants whose mothers were dispensed an antidepressant in the third trimester and 1,104 full-term infants whose mothers did not receive an antidepressant in the third trimester (Pharmacoepidemiol. Drug Saf. 2009 January 15 [doi:10.1002/pds.1710]).

Possible cases of PPHN were identified using different diagnosis and procedure codes and confirmed with reviews of hospital records. There was no difference in risk for PPHN between exposed and unexposed children: The prevalence of PPHN was 2.14 per 1,000 among infants exposed to an SSRI during the third trimester and 2.72 per 1,000 among the infants not exposed to SSRIs. Only a small number of cases of possible PPHN were confirmed—two among SSRI-exposed infants and three among those not exposed—and some cases may have been missed, hence one of the limitations of the study.

The conflicting data are not terribly surprising because these studies are not prospective and they use various databases; each has its own respective limitations. It is noteworthy, however, that in the most recent study, the frequency of PPHN was similar to rates reported in the literature and the general population, suggesting that the methods used were comprehensive and that the results may reflect what we see in the real world. Also noteworthy is that maternal diabetes and asthma, two known risk factors for PPHN, were common in the exposed group, compared with the unexposed group, but other risk factors known to drive PPHN—increased body mass index, alcohol and cigarette smoking, or African American ethnicity—were not ascertained in this study.

Hence, we are faced once again with studies addressing critical questions for patients that have provided different results, which certainly makes it challenging for clinicians to attempt to navigate a thoughtful clinical course for their patients.

When counseling patients, one concern is how these data cumulatively inform the care of patients with histories of recurrent major depression treated with SSRIs during pregnancy. Given the warnings in the SSRI labels regarding PPHN, many patients—in collaboration with their doctors—may elect to discontinue antidepressants just before delivery because of concern over PPHN, an extremely serious outcome. Given the study with the sixfold increased risk, the Swedish registry data indicating a twofold increased risk, and these new data, which suggest the absence of risk, the answer regarding the true risk for PPHN may fall somewhere in the middle, with perhaps some modest increase in risk.

Even if we assume a modest increase in the risk for PPHN in this scenario, the absolute risk is extremely small and it may not justify discontinuing antidepressants close to delivery because this clearly puts patients at risk for depressive relapse and at a very high risk for worsening of mood in the postpartum period, with its attendant morbidity and adverse sequelae for both the mother and child.

Clinicians and patients together will make decisions based on the available information, and those decisions will vary from patient to patient, based on patients' wishes and individual clinical situations. We make the best clinical decisions possible on a case by case basis, and we welcome more of these analyses from rich datasets so we can continue to refine risk estimates—particularly for rare but serious outcomes such as PPHN.

DR. COHEN *directs the perinatal psychiatry program at Massachusetts General Hospital, Boston, which provides information about pregnancy and mental health at www.womensmentalhealth.org. He also is a consultant to manufacturers of SSRIs.*