Nevirapine Monotherapy Needs to Be Reassessed

Giving HIV+ women multidrug regimens in late pregnancy may do more to reduce virus transmission.

BY DIANA MAHONEY
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BOSTON — Short-term treatment with one or more antiretroviral drugs starting in late pregnancy—in addition to or instead of single-dose nevirapine—may reduce the likelihood that HIV-infected women will transmit the virus to their newborns and that the women will develop nevirapine resistance, research has shown.

The practice of giving pregnant women with HIV a single dose of nevirapine (Viramune) during labor has significantly reduced maternal/child transmission rates in the developing world. It also has been heralded as an optimal approach for lowering the transmission rates among women in the United States who are identified as HIV positive very late in pregnancy or at the time of labor, and who also may be unlikely to follow extended treatment regimens because of lifestyle or health care inaccessibility.

There is growing evidence, however, that many women who receive this treatment develop mutated strains of the virus that resist future treatment with nevirapine and, potentially, other drugs, said James McIntyre, M.D., at a conference on retroviruses and opportunistic infections.

"While people have been lauding [single-dose nevirapine] as a stunning breakthrough, others have said it represents a less-than-optimal regimen" to which women in developing countries should not be subjected, said Dr. McIntyre of the perinatal HIV research unit at the University of Witwatersand, Johannesburg, South Africa. "In my country, this has been seen as a U.S. and pharmaceutical company conspiracy."

The value of nevirapine monotherapy should be reassessed, Dr. McIntyre stressed, in light of new evidence suggesting that possible alternatives to the single-dose, single-drug regimen may be as effective at preventing vertical HIV transmission minus the potential for drug resistance.

In one of the studies presented at the conference, which was sponsored by the Foundation for Retrovirology and Human Health, 329 HIV-infected pregnant women in the West African nation of Cote d'Ivoire began therapy with a combination of zidovudine (AZT) and lamivudine (3TC [Epivir in the U.S.]) in their 32nd week of pregnancy through 3 days post partum, in addition to single-dose nevirapine during labor, reported lead investigator Francois Dabis, M.D., of Victor Segalen University in Bordeaux, France. The newborns in the study were treated with AZT for 1 week and a single dose of nevirapine.

The 6-week HIV type 1 (HIV-1) maternal/child transmission rate was 4.7%, representing "among the lowest transmission rates ever reported in Africa," said Dr. Dabis. Single-dose nevirapine alone typically reduces the transmission rate from an estimated 35% to approximately 12%, he noted. (Maternal/child HIV transmission rates in the United States, where women have more access to antiretroviral therapy, are approximately 2%, according to CDC data.)

The drop in nevirapine resistance was even more dramatic, with a reported rate among the mothers of 1.1%. Although the exact mechanism for the reduced resistance rate has yet to be identified, the multidrug strategy "may impair the ability of the virus to mutate into a [nevirapine-] resistant strain," according to Dr. Dabis.

A second study of 1,179 live births conducted in Botswana compared the effect of giving HIV-infected mothers multiweek zidovudine alone versus giving it in combination with single-dose nevirapine. Initially, each mother in the study was given zidovudine from 34 weeks' gestation and each mother/infant pair was randomized to receive blinded maternal and infant single-dose nevirapine or maternal and infant placebo. The study protocol was changed at 17 months because the infant nevirapine placebo was deemed unethical. Under the revised protocol, all infants received nevirapine as soon as possible after birth, while half of the mothers still got placebo, explained lead investigator Roger Shapiro, M.D., of Beth Israel Deaconess Medical Center in Boston.

Before the revision, the 1-month HIV transmission rates in 485 births were 5.3% in babies given nevirapine and 6.2% in babies who received placebo. In the 694 births that occurred during the revised study period, the 1-month transmission rates were 3.7% in babies born to mothers who received nevirapine and 4.3% in babies born to mothers given a placebo. The overall transmission rate for the entire study was approximately 4%, Dr. Shapiro said.

The results suggest that maternal single-dose nevirapine may not be needed to reduce mother/child transmission rates when both mother and infant are treated with zidovudine and when the infant receives nevirapine at birth—an important possibility, given that a substudy of the investigation found that 44% of the women who received the single-dose nevirapine developed resistance mutations, Dr. Shapiro noted.

Although the findings from both studies are promising, "the translation from trials to programs is incredibly challenging," said Mary Glenn Fowler, M.D., chief of maternal-child transmission, Centers for Disease Control and Prevention, Atlanta. "It's important not to be rapidly overoptimistic. We need to see what happens when those women start therapy [after delivery]."

Advocates for AIDS research and treatment agree. A press release issued by the Elizabeth Glaser Pediatric AIDS Foundation stressed the importance of preserving single-dose nevirapine as an option: "Even simple interventions like nevirapine are still available to less than 10% of the women who need them worldwide. Therefore, we must continue to aggressively expand access to services and improve our ability to offer the most effective drug regimens in all instances." ■

Antiviral Therapy Missed by Those in Need

BY DIANA MAHONEY
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BOSTON — Almost half of HIV-positive individuals in the United States who meet federal guidelines for antiretroviral therapy may not be receiving the treatment, according to a recent estimate by the Centers for Disease Control and Prevention.

Late diagnoses, unawareness of HIV risk factors and risk status, and treatment inaccessibility are among the likely factors contributing to the insufficient care of as many as 44% of the country's treatment-eligible HIV-positive individuals, CDC medical epidemiologist Eyasu Teshale, M.D., reported at a conference on retroviruses and opportunistic infections.

Using data from an analysis of AIDS diagnoses reported by all 50 states and HIV diagnoses reported by 30 states with well-established integrated HIV/AIDS reporting systems and lab-based CD4 reports, the CDC investigators estimated that, through 2003, there were about 480,000 treatment-eligible HIV/AIDS patients in this country.

Federal treatment guidelines recommend antiretroviral therapy for HIV-infected patients with CD4 white blood cell counts of 350 cells/μL or lower; yet according to a statistical model, only 56% of eligible patients likely received the recommended therapy, said Dr. Teshale.

To estimate the number of HIV/AIDS patients receiving antiretroviral therapy, the CDC investigators extrapolated treatment percentages from CDC's Adult/Adolescent Spectrum of HIV Disease (ASD) project, a 10-city medical records–based surveillance project that prospectively collected information from more than 60,000 HIV/AIDS patients from 1990 through June 2004.

About 79% of the HIV-infected patients in the ASD population with CD4 counts below 350 cells/μL received antiretroviral therapy. "We applied that proportion to the 340,000 patients estimated to be 'in care' on a national level," Dr. Teshale said. Using this approach, the investigators estimated that 268,000 (79%) of the 340,000 patients diagnosed and receiving care in the U.S. received ART at the end of 2003. These 268,000 people represent only about 56% of the 480,000 Americans aged 15-49 who were living with HIV/AIDS and were eligible for ART at the end of 2003.

An estimated 42% of eligible patients not getting antiretroviral therapy have not even been diagnosed with HIV infection, and as many as 25% are likely aware of their HIV status but are not receiving medical care for it, Dr. Teshale said at the conference, sponsored by the Foundation for Retrovirology and Human Health.

Among patients who have access to health care and are being treated for HIV, barriers to receiving recommended antiretroviral treatment include the expense of the multidrug cocktails, which can cost more than $10,000 per year. Although private insurance will often cover this expense, patients receiving public health assistance are often placed on waiting lists for the drugs. Finally, some patients choose not to take the antiretroviral medications because of the side effects.

The new estimates, though limited by variations in data collection by states and inconsistencies in the medical records included in the analyses, support previous research demonstrating the unmet need for antiretroviral therapy.

The findings need to be validated by additional research, and the factors contributing to insufficient care for HIV-infected individuals deserve more study.

However, efforts to reduce the scope of the problem should be implemented without waiting for further research, Dr. Teshale said. These include increasing individuals' awareness of their HIV status, providing more methods for linking at-risk individuals to prevention and care programs, and encouraging health care providers to prescribe antiretroviral therapy, according to federal guidelines. ■

OraQuick Test Doubles HIV Detection Rates

WASHINGTON — The first 1,000 uses of the OraQuick Advance Rapid HIV-1 Antibody Test in New Jersey identified nearly double the number of HIV-positive patients, compared with the traditional blood tests, Evan Cadoff, M.D., wrote in a poster presented at the annual meeting of the American College of Preventive Medicine.

However, the data represent rates of seropositivity, not necessarily new infections, wrote Dr. Cadoff of the University of Medicine and Dentistry of New Jersey.

The test requires an oral fluid sample and gives results in 20-40 minutes. Rapid testing in New Jersey began in November 2003 at publicly funded counseling and test sites. After the first 1,000 results, the seropositive rate rose to 4.72%, almost double the 2.36% seropositive rate recorded with traditional testing in the previous year.

Overall, 63% of the people who tested positive had not been diagnosed with HIV. However, whether the numbers represent improved detection rates in previously targeted at-risk populations or new groups of patients who previously went untested remains uncertain, the investigators noted.

—Heidi Splete