The Conundrum of Lamivudine and Tenofovir Disoproxil Fumarate for Hepatitis B: Fetus Versus Infant

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(See the Invited Article by Ehrhardt et al on pages 275–8.)

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Despite worldwide efforts utilizing universal infant hepatitis B vaccination, hepatitis B virus (HBV) infection remains a significant problem worldwide. The article by Ehrhardt et al [1] in this issue of *Clinical Infectious Diseases* focuses on a bureaucratic snafu in which the use of the drugs lamivudine and tenofovir disoproxil fumarate (TDF) can be utilized during pregnancy when the fetus is exposed but are not approved for use during breastfeeding of the newborn infant; the authors review the evidence for and against their use during these time frames. It is ironic that both drugs are approved for use during pregnancy to treat mothers with HBV, but are not approved for use during breastfeeding. Even more ironic is that World Health Organization human immunodeficiency virus (HIV) guidelines recommend continued antiretroviral treatment while breastfeeding and one of the recommended drugs is TDF. So what is the evidence?

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The authors clearly provide proof that fetal exposure to both lamivudine and TDF is much higher than the exposure associated with breastfeeding. The incidence of newborn defects in association with these drug exposures is no different than that found in the general population. TDF is known to alter bone mineral density, but in pediatric trials overall skeletal growth was not adversely affected. However, the effect of TDF exposure on long-term growth is not currently known.

So, what is one to do when faced with a mother who is infected with HBV and has been treated with one of these drugs during pregnancy? Do you recommend stopping the drugs after birth to allow the mother to breastfeed knowing that the drug labeling does not approve of breastfeeding with these drugs? Do you allow the mother to risk a flare of her hepatitis B when you discontinue the drug immediately postpartum so that she can breastfeed her infant? Do you turn to the HIV literature where it is recommended that these drugs can be continued for breastfeeding the infant? Do you just ignore the recommendations and allow the mother to breastfeed? Or do you prohibit breastfeeding and continue the mother on the drugs?

The first lesson I learned in medical school was to do no harm. But in this case, who has precedence? Do we protect the mother or the newborn? As a pediatrician, I certainly am biased and would vote in favor of the newborn. But of course I do want the newborn to have a healthy mother. It would make the most sense to have the agencies responsible for drug approvals to review the available literature as evidenced by Ehrhardt et al and reconsider their labeling of lamivudine and TDF for breastfeeding. Also, the drug manufacturers could go to the drug agencies and petition for a label change based on the available literature. This, of course, is costly and time-consuming. Does it make business sense for the drug manufacturers to take on this task? My suspicion is no, or they would have already done so. So, is it the responsibility of physicians and healthcare advocates to request a reexamination of the facts by the drug agencies? It seems to me that this makes the most sense. In the interim, I suspect that each individual physician will need to have a frank conversation with their patients prior to delivery, explaining the benefits and risks, both known and unknown, of continuing these drugs following delivery and during breastfeeding. It is hoped that together, they will decide on the best course of action for both mother and child.

Note

Potential conflict of interest. Author certifies no potential conflicts of interest.

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Reference

1. Ehrhardt S, Xie C, Guo N, Nelson K, Thio CL. Breastfeeding while taking lamivudine or tenofovir disoproxil fumarate: a review of the evidence. Clin Infect Dis **2015**; 60: 275–8.