

Resistance After Single-Dose Nevirapine Is Time Related

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SAN FRANCISCO — Pregnant women given a single dose of nevirapine during pregnancy to prevent vertical transmission of HIV were more likely to fail their own HIV treatment if it was started within 6 months of taking the nevirapine, Shahin Lockman, M.D., reported.

The randomized study of 218 women and 30 infants in Botswana found that, for the cohorts as a whole, the peripartum nevirapine dose led to higher rates of virologic failure in women and their infants, compared with women who received a peripartum dose of placebo and their infants, she said at the annual meeting of the Infectious Diseases Society of America.

Most resource-poor nations include nevirapine in their first-line treatment regimens for women and infants. More than 500,000 women each year are believed to receive single-dose nevirapine during pregnancy. This is a simple and affordable measure that halves the risk of vertical transmission, but previous data suggest that it can cause resistance to subsequent nevirapine therapy in 25%-70% of women and 40%-90% of infants, said Dr. Lockman of Brigham and Women's Hospital, Boston.

The current data came from the Mashi study of 12,000 HIV-infected women and 491 infants randomized to receive a single peripartum dose of nevirapine or placebo plus a short course of zidovudine starting at 34 weeks' gestation. Infants received 1 month of zidovudine if formula-fed or 6 months of zidovudine if breast-fed.

Women who developed an AIDS-defining illness or whose CD4 counts fell below 200 cells/mm³ during or after delivery were offered combination antiretroviral therapy with nevirapine, zidovudine, and lamivudine.

Of the 218 women who started antiretroviral therapy and had adequate follow-up, 18% of 112 who previously received single-dose nevirapine and 5% of 106 who previously received single-dose

placebo developed virologic failure by 6 months after starting the combination antiretroviral regimen.

At 12 months, 20% of the nevirapine group and 10% of the placebo group had developed virologic failure, defined as an HIV RNA load greater than 400 copies/mL. At 24 months, 28% of the nevirapine group and 11% of the placebo group had failed combination therapy. All differences were statistically significant.

Further analysis showed that the failures occurred in women who started their antiretroviral therapy within 6 months of receiving the single dose of nevirapine but not in women whose therapy began at least 6 months after the single nevirapine dose.

Of the 60 women who started combination antiretroviral therapy within 6 months of the peripartum dose, 42% of the 24 women in the nevirapine group and none of the 36 women in the placebo group developed virologic failure by 6 months. Virologic failure was seen at 12 and 24 months in 46% of the nevirapine group and 3% of the placebo group. All differences were highly significant.

Virologic failure rates did not differ significantly between the nevirapine and placebo groups in the 158 women who started combination therapy at least 6 months after the peripartum dose.

A total of 30 HIV-infected infants were given the same combination antiretroviral therapy. Of 15 infants whose mothers got single-dose nevirapine during pregnancy, 10 developed virologic failure during 2 years of follow-up, compared with 2 of 15 infants in the placebo group. Two infants in the nevirapine group and three in the placebo group died.

Infants in the nevirapine group showed a smaller increase in CD4 counts on combination therapy vs. those in the placebo group. For mothers, the CD4 counts did not differ significantly between groups.

Only nevirapine exposure predicted the risk of virologic failure in women and infants. Other factors such as maternal age, clinic location, or infant feeding strategy (breast vs. formula) were not predictors. ■

Severe Disease in Pregnancy Typical of Hepatitis E Infection

SAN FRANCISCO — Acute hepatitis E is rare in the United States, but an increasing number of travelers to India and China could make the disease more common here, Gregory L. Armstrong, M.D., said at the annual meeting of the Infectious Diseases Society of America.

Most U.S. patients with hepatitis E have traveled to countries where the virus is endemic.

Although hepatitis E shares many commonalities with hepatitis A, it has a number of unique characteristics—most notably severe disease during pregnancy, said Dr. Armstrong of the Centers for Disease Control and Prevention, Atlanta.

Clinically, acute hepatitis E is indistinguishable from acute hepatitis A, B, or C. Its clinical spectrum is highly variable, ranging from asymptomatic infection to fulminant hepatic failure. Hepatitis E disease is most severe when it is acquired in the third trimester of pregnancy, he said. The reasons for poor outcomes in pregnancy are unclear.

About half of pregnant women who acquire the virus during the third trimester remain asymptomatic. In the resource-poor settings where these cases usually occur, the other half of third-trimester infections result in acute hepatitis E, with fulminant hepatic failure in about a third

and preterm delivery in about two-thirds of pregnant women with acute hepatitis E. Clinical outcome in infants also is variable, ranging from asymptomatic infection to hepatic necrosis.

Commercially available serologic assays to diagnose hepatitis E are not very sensitive or specific, and results must be interpreted based on the pretest probability of

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hepatitis E infection, he said. A better serologic assay developed by the National Institutes of Health is not commercially available. Viral RNA testing is even more accurate, but also is available only for research.

There is no specific antiviral therapy for hepatitis E; treatment is supportive care. There are no published data on the benefits of early delivery of the child in cases of acute hepatitis E during pregnancy.

Results of a phase II/III trial of a hepatitis E vaccine developed by the National Institutes of Health should be released soon. "Most people who work in this field feel that this vaccine is likely to be very effective," Dr. Armstrong said.

There have been five domestically acquired cases of acute hepatitis E in addition to travel-related cases, he added. All five cases involved a viral genotype found in almost all U.S. pigs. Workers in the swine industry also have higher rates of hepatitis E antibodies. ■

Universal Culture-Based Screening Reduces GBS in Term Infants

SAN FRANCISCO — The incidence of early-onset group B streptococcal disease fell significantly in term infants after 2002 recommendations called for culture-based screening of all pregnant women, Matthew Eberly, M.D., said.

A retrospective review of all 736,984 live births at U.S. Department of Defense hospitals from October 1992 to December 2004 found 828 term infants and 128 preterm infants who developed group B streptococcal (GBS) disease in the first 7 days of life, he said in a poster presentation at the annual meeting of the Infectious Diseases Society of America.

Dr. Eberly and his associates at the San Antonio Military Pediatric Center divided these births into three periods: the years before the Centers for Disease Control and Prevention's 1997 recommendations to give antibiotics to women who had either clinical high-risk factors for GBS colonization or culture results showing colonization; 1997 through November 2002, before the CDC's 2002 recommendation to screen all women via vaginal-rectal culture at 35-37 weeks' gestation; and December 2002 to the present (the period since the recommendation for universal culture-

based GBS screening and treatment).

The incidence of early-onset GBS disease in all infants fell from a rate of 2.18 per 1,000 live births before 1997, to 0.84 per 1,000 through November 2002, and to 0.70 per 1,000 in the third period. The differences were significant. "The new guidelines since 2002 are more effective in preventing early-onset GBS disease," he said.

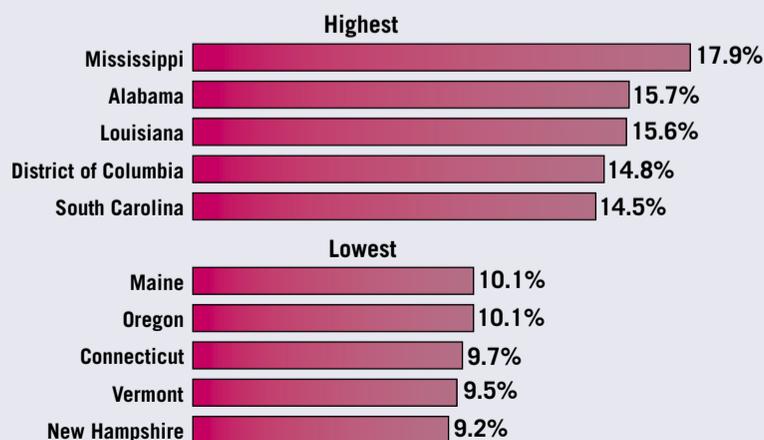
The universal culture-based screening strategy did not reduce early-onset GBS infections in preterm infants, since cultures are not obtained until about 36 weeks' gestation.

As the incidence of early-onset GBS in term infants fell from 2.08 per 1,000, to 0.76 per 1,000, to 0.50 per 1,000 over time, the proportion of preterm infants among those with early-onset GBS disease increased from 10% to 15% to 33% over the three periods studied, he noted.

Of the 78 cases of early-onset GBS disease since the 2002 guidelines were issued, 26 occurred in preterm infants. Twelve weighed less than 1,000 g at birth, and 14 were delivered before 30 weeks' gestation. "These are the extremely low-birth-weight infants" who are most likely to develop early-onset GBS disease under the current strategy, Dr. Eberly said. ■

DATA WATCH

Live Births That Were Preterm in 2003



Notes: Preterm defined as <37 weeks' gestation. Based on final natality data from the National Center for Health Statistics.

Source: March of Dimes Perinatal Data Center