

HIV Drugs in Breast Milk May Help At-Risk Babies

BY DIANA MAHONEY
New England Bureau

BOSTON — High levels of antiretroviral drugs measured in the breast milk of HIV-positive mothers and in the blood of their breast-fed infants could protect against transmission of the virus from mother to baby, Roger L. Shapiro, M.D., said at the annual meeting of the Infectious Diseases Society of America.

His study's "surprising" findings also suggest that it may not be necessary to prophylactically treat infants of infected mothers directly, provided the at-risk babies are getting therapeutic doses of the highly active antiretroviral drugs from their mothers' milk, reported Dr. Shapiro of the Harvard School of Public Health in Boston.

It is standard practice for physicians to advise HIV-positive women to take antiretroviral drugs while pregnant and during childbirth to prevent transmission of the virus to their babies. The babies themselves are also routinely treated with daily doses of an antiretroviral drug such as zidovudine (AZT) for up to a month, sometimes in combination with a single dose of nevirapine at birth, Dr. Shapiro said.

Breast-feeding is typically not recom-

mended for infected mothers, however, because as many as one in eight babies born to women with HIV/AIDS acquires the virus during breast-feeding, he said.

Because formula feeding is not a reasonable option for some women, particularly those in developing countries with limited access to infant formula and clean water, researchers worldwide have been investigating options for preventing transmission of HIV during breast-feeding. Toward this end, Dr. Shapiro and his colleagues at Harvard sought to determine what, if any, therapeutic or protective effect maternal antiretroviral therapy could have on breast-fed infants.

The investigation, which was part of a larger transmission-prevention study funded by the National Institutes of Health, included 20 HIV-positive breast-feeding mothers with full-blown AIDS in Botswana. All of the women had been placed on an antiretroviral combination drug regimen comprising nevirapine (NVP), lamivudine (3TC), and AZT. Their

infants also received a single dose of nevirapine and oral AZT during the course of breast-feeding.

Laboratory testing at 2 and 5 months after birth showed high levels of all three drugs in the mothers' breast milk samples. Blood tests showed that the infants might have achieved high enough levels of NVP and possibly 3TC and AZT from breast-feeding to prevent transmission of the virus through breast milk, said Dr. Shapiro. "What was surprising about what we found is that the infants of mothers who were receiving [the drug combination] had higher than expected levels" of NVP and 3TC, he said.

At 971 ng/mL, the median serum concentration of NVP was 36-360 times higher than the IC50 (the level that inhibits 50% viral growth in vitro) for that drug. The 3TC levels were 0.8-47 times the IC50 levels, which "was higher than we expected it to be, but still lower than what we want the target concentrations for prophylaxis to be," said Dr. Shapiro. The serum levels of

AZT transmitted through breast milk could not be determined because the infants were receiving that drug directly.

The observed effect could represent a "two-for-one" deal, he said. "It's believed that maternal antiretroviral therapy decreases the risk of transmission to breast-feeding infants by reducing virus levels in the mother's breast milk. It now appears possible the transmission risk may be reduced by breast-feeding because the infants are getting enough of the drugs directly," he said.

Additional studies are needed to determine whether exposure to the AIDS medications through breast milk alone will be risky for infants who have acquired HIV in utero or during birth. "It may be that exposure to lower-than-therapeutic drug levels could cause resistance mutations to develop, potentially compromising future treatment," said Dr. Shapiro. It also is possible that exposed infants could develop toxicities from the antiretroviral drugs, including lowered blood counts, liver problems, or allergic reactions, he noted.

Dr. Shapiro reported that neither he nor his coinvestigators have a financial interest in the manufacturers of the drugs used in the study. ■

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Lymphogranuloma Venereum Poised to Make Comeback in Men

BY ROBERT FINN
San Francisco Bureau

SAN FRANCISCO — Lymphogranuloma venereum, once common among gay men but rare in the United States for the last decade, may be poised to make a comeback, Gail Bolan, M.D., said at a meeting on HIV management sponsored by the University of California, San Francisco.

The Centers for Disease Control and Prevention recently reported on an outbreak of lymphogranuloma venereum (LGV) among men who have sex with men in the Netherlands (MMWR 2004;53:985-8).

There has been one confirmed U.S. case of the opportunistic infection out of Emory University (Atlanta), and the New York City Department of Health and Mental Hygiene announced the discovery of two others in New York in February. Another possible case from San Francisco has not yet been confirmed, said Dr. Bolan, chief of the sexually transmitted disease control branch of the California Department of Health Services, in Berkeley.

LGV is common in Africa, Southeast Asia, Central and South America, and the Caribbean but has been rare in developed countries in recent years.

The outbreak in the Netherlands included 92 confirmed cases during an 18-month period in 2003 and 2004, compared with an average of 5 cases annually during previous years.

Chlamydia trachomatis is the causative organism in LGV, but only certain serotypes are involved, not the ones responsible for garden-variety chlamydia infections. The classic presentation includes inguinal adenopathy (buboes). These start as painless papules, nodules, or ulcers that resolve spontaneously.

In the outbreak in the Netherlands, however, only one of the patients had a genital bubo. Most patients presented with GI symptoms, including bloody proctitis and mucopurulent anal discharge.

Other symptoms in this presentation, which is sometimes mistaken for Crohn's disease, include bleeding, tenesmus, fever, and constitutional symptoms. Anoscopy shows diffuse friability and discrete ulcerations.

The destructive granulomatous process can cause complications such as scarring, genital elephantiasis, fistulas, rectal strictures, and perianal abscesses.

The CDC's study of the Netherlands outbreak identified several risk factors, including unprotected receptive anal intercourse or fisting; casual-sex gath-

erings; and other concurrent STDs. Of the patients whose HIV status was known, 77% were HIV-positive.

A positive chlamydia test from the mucosal site or a bubo aspirate is necessary to confirm the diagnosis. For rectal lesions, it's better to get a swab under control by anoscopy than by taking a blind rectal swab, Dr. Bolan said.

But the available serologic tests are poorly standardized, she added. It's better, when possible, to confirm the presence of the specific LGV serotype by polymerase chain reaction sequencing or tissue culture and monoclonal antibodies.

The CDC's treatment guidelines recommend oral doxycycline, 100 mg b.i.d., for 21 days. Oral erythromycin, 500 mg four times daily for 21 days, is an alternative. Some experts also recommend oral azithromycin, 1 g weekly for 3 weeks, but this has never been formally evaluated.

Partners of affected patients (within the 30 days prior to the onset of symptoms) need evaluation. If these individuals are asymptomatic, they should be treated with doxycycline, 100 mg b.i.d., for 7 days, or with a single dose of 1 g of azithromycin.

Dr. Bolan stated that she has no financial relationships relevant to her presentation. ■

Treat Pregnant HIV Patients Even if Asymptomatic

HOUSTON — Pregnant women should be treated for human immunodeficiency virus infections even if they are asymptomatic with normal CD4 counts and have a low viral load, said Hunter A. Hammill, M.D.

Pregnancy itself does not affect the course of the disease. The woman's condition will not become worse, but the baby is at risk, he said at a conference on vulvovaginal diseases sponsored by Baylor College of Medicine.

"Optimum therapy should be offered to minimize vertical transmission to the infant," said Dr. Hammill of the college.

Infants of HIV-positive mothers will test positive for 6-8 weeks after birth. Without treatment, about one-third will be infected and remain positive. Breast-feeding can increase the vertical infection rate by 20%.

Studies summarized by Dr. Hammill have reported transmission rates of less than 1%-13% when various therapies were tested in pregnant women. "My series is now down to less than a tenth of a percent vertical transmission with vaginal delivery when treating with HAART [Highly Active Antiretroviral Therapy]," he said.

Dr. Hammill urged practi-

tioners to get up to date on new antiretroviral treatments. About 30 different treatment options are available, he said, and these are typically given in three-drug combinations.

Patients have to be monitored as some agents will have side effects. Among these, he listed unusual dreams, yellow skin, liver and renal toxicities, and nausea lasting several weeks until the patient's body adapts.

Some HAART drugs do pose special risks. He cited rash and hepatic toxicity with nevirapine (Viramune), hyperglycemia with protease inhibitors, and mitochondrial toxicity with nucleoside analogs.

His greatest concern is efavirenz (Sustiva), which is sometimes prescribed because it is considered safe in pregnancy. Because one animal study has linked it to monkey anencephaly, Dr. Hammill said he switches his patients to another drug. "If you see an HIV patient on Sustiva, please think of birth control."

Dr. Hammill also urged physicians to provide intensive counseling about the importance of complying with treatment. "The big thing in AIDS is adherence. If you don't take the drug, it doesn't work."

—Jane Salodof MacNeil