Tenofovir Accumulates In Fetal Compartment

BY SHERRY BOSCHERT
San Francisco Bureau

MONTEREY, CALIF. — Multiple doses of tenofovir produced much higher drug concentrations in fetuses, compared with other antiretrovirals taken by pregnant women with HIV, Dr. Kim A. Boggess said at the annual meeting of the Infectious Diseases Society for Obstetrics and Gynecology.

Few data exist on the fetal effects of antiretroviral regimens for HIV, and those few mostly look at single doses. The current study of eight HIV-infected women who had been on antiretrovirals for at least 26 weeks had them take their usual doses of antiretroviral medications on the day before and the day of a scheduled prelabor cesarean delivery. They also received intravenous zidovudine 4 hours before delivery to reduce the risk of vertical transmission.

Blood samples taken from the mother and mixed umbilical venous/arterial blood before administration of zidovudine and afterward (a mean of 16 hours after their last dose of usual antiretrovirals) found that tenofovir accumulates within the fetal compartment, said Dr. Boggess of the University of North Carolina, Chapel Hill, and her associates.

Results showed levels of tenofovir in umbilical cord blood were six times levels in maternal blood, nine times higher than reported following a single dose of tenofovir. Umbilical:maternal ratios for other antiretrovirals were similar to concentrations reported for single doses.

Three of the eight women were taking tenofovir (Viread), two women were on nelfinavir (Viracept), six were taking Kaletra (lopinavir/ritonavir), and all were exposed to Combivir (lamivudine/zidovudine) in their antiretroviral regimens.

Dr. Boggess has no affiliation with any of the companies that make these drugs.

The implications of tenofovir accumulating in the fetal compartment are unclear; it could be both helpful and harmful. Higher concentrations of an antiretroviral may help reduce the risk of vertical transmission of HIV from women who cannot undergo cesarean delivery, but also may cause more adverse side effects.

The infants are being followed, some with x-rays, to monitor potential bone changes from exposure to antiretrovirals, a concern raised by studies in monkeys.

Approximately 1,800 children are infected with HIV daily worldwide, usually via pregnancy or breast-feeding. Higher fetal antiretroviral concentrations might be especially useful in areas of the world where access to C-sections is limited, Dr. Boggess said. ■

Few Web Sites Good Sources of Patient Info on Labor Analgesia

HOLLYWOOD, FLA. — A search of more than 100 Web sites that provide information about labor epidurals yielded very few with reliable information, Dr. Edgar M. Wayne reported in a poster at the annual meeting of the Society for Obstetric Anesthesia and Perinatology.

Of 117 sites reviewed by two experienced obstetric anesthesiologists using two popular search engines and a Microsoft Accuracy rating tool that was shown to be reliable, only 33 were rated as accurate, and only 13 of those were deemed relevant and acceptable as educational tools for patients. An additional 36 sites were rated as inaccurate, and 33 were rated as misleading, reported Dr. Wayne of the University of Michigan Health System, Ann Arbor.

The remaining 15 were peer-reviewed articles only and were not included in the analysis.

Sites based on information from peer-reviewed sources such as textbooks or journals were significantly more likely to be accurate, relevant, and reliable; inaccurate Web sites were significantly more likely than the others to be based on nonscientific sources such as anecdotes or human interest stories. In addition, the inaccurate sites were more often written or sponsored by special interest groups.

Dr. Wayne emphasized that it is important to direct patients to Web sites that provide accurate, reliable information, because the Internet is widely and increasingly used by patients for medical information and the information they find there could influence them to decline safe and potentially beneficial labor pain management.

Interdisciplinary, hospital-based antepartum educational programs could help address the need for accurate patient education regarding neuraxial labor analgesia, he said.

—Sharon Worcester

DRUGS, PREGNANCY, AND LACTATION

Accumulating Data on Prenatal Exposure to SSRIs

BY LEE COHEN, M.D.

Over the last year, several studies on possible neonatal effects of prenatal exposure to SSRIs have been reviewed in this column. These studies have raised concerns about potential risks, including congenital malformations—as may be the case with paroxetine (associated with a putative increased risk for cardiovascular malformations, prompting a change in the pregnancy risk category label from C to D)—and perinatal distress and pulmonary complications, as noted in two recent studies (OB.GYN. NEWS, January 15, April 15, 2006). Other studies discussed here have highlighted the high risk of depressive relapse associated with discontinuation of antidepressants during pregnancy.

These and further studies reported over the last few years reflect the heightened interest in perinatal psychopharmacology and have provided a more refined scientific focus on the relative risks of prenatal SSRI exposure vs. the potential risks of untreated mood disorder during pregnancy. These are relative risks that physicians need to discuss with patients, making the best clinical decision possible based on the patient's individual clinical situation.

Until recently, few studies have attempted to parse out the neonatal effects of untreated depression and prenatal SSRI exposure. Most of the available data have been in women treated with an SSRI for underlying depression, and have not included a comparison group of unmedicated women suffering from depression.

However, a study published in August by investigators at the University of British Columbia, Vancouver, using population-based health data in British Columbia and linking records of neonatal birth outcomes with hospital records of psychiatric diagnoses at maternal discharge and prenatal SSRI prescriptions, provides an opportunity to tease apart these two potentially important predictors of neonatal outcomes (Arch. Gen. Psychiatry 2006;63:898-906).

The study compared outcomes of babies born to women diagnosed with depression and treated with an SSRI to outcomes of babies born to women diagnosed with depression who were not treated with medication, and to a control group of babies whose mothers were neither depressed nor on antidepressant medication, between 1998 and 2001.

Among babies exposed to SSRIs, birth weights were lower, hospital stays were longer, and gestational ages were shorter, compared with babies in the control group. A similar pattern was seen when the SSRI-exposed babies were compared with those of depressed mothers who were not treated, except for birth weight for gestational age. In addition, significantly more of the infants of medicated women had respiratory distress and jaundice, compared with babies in the other two groups. Feeding problems were significantly more common among SSRI-exposed infants than among infants of unmedicated women with depression. The rate of convulsions was not significantly different between the groups.

Using propensity scores to match severity of depression in untreated and treated women, the investigators attempted to match women by degree of depression in the year before and during pregnancy, essentially controlling for illness severity while looking at neonatal outcomes. When they compared birth outcomes in these two groups, the associations between prenatal SSRI exposure and feeding problems and jaundice were no longer present. What remained significant was a greater rate of respiratory distress among infants of SSRI-treated mothers and the incidence of birth weight below the 10th percentile. These findings suggest that the effect on respiratory distress may be due to SSRI exposure, rather than maternal depression.

The authors appropriately acknowledge the limitations of using claims data and discharge diagnoses as proxies for real diagnostic assessments. They also note that alcohol or illicit drug use, smoking, or socioeconomic conditions beyond income—all of which can affect neonatal well-being—could not be ascertained. Not factored into the study is another critical issue, the risk of postpartum depression, which is strongly associated with depression during pregnancy. In many respects, postpartum depression may have more enduring long-term outcome than other types of fetal exposures. Also unknown is the nature of respiratory distress, and whether it persisted. In one recent study, for example, symptoms of a "neonatal abstinence syndrome" were transient and did not require clinical intervention (Arch. Pediatr. Adolesc. Med. 2006; 16:173-6).

The conclusion from the Canadian study, considering its limitations, is that there may be an independent effect of maternal depression on neonatal outcome and an independent effect of medication exposure, and that these effects may be additive. Confirming this finding may only be possible with a prospective study that more accurately assesses maternal diagnosis and severity over time and where medication exposure is confirmed prospectively.

In considering the increasing amount of data on both sides of this relative risk equation, it is critical for clinicians to discuss with patients the range of issues, from the potential neonatal effects of these medicines, to the high risk for relapse when antidepressants are discontinued, to the impact of untreated illness on the baby and mother.

Our own research and clinical experience with this population suggest that patients presented with the same information, including women with extremely similar clinical illness histories, will make very different decisions about medication use during pregnancy. So, there is our task: to present this information and to let patients make decisions consistent with their wishes. With the backdrop of continually evolving data, patient decisions will also evolve, decisions not driven by the clinician, but by collaboration between the clinician and patient.

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 serves as a consultant to manufacturers of several antidepressants, including SSRIs.