Tenoforv Accumulates In Fetal Compartment

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MONTREY, CALIF.—Multiple doses of tenoforv 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 umbilical cord were analyzed for tenoforv. Of the eight women, all but one were taking tenoforv and the other was taking a combination of tenoforv, lamivudine, and zidovudine. The babies had high tenoforv concentrations, with nine times higher than reported following a single dose of tenoforv. Umbilical maternal ratios for other antiretrovirals were similar to concentrations reported for single doses.

Three of the eight women were taking tenoforv (Virad, two women were on nelfinavir (Vira-cept), 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 tenoforv 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.

Accumulating Data on Prenatal Exposure to SSRIs

BY LEE COHEN, M.D.

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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—and an increased risk for cardiovascular malformations, prompting a change in the pregnancy risk category labeling 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 to the potential risks of untreated mood disorders 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 the effects of 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 unmicated 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 weights 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 the exposed infants than among infants of untreated women with depression. The rate of convulsions was not significantly different among the groups.

In one recent study, for example, symptoms of postpartum depression, which is the nature of respiratory distress, and whether it persisted. Concerns about the 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. Considering these findings may only be possible with a prospective study that more accurately assesses maternal diagnosis and severity over time and where medication exposure is controlled 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 let patients make decisions consistent with their wishes. With the backdrop of continuing 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.