Asthma Drugs, Anorectal Atresia May Be Related

BY ROBERT FINN
San Francisco Bureau

MONTEREY, CALIF. — Women who take anti-inflammatories for asthma during the first trimester of pregnancy have an elevated risk of giving birth to an infant with anorectal atresia, according to results of a multicenter, case-control study of more than 7,000 women.

Anti-inflammatory use was not associated with any other birth defects, nor was the use of bronchodilators, Shao Lin, Ph.D., and colleagues at the New York State Department of Health reported in a poster presentation at the annual meeting of the Teratology Society.

The multicenter case-control study was part of the National Birth Defects Prevention Study, which collects data from 10 regions in the United States.

The investigators included women exposed to asthma medications at least once during a critical period defined as between 1 month prior to pregnancy and the end of the third pregnancy month. They focused on babies born between 1997 and 2003 with one of seven birth defects: diaphragmatic hernia, esophageal atresia, intestinal atresia, anorectal atresia, neural tube defects, omphalocele, and limb reduction.

In all, the investigators identified 2,248 infants with birth defects born to mothers taking asthma medications. They compared them with 4,986 nonmalformed, live-born infants identified by birth certificates or birth hospitals.

After adjusting for age, body mass index, parity, race/ethnicity, education, alcohol use, smoking, gender, folic acid use, fever, cocaine use, and the use of seven different vasoactive medications, the investigators found no significantly increased risks of birth defects associated with maternal bronchodilator use. Maternal anti-inflammatory use, on the other hand, was associated with a statistically significant 2.6-fold increase in the risk of anorectal atresia. There were no other statistically significant associations between anti-inflammatory use and birth defects.

The investigators acknowledged that their study could not determine whether it was the anti-inflammatories or the asthma itself that was the causal agent. The use of asthma medications during the entire critical period could be an indication of especially severe asthma. They wrote that further studies would be needed to separate the effects of asthma from the effects of asthma treatment.

Dr. Lin disclosed no conflicts of interest associated with the study. ■

Screen, Intervene to Help Pregnant Substance Abusers

BY SUSAN BIRK
Contributing Writer

CHICAGO — Careful screening for substance abuse in pregnant women and recognizing that intervention can make a difference for these patients and their offspring are two important ways to improve obstetric outcomes.

Physicians might also examine the attitudes and biases they bring to their treatment of expectant patients who are chemically dependent.

"We need to remember that addiction is a disease, not a moral failure, and that patients can change," said Dr. Ellen Mason, an internist and attending physician in the department of obstetrics and gynecology at John H. Stroger Jr. Hospital, Chicago, in a presentation on substance abuse and psychiatric disorders among pregnant women.

"For doctors, [pregnancy and substance abuse] is not just a medical issue, it's a personal issue. In medicine, regardless of how much [physicians] think they're detached or nonjudgmental, they have a lot of trouble being nonjudgmental about [chemically dependent] women" and often view these patients as neglectful or deliberately hurting their fetuses, she said.

She stressed, however, that "treatment is ultimately more successful for women when they are not made to feel like monsters or made to feel more guilty than they already feel. Some patients, regardless of how much bravado they display … feel terrible about it."

In her presentation, Dr. Mason cited the 2005 National Survey on Drug Use and Health (www.oas.samhsa.gov), which indicated that an estimated 12.1% of pregnant women aged 15-44 reported current alcohol use, 3.9% reported binge drinking, and 3.9% reported illicit drug use during the month preceding the survey.

She urged physicians to "translate ethical principals into [practices] that will serve our patients well and help them succeed."

These practices include using the "Five A's," the screening and behavioral counseling intervention for alcohol misuse recommended by the U.S. Preventive Services Task Force (Ann. Intern. Med. 2004;140:554-6), which asks physicians to take these steps:

- ► Assess alcohol consumption with a brief screening tool followed by clinical assessment as needed.
- ► Advise patients to reduce alcohol consumption to moderate levels.
- ► Agree on individual goals for reducing alcohol use or abstinence (if indicated).
- ► Assist patients with acquiring the motivation, self-help skills, and support needed for behavior change.
- ► Arrange follow-up support and repeated counseling, including referring dependent drinkers for specialty treatment. ■

DRUGS, PREGNANCY, AND LACTATION

FDA to Revise Risk Categories

BY LEE COHEN, M.D.

The Food and Drug Administration has proposed revisions to the longstanding system of pregnancy category labeling for all medications. The current system has classified the reproductive safety of medications across five risk categories—A, B, C, D and X—usually based on available data when a drug is approved. The proposed system will eliminate the letter categories and instead will include sections on pregnancy and lactation, each with information summarizing risks, clinical considerations, and available data.

The implications of the proposed system with respect to psychiatric medications are significant. In previous columns, I have discussed some of the limitations of the category label system for various psychiatric medications. There are examples of medications with a sparse amount of reproductive safety information that does not indicate an adverse effect, which bear a more favorable category label than other medicines for which very extensive reproductive safety are available, but perhaps where animal safety data suggest some cause for concern. There are also examples where evidence of adverse reproductive effects in animals dosed with toxic amounts of a medicine can trump significant amounts of human data supporting reproductive safety.

A dramatic example of the current system's limitations is lithium, a category D drug because of clear evidence of Ebstein's anomaly associated with first-trimester exposure. Yet the absolute risk of the cardiac anomaly is only 0.05% following first-trimester exposure. Considering the high rate of relapse of bipolar disorder associated with stopping lithium before or during pregnancy, this may be a risk many patients are willing to take, in collaboration with their psychiatrists.

The current system also does not distinguish between relative amounts of data, and typically lumps a class of medications into one category, instead of considering the drugs as individual molecules. All the selective serotonin reuptake inhibitors are labeled category C, yet the amount of reproductive safety data available for the individual SSRIs is highly variable. Moreover, information in the letter category system has been limited to reproductive safety during the first trimester and does not address some of the potential risks of exposure during the second and third trimesters, and peripartum period

Part of the problem is that with few exceptions, industry has failed to embrace a global product safety initiative regarding establishing registries for these products in a systematic way shortly after a drug is marketed.

In May, almost a decade after indicating that the pregnancy and lactation labeling system would be changed, the FDA announced the proposed changes, which address these limitations.

The pregnancy section would include a fetal risk summary, which would describe the risks to the fetus associated with exposure to the medicine based on available data; and clinical considerations, which would include information about the effects of the drug if a woman takes it before she knows she is pregnant and the risks of the disease for the mother and baby. A third section would summarize the available human and animal data that provide the basis of the fetal risk summary. The labor and delivery section in the current drug label would be eliminated, with this information included in the pregnancy section. The section on lactation would include the same sections on risk summary, clinical considerations, and data.

The clinical implications of dropping the letter category system are considerable. These categories have frequently been used to switch patients from one medicine to another somewhat arbitrarily. Even well-intentioned doctors have switched a patient to a medicine based on the category label, when there are less available reproductive safety data in humans, but perhaps animal data were of some concern.

Once the new system is in place, this type of arbitrary change in a patient's medication based on the category label will hopefully cease. Moving from a categorical system of classification to a system that is more inclusive of available reproductive safety information should help providers rather than confuse them. Physicians will be provided with more information in a drug's label that actually describes results of studies and will be able to see firsthand the type of information that is available and the quality of data, as well as references to studies. As a result, we will be provided with a more global risk assessment across pregnancy, including the peripartum period and lactation.

Regardless of the system used, the process of making decisions about the use of any medicine, particularly psychotropics, during pregnancy should be made on a case-by-case basis.

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