Tenoforv Accumulates In Fetal Compartment

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MONTEREY, CALIF. — Multi- ple 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 med- ications on the day before and the day of a scheduled prelabor ce- sarian 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 vein blood after birth of each infant were analyzed for tenoforv and d4T. The results showed that tenoforv levels in umbilical cord blood were nine times higher than reported following a single dose of tenoforv. Umbilical maternal ratios for other antiretroviral were similar to concentrations reported for single doses.

Three of the eight women were taking tenoforv (Viread), two women were on nelfinavir (Vira- crix), six were taking Kaletra (lopinavir/ritonavir), and all were exposed to Combivir (lamivu- dine/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 comp- artment 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 ce- sarian delivery, but also may cause more adverse side effects. The infants are being followed, some with x-rays, to monitor po- tential bone changes from expo- sure to antiretrovirals, a concern raised by studies in monkeys.

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

Tenofovir Accumulating Data on Prenatal Exposure to SSRIs

O ver the last year, several studies on pos- sible neonatal effects of prenatal ex- position to SSRIs have been reviewed in this column. These studies have raised con- cerns about potential risks, including congen- ital malformations—as may be the case with patients on tenoforv and a putative in- creased risk for cardiovascular malformations, prompting a change in the pregnancy risk cat- egory label from C to D—and perinatal dis- tress 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 antide- pressants during pregnancy.

These and further studies re- ported over the last few years re- flect 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 de- pression and the 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 un- medicated women suffering from depression.

However, a study published in August by in- vestigators at the University of British Colum- bia, 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;63:988-906).

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 med- ica- tion, 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 untreated group. A similar tend- ern was seen when the SSRI-exposed babies were compared with those of depressed moth- ers who were not treated, except for birth weight for gestational age. In addition, signifi- cantly 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 com- mon in the SSRI-exposed infants than among infants of unmedicated women with depres- sion. The rate of convulsions was not signifi- cantly different between the groups.

Using propensity scores to match severity of depression in the year before and dur- ing 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 jaun- dice were not longer present. The most sustained significant was a greater rate of respiratory dis- tress 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 ex- posure, rather than maternal depression.

The authors appropriately ac- knowledge the limitations of using claims data and discharge di- agnosises 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-be- ing—could not be ascertained. Not factored into the study is an- other critical issue, the risk of postpartum depression, which is strongly associated with depres- sion 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.

This recent study of symptoms of a “neonatal abstinence syndrome” were tran- sient 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 ef- fect of medication exposure, and that these ef- fects may be additive. Considering this finding may only be possible with a prospective study that more accurately assesses maternal diag- nose and severity over time and where med- ication 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 ef- fects of these medicines, to the high risk for relapse when antidepressants are discon- tinued, to the impact of untreated illness on the baby and mother.

Our own research and clinical experience with this population suggest that patients pre- sented with the same information, including women with extremely similar clinical illness his- tories, 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 ac- cumulating data, patient decisions will also evolve, deci- sions not driven by the clinician, but by collabor- ation 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.

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 ex- pected obstetric anesthesiolo- gists using two popular search en- gines and a Microsoft Accuracy rating tool that was shown to be reliable, only 33 were rated as ac- curate, and only 13 of those were deemed relevant and acceptable as educational tools for patients. An additional 36 sites were rated as in- accurate, some as misleading, leading, reported Dr. Wayne of the University of Michigan Health System, Ann Arbor.

The remaining 15 were peer-re- viewed articles only and were not included in the analysis. Sites based on information from peer-reviewed sources such as text- books or journals were significant- ly more likely to be accurate, re- levant, and reliable; inaccurate Web sites were significantly more likely than the others to be based on nonscientific sources such as anec- dotes 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, re- liable information, because the In- ternet is widely and increasingly used by patients for medical in- formation and the information they find there could influence them to decline advice potentially ben- efitl labor pain management.

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

—Sharon Worcester