Antibacterial Use in Pregnancy

Prenatal Exposure to SSRIs May ‘Modestly’ Raise Autism Risk

BY MARY ANN MOON
FROM ARCHIVES OF GENERAL PSYCHIATRY

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ntibacterial medications are among the most commonly used in pregnancy. Despite decades of use in obstetric practice for some of these medications, large-scale studies of human teratogenicity have been lacking. In recent years, some of the gaps in knowledge, and real-time updates of medications and risks for specific birth defects have been addressed by ongoing work being conducted through the National Birth Defects Prevention Study, a multisite U.S. population-based case control study with sufficient sample size and power to explore associations between medication exposure in the first trimester and approximately 30 selected major birth defects.

However, as data emerge from this study, interpretation can present dilemmas in obstetric practice when commonly used treatments are called into question regarding safety. One such analysis published in 2009 explored the relationship between selected major congenital anomalies and 11 categories of antibacterial medications taken for any number of days in the month before pregnancy through the first trimester. A total of 13,115 mothers of infants with birth defects were interviewed and the prevalence of maternally reported exposure to antibacterial medications in the periconceptional period was compared to that reported by 4,941 mothers of nonmalformed control infants (Arch. Pediatr. Adolesc. Med. 2009;163:978-85).

This study confirmed the high prevalence of exposure in pregnancy to at least one of these agents — about 30% of women in both groups recalled taking an antibacterial medication sometime in pregnancy, although over 30% of those could not recall the specific type. The study findings were reassuring regarding most categories of treatments studied, including penicillins and erythromycins. However, of concern, two categories of medications used to treat urinary tract infections, nitrofurantoin and sulfonamides, were found to be significantly associated with four and six types of congenital anomalies, respectively.

The authors acknowledged the limitation that documentation of exposure to antibacterials was based on maternal recall up to 2 years post partum, and that the underlying disease being treated could have been contributory. In addition, more than 300 comparisons were made in this study, and it was impossible to pinpoint specific gestational days of exposure to the medications that might have plausibly been related to the wide variety of embryologic timing for each of the specific defects. Furthermore, a previously published Hungarian case-control study of nitrofurantoin use in pregnancy found no evidence of an increased risk with first trimester exposure to this drug. The authors of the U.S. study appropriately concluded that their findings called for additional scrutiny.

However, taken in context, further research takes time, and clinical treatment decisions must be made now. As a result, in June of 2011 the American College of Obstetricians and Gynecologists issued a Committee Opinion (1494) on this topic. Based on the limitations of the study, lack of corroborating evidence, and the necessity of treatment, the committee concluded that the two antibiotics in question could be used by pregnant women in the first trimester if there was no appropriate alternative.

This is one example of many similar situations that are likely to occur in the future as findings from large case-control studies like the National Birth Defects Prevention Study are published. More good quality research on the risks or lack of risks of medications in pregnancy is a huge positive step forward for public health, and is long overdue. However, at the same time, a systematic and swift means for evaluating how these often hypothesis-generating findings should impact clinical practice (e.g., the ACOG Committee Opinion) is needed, as well as a systematic and relatively quick means for testing the hypothesis in one or more other data sets — whether it’s a large claims database or one of the many other rich data resources that are being developed to explore the risks and benefits of drugs in pregnancy.