HIV DIAGNOSIS

The Rapid Diagnosis of HIV-1 Infection in Mothers in Puerto Rico: a Crucial Testing Strategy for Maximal Reduction of Perinatal Transmission

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This study was designed to evaluate early post partum rapid HIV testing of infants as surrogates for their mothers. In a screening of 971 infants whose mother's HIV-1 status was not known at delivery, 22 (= 2.26 %) were found positive for antibodies by ELISA. Five were new cases and two (40%) were from transmitting mothers. This is in contrast with the UPR Women and Infants Transmission Study (UPR WITS) in which of 186 HIV-1 infected mothers none were transmitters. These were selected among thousands screened for anti-HIV-1 antibodies over a period of almost 5 years studied (September, 1996 through August, 2001). These results clearly indicate that all mothers at delivery should have a rapid test to determine their HIV-1 status to allow in the positive cases rapid intervention strategies to prevent perinatal transmission. *Key words: HIV-1, Rapid test*

Protection against perinatal HIV transmission became a reality in 1994, when Pediatrics AIDS Clinical Trials Group (PACTG) completed Protocol 076. This study demonstrated that a three-part zidovudine (ZDV) regimen administered during pregnancy, intrapartum, and to the neonate reduced the risk of vertical transmission from 25.5% in the placebo group to 8.3% in the ZDV group. Thirteen percent of the children in that study were from Puerto Rico (1). Implementation of this finding and the use of more aggressive therapies have resulted in substantial declines in perinatal transmission in the United States and industrialized countries. At present, perinatal transmission in the United States is 5% or less (2,3).

In San Juan, Puerto Rico the prevalence of HIV infection among pregnant women is higher than among childbearing women in the United States (4). As of 31 July, 2001 Puerto Rico has reported 26,242 cases of HIV-1/AIDS, of which 395 were pediatric cases and 299 were in children under 5 years of age (5). In 1998, the Centers for Disease Control and Prevention reported 12 pediatric cases from Puerto Rico (6).

In contrast, the Puerto Rico site for the Women and Infants Transmission Study (WITS) found no cases of perinatal transmission in the past 5 years. The WITS is a prospective epidemiological study of the natural history of HIV infection in pregnant women and their infants carried out at obstetric/gynecologic and pediatric clinics in San Juan, University of Puerto Rico (UPR), Boston, Manhattan, Brooklyn, Chicago, and Houston (7). The UPR WITS site engages in a more aggressive risk-reduction intervention than other local clinics.

Materials and Methods

Peripheral blood samples were obtained from 973 infants at the University of Puerto Rico University Hospital in the Puerto Rico Medical Center in San Juan between August, 1998 and August, 2000. The samples were from infants born of women of uncertain HIV-1 status presenting at the UPR obstetric delivery room with no evidence of HIV-1 screening tests during pregnancy. Pre-HIV test counseling with HIV-1 screening was made available for those infants

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whose mothers agreed to participate and signed informed consent forms. Only 2 of 973 delivering mothers declined, for a 0.2 % refusal rate. Blood samples were sent to an ACTG certified laboratory in the UPR generally within 24-48 hours of birth. The serum collected from the samples was tested, using an ELISA for antibodies to HIV-1, commonly within one day of receipt of specimens.

The ELISA test used from August, 1998 through December, 1999 was the Abbott (Abbott Park, IL) Human Immunodeficiency Virus Type 1 HIVAB HIV-1 EIA. A total of 474 serum samples were examined using this test. Afterwards, the third generation Abbott HIV1/2 EIA assay was used, viz: Human Immunodeficiency Virus Types 1 and 2: (*E. coli*, *B. megaterium* Recombinant Antigen) HIVABTM HIV-1/HIV-2 (rDNA) EIA. Those found positive were verified using a second ELISA and further confirmed using a Western Blot using the Human Immunodeficiency Virus Type 1 Cambridge Biotech (Rockville, MD) HIV-1 Western Blot Kit for Detection of Antibodies to HIV-1. The UPR ACTG laboratory has been a participant since 1992 in the Centers for Disease Control and Prevention Model Performance Evaluation Program for antibodies to HIV-1 by ELISA (Abbott) and Western Blot (Cambridge Biotech).

Results

Of the 971 pediatric peripheral blood serum samples tested, 22 (2.26 %) were positive by ELISA. After these were identified, a more rigorous query showed that 17 of these infants were from mothers who had been in fact tested and found positive for anti-HIV-1 antibodies. The other 5 were new cases that were found through this screening mechanism. Significantly, two of the five were born of transmitting mothers. Moreover, these two infected infants were born by vaginal delivery. Within one month of birth one of the two infants had over 750,000 HIV-1 copies/ml of serum and the other had 25,000 copies/ml as measured by RNA (Roche) PCR.

Mothers and their infants positive to our screen were recalled for confirmatory testing and viral burden. The two transmitting mothers and their infants were begun on treatment and HIV-1 follow-up.

These findings contrast with the multi-center Women and Infants Transmission Study where at the UPR site no infected babies have been recorded since September 1996. Since then and through August, 2001, 186 HIV-1 infected mothers have delivered virus-free babies. All positive pregnant women were enrolled in the WITS project and received prenatal care. None of these were transmitting mothers and our study has not had a single infected infant through mother-infant transmission during the past 5 years.

Discussion

Our studies reported herein support the implementation of a policy that rapid testing for antibodies to HIV-1 should be mandatory for all women whose HIV-1 status is unknown at delivery. This is important in order to maximally suppress all possible transmission of HIV from mother to her infant because unprotected delivery can lead to high transmission of HIV-1 from mother to their infants. Moreover, HIV-1 infected women who are pregnant and whose first contact with health care comes at delivery might be diagnosed immediately using rapid tests, thereby increasing the chance for drugs to be administered right away to their infants (8,9). This would result in decreased perinatal transmission of HIV-1 and obvious improved health care. Failure to implement rapid testing could lead to potentially staggering economic consequences with the cost of patient care of infected infants. Thus, rapid testing should be implemented in Puerto Rico routinely as a strategy for significantly reduced perinatal transmission of HIV-1 from mothers to their infants.

The U.S. Food and Drug Administration has recently approved the Murex Single-Use Diagnostic System (SUDS; Abbott Laboratories). In this test HIV antigen is a suspension of p24 Gag lysate and a synthetic envelope protein. The test consists of a subjective determination by examining the blue color produced in three circles on the bottom of the test cartridge. A positive test can result in several shades of blue, which are graded from 1+ to 4+. A recent prospective study in lower Michigan found that of 888 SUDS-tested sera, 875 (98.4 %) were both SUDS and Abbott HIV1/2 EIA negative and 5 (0.6 %) were SUDS, EIA, and Western Blot positive (10). This SUDS test which offers on-site availability, apparent simplicity and rapid (30-60 min.) turnaround time, performs as well as the traditional EIA as a screen in laboratories with experienced personnel (10). However, use of rapid test such as SUDS needs to be validated in each specific geographic zone to ensure that the test is adequately sensitive to circulating HIV-1 subtypes. Moreover, another study found the SUDS test to give false-positive results in 5 of 69 seronegative specimens for a 93 % specificity (11). Nevertheless rapid testing is so important as a strategy for rapid intervention to decrease perinatal transmission that the CDC is implementing a "Mother-Infant Rapid Intervention At Delivery (MIRIAD) Study" in five U.S. metropolitan areas to test the feasibility of offering rapid testing to women presenting late in pregnancy or at delivery with undocumented HIV status (12). Puerto Rico should do the same.

Resumen

Se diseñó este estudio para utilizar pruebas rápidas para la detección de anticuerpos contra el VIH en niños para identificar infección en sus respectivas mamás. El cernimiento se realizó en 971 infantes cuyas madres desconocían su estatus de infección con VIH al momento del parto. Se identificaron 22 casos positivos para anticuerpos de VIH. De estos 22, se encontró que 5 fueron identificados como casos nuevos y 2 de los 5 (40%) fueron madres que trasmitían la infección a sus bebés (madres transmisoras). Este hallazgo contrasta con los resultados obtenidos en el estudio "WITS" (Women and Infants Transmission Study) de la Universidad de Puerto Rico, Recinto de Ciencias Médicas, en el cual ninguno de los 186 casos de mamás infectadas con VIH-1 se transmitió el virus a sus infantes. Estos fueron seleccionados entre miles a los cuales se les realizó una prueba de anticuerpos para VIH-1, durante un período de casi 5 años que comprendió el estudio (Septiembre 1996-Agosto 2001). Estos resultados claramente indican que todas las mamás deben ser sometidas al momento del parto a una prueba rápida de detección para VIH-1, lo que permitirá en los casos positivos una intervención rápida y el uso de estrategias para prevenir la transmisión perinatal.

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