Hair samples from infants show exposure to anti-HIV drugs in the womb and during breast-feeding

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Researchers from the University of California, San Francisco (UCSF) and Makerere University in Uganda have used hair and blood samples from three-month old infants born to HIV-positive mothers to measure the uninfected babies' exposure—both in the womb and from breast-feeding—to antiretroviral medications their mothers were taking. The results, they said, are surprising.

"We found high levels of exposure to three antiretroviral medications in the hair samples of HIV uninfected infants at twelve weeks of life," said study senior author, Monica Gandhi, MD, MPH, associate professor of medicine at the UCSF Division of HIV/AIDS at San Francisco General Hospital and Trauma Center (SFGH).

"From looking at plasma level data at the same time point, we believe that transfer of two of the medicines from mother to baby occurs exclusively in the womb and transfer of the third medication occurs both in the womb and through breastfeeding."

The findings could lead to new ways to protect infants from HIV transmission and to better understand the development of toxicities and resistance to the drugs, the researchers said.

A single plasma level of a medication reflects drug exposure over approximately 24 hours. Measuring the concentrations of antiretrovirals in a small hair sample reveals exposure over the past month. The team therefore measured both plasma and hair levels of medications in babies whose mothers were taking HIV medications to get a better idea of when drugs are being passed from mother to baby. "Since fetuses start growing hair in the womb, hair sampling gives us an opportunity to examine exposures to drug before birth," said Gandhi.

UCSF researchers have pioneered the use of hair sampling for measuring antiretroviral levels. The procedure is now a standard measure in many research studies, equivalent in HIV clinical care to measuring hemoglobin A1C to monitor average blood glucose levels in patients with diabetes.
In the study, the team took hair and blood samples from two groups of HIV-positive mothers, all of whom breast-fed their infants. For 45 mother/infant pairs, the mothers’ antiretroviral regimens included a protease inhibitor, lopinavir, boosted by ritonavir, another antiretroviral medication. The other 64 mothers were on an efavirenz-based regimen.

Infants in the lopinavir group had levels of the drug in their hair that measured 87 percent of the levels found in their mothers’ hair. The levels of ritonavir were about 45 percent of the levels found in their mothers’ hair. When the researchers looked at the drug levels in the blood drawn from the mothers and infants at 12 weeks, they found the expected levels of lopinavir and ritonavir in the mothers, but none of either in the blood of the infants.

“The inability to find drug in the infants’ blood at 12 weeks tells us that the lopinavir and ritonavir in their hair is not due to recent exposure, so breast-feeding did not transfer these drugs to the infants. Our conclusion is that the lopinavir and ritonavir were transferred to the babies in the womb, and lopinavir at quite a high level,” said Gandhi.

In the efavirenz group, researchers found infant drug levels in hair samples that were about 40 percent of the levels found in their mothers. Additionally, they found that infants had levels in their blood that were about 15 percent of what was found in their mothers.

These findings indicate a moderate transfer of efavirenz both in the womb and during breastfeeding said Gandhi.

“Our findings, as we verify them, will have important implications. One, being able to measure drug exposures of fetuses in the womb and during breast-feeding can help us understand how to better protect infants from HIV transmission from HIV-positive mothers during pregnancy, birth and after birth. Antiretroviral medications are delivered prophylactically to HIV-positive mothers and newborns to prevent transmission, and fetuses derive protection from transmission if their HIV-positive mothers are on an antiretroviral regimen,” she said.

“Second, the development of resistance to antiretroviral medications in infants is an important issue. HIV develops resistant mutations after fairly low levels of exposure to the class of medications to which efavirenz belongs, non-nucleoside transcriptase inhibitors (NNRTIs). Additionally, hair sampling for antiretroviral exposure levels will ultimately help us monitor toxicities associated with these medications in infants.”

Using hair to measure exposure to antiretrovirals has advantages in that it is a painless, bloodless, biohazard-free method of collecting a stable specimen from HIV patients. It measures drug exposure over time and has been shown to be more predictive of treatment response than the “snapshot” of exposure provided by a single plasma level of medication.

Gandhi said that researchers are finding hair sampling to be a very useful tool in several settings. One use is in resource-limited settings where collecting, storing and handling blood draws is difficult and expensive. Hair is snipped, wrapped in foil and needs no refrigeration.

Another setting is in monitoring drug exposures in uninfected people. Researchers have been using the technique to measure adherence/drug levels in some of the pre-exposure prophylaxis trials, where high-risk uninfected patients take antiretrovirals to prevent getting infected with HIV. Non HIV-infected individuals cannot be monitored for adherence to antiretrovirals like HIV-infected individuals (where levels of HIV in the blood are measured routinely to indicate how well they are taking their pills) so hair levels provide a novel and reliable indicator of adherence.

A third setting is for monitoring prenatal exposures. Hair sampling is the only way currently to measure how much antiretroviral exposure fetuses are getting in the womb long-term. Cord blood measurements of antiretrovirals at birth, which are expensive and cumbersome to collect, still only reflect exposure to the babies over the short-term. And collecting
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This work will be presented on Saturday July 21, 2012 during the 4th International Workshop on HIV Pediatrics, which takes in Washington, D.C. preceding the XIX International AIDS Conference. A poster presentation of the same data, titled, "Lopinavir and efavirenz concentrations in paired hair samples as a marker of cumulative exposure among postpartum women and breastfeeding infants in Tororo, Uganda" will be unveiled at the XIX International AIDS Conference on Sunday, July 22, 2012.

Provided by University of California, San Francisco

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