Bleeding, Oral Pathogens Linked to Preterm Birth

BY SHARON WORCESTER
Southeast Bureau

MIAMI BEACH — Unexplained vaginal bleeding and fetal exposure to oral pathogens have been linked individually with spontaneous preterm birth, and new data suggest the presence of both is associated with greater risk than either alone.

Of 660 pregnancies analyzed, 229 (35%) demonstrated fetal exposure to oral pathogens. Pregnancies that demonstrated such exposure were more likely to be in white women, women who had symptomatic bacterial vaginosis, and women who experienced vaginal bleeding, which was the most significant variable associated with oral pathogen exposure (adjusted risk ratio 1.6).

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DR. BOGGESS

A total of 51 women (8%) in this planned secondary analysis of the Oral Conditions and Pregnancy Study—a prospective observational study of oral health and pregnancy outcomes—delivered before 35 weeks' gestation, Dr. Kim Boggess reported at the annual meeting of the Society for Maternal-Fetal Medicine.

When women with vaginal bleeding were stratified according to whether fetal exposure to oral pathogens occurred, preterm birth rates were significantly higher in those with both factors. Preterm birth occurred in 30% of those with both factors, compared with 8% in those with only vaginal bleeding, 9% of those with only oral pathogen exposure, and 6% of those with neither.

After adjusting for age, race, prior preterm birth, prior elective or spontaneous abortion, bacterial vaginosis, and enrollment weight, the differences remained. The adjusted hazard ratio for spontaneous preterm birth, compared with those with neither risk factor, was 6.4 for those with both factors, 1.9 for those with only vaginal bleeding, and 2.0 for those with only exposure to oral pathogens, said Dr. Boggess of the University of North Carolina at Chapel Hill.

Fetal exposure to oral pathogens was considered to have occurred if umbilical cord serum at delivery demonstrated an immunoglobulin M-positive (IgM-positive) response to at least one of five oral pathogens, she explained.

"Our findings show that antepartum vaginal bleeding is associated with fetal exposure to oral pathogens, and that the combination of fetal exposure to oral pathogens and vaginal bleeding provides the highest risk for premature birth at less than 35 weeks," Dr. Boggess said.

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Unexplained vaginal bleeding may be one of the mechanisms of fetal exposure to oral pathogens during pregnancy, but further study is needed to determine whether vaginal bleeding is the cause or the effect of fetal exposure to oral pathogens, she said.

The findings also suggest that clinical determination of periodontal disease is a poor marker for fetal exposure to oral pathogens, she noted.

Dr. Boggess indicated two weaknesses of the study: Detected pathogens could reside in the vagina of affected patients, causing fetuses to be exposed via pathogen ascent through the vagina; and the vaginal bleeding detected in this study may have actually been from some undetected underlying cause.

More data are needed before a position on interventions in women with periodontal disease can be officially taken, but two ongoing intervention trials may shed some light on the impact of treatment of periodontal disease during pregnancy, Dr. Boggess noted. ■

Depression Doubles With Menopause

Women entering menopause are nearly twice as likely to develop depression as are women the same age who are not yet making the transition to menopause, reported Dr. Lee S. Cohen and his associates in the Harvard Study of Moods and Cycles.

A cross-sectional sample of 460 women, aged 36 to 45 years, were prospectively followed every 6 months for several years. Changes in menstrual cycle length and menstrual flow amount and duration were tracked, and symptoms were assessed, said Dr. Cohen and his associates at Harvard Medical School, Massachusetts General Hospital, and Brigham and Women's Hospital, all of Boston.

None of the women had a history of major depression. A total of 134 were still premenopausal at the end of the last follow-up period, which occurred between 59 and 92 months after study enrollment. The remaining 326 women had entered menopause during that interval.

The rate of new-onset major depression was 16.6% in the menopausal women, compared with 9.5% in those who had not yet entered menopause, after the data had been adjusted to account for age at study enrollment and history of negative life events. "To our knowledge, this prospective documentation of increased risk for depression among women without a history of depression is unique," the investigators said (Arch. Gen. Psychiatry 2006;63:385-90).

—Mary Ann Moon

DRUGS, PREGNANCY, AND LACTATION

Weighing New Evidence on SSRI Use

Until fairly recently, studies and reviews of global teratovigilance data have been relatively reassuring that SSRIs were particularly safe, especially with regard to their teratogenicity. In fact, there are more reproductive safety data available for SSRIs than for many medicines women take during pregnancy. But new reports have raised concerns about the teratogenicity of paroxetine, which we have previously discussed (FAMILY PRACTICE NEWS, Nov. 1, 2005, p. 41), as well as risk for putative neonatal distress syndromes and, most recently, possible increased rates of persistent pulmonary hypertension of the newborn (PPHN) following late-pregnancy exposure to SSRIs.

BY LEE S. COHEN, M.D.

What do the new reports describe and how do the findings inform clinical care? One study supports previous reports of a "neonatal abstinence syndrome" with characteristic symptoms of jitteriness, sleep disturbance, dysregulation, tachypnea, and myoclonus in infants whose mothers used antidepressants during pregnancy. In this prospective cohort study of 120 infants, examiners used a systematic scale to assess full-term SSRI-exposed newborns with respect to the presence or absence of a wide range of previously reported symptoms.

Of the 60 infants exposed in utero to various SSRIs for a mean of 35.5 weeks, 8 had severe symptoms and 10 had mild symptoms, compared with none of the 60 infants who had not been exposed in utero to these drugs (Arch. Pediatr. Adolesc. Med. 2006;160:173-6). A particularly noteworthy finding is that no infant with symptoms required treatment intervention; symptoms were transient and of little if any clinical significance.

In the second study, investigators using a case-control design described an elevated risk for PPHN, a far more serious syndrome associated with severe respiratory failure, in newborns with in utero exposure to SSRIs late in pregnancy. In this study, which enrolled almost 400 women whose infants had PPHN, matching them to more than 800 control mothers and infants, the use of SSRIs at any point during pregnancy was not associated with PPHN, but there was a significant association between PPHN and in utero exposure to an SSRI after 20 weeks' gestation (N. Engl. J. Med. 2006;354:579-87).

The study describes a very disturbing and striking finding. But an accompanying editorial points out that the number of cases reported is small (N. Engl. J. Med. 2006;354:636-8). And though not mentioned in the editorial, the vulnerability to reporting bias in such a study is great. One wonders whether women without an adverse outcome may be reluctant to disclose use of an antidepressant during pregnancy, compared with those with an adverse outcome as serious as PPHN. Because the conclusions are based on a small number of PPHN cases, a difference of a small number of cases in either direction can strengthen or attenuate a positive finding.

The authors of the second study suggest that the incidence of PPHN associated with SSRI exposure in late pregnancy approaches 1%. However, given the hundreds of women who have used SSRIs during late pregnancy, it is unlikely such a dramatic clinical finding would not have been reported, even anecdotally, before this study—the first of such reports.

These studies, which have had considerable media attention, have alarmed women who are taking antidepressants. In fact, they were published just weeks after we reported the results of a prospective study of 201 women with a history of major depression who were prospectively followed during pregnancy. Women who discontinued their antidepressant medication proximate to conception were at a fivefold greater risk for depressive relapse during pregnancy, compared with those who continued with an antidepressant (JAMA 2006;295:499-507). These data certainly suggest pregnancy is not protective with respect to depression and many women who stop antidepressants will relapse during pregnancy.

Although some women will still stop antidepressant therapy during pregnancy, patients should be informed that depression during pregnancy can increase the risk for other neonatal complications and substantially increase the risk for postpartum depression. Other women will choose to continue antidepressant use during pregnancy, regardless of the findings of these more recent studies, given what for some patients will be viewed as a modest risk for the neonatal outcomes described. Regardless of individual choices, which can vary greatly, it is crucial to present all available information to reproductive-age women on antidepressants who plan to conceive or who are pregnant, so collaborative decisions can be made based on the data and personal wishes. No decision is perfect or risk free. Women provided with the same information may make very different decisions.

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