

Diagnosis of Perinatal Transmission of HIV-1 Infection by HIV DNA PCR

Ira Shah

Abstract

To determine the sensitivity and specificity of HIV DNA PCR (Qualitative) at various age groups to detect or rule out HIV infection in infants born to HIV infected mothers. Pediatric and perinatal HIV clinic in a tertiary pediatric hospital. Sixteen infants born to HIV positive mother enrolled in the prevention of mother to child transmission of HIV at our center were tested for HIV infection by HIV DNA PCR at 1.5 months, 3 months, 5.5 months and/or 7 months of age. Their HIV status was confirmed by an HIV ELISA test at 18 months of age by 2 different ELISA kits. Eight patients (50%) had a negative HIV DNA PCR whereas 8 patients (50%) had a positive DNA PCR of which 6 patients (75%) had a false positive HIV DNA PCR and no false negative DNA PCR. Thus, the sensitivity of HIV DNA PCR was 100% and specificity was 57.1% with a total efficiency of the test being 62.5%. The efficiency of HIV DNA PCR at 1.5 months of age was 50%, at 3 months of age 42.9%, at 5.5 months of age 60% and at 7 months of age was 100%. HIV DNA PCR has a high sensitivity but low specificity to diagnose HIV infection in infants less than 7 months of age. Hence, the results of the test have to be interpreted with caution in infants born to HIV positive mothers.

Keyword

HIV DNA PCR, Perinatal HIV.

Introduction

The predominant mode of transmission of HIV in children is through the vertical route (1). Without intervention, the mother to child transmission of HIV ranges from 15 to 40% (2,3). Perinatal administration of zidovudine has shown to substantially reduce vertical HIV transmission (4,5). Infants infected with HIV must be diagnosed as rapidly as possible to ensure the early institution of therapy to limit HIV related morbidity and to prevent opportunistic infections. In 1989, Science selected the polymerase chain reaction (PCR) as the major scientific development of the year (6). The potential utility of DNA PCR for the diagnosis of vertical HIV infection soon became readily apparent as passively transferred maternal antibodies make HIV serological

tests uninformative for diagnosis in the first year of life; and HIV culture is slow, labor-intensive and expensive. HIV DNA PCR has been found to be highly sensitive and specific for early diagnosis of pediatric HIV infection (7,8). However, false positive and false negative results with HIV DNA PCR may occur (9). Thus, we undertook this study to determine the sensitivity and specificity of HIV DNA PCR at different age groups to detect or rule out HIV infection in infants born to HIV infected mothers enrolled in our perinatal prevention programme.

Material and Methods

All pregnant women were screened for HIV infection as part of the prevention of mother to child transmission of HIV at our center. All pregnant women

From the Pediatric HIV Clinic, B.J.Wadia Hospital for Children, Mumbai, 400 012.

Correspondence to : Dr. Ira Shah, Incharge, Pediatric HIV Clinic, B J Wadia Hospital for Children, Mumbai, 400 012.

infected with HIV were treated with antenatal zidovudine (100 mg five times a day) starting from 14 weeks of gestation onwards and underwent an elective LSCS delivery. All infants born to these mothers were treated with zidovudine (2 mg/kg/dose 4 times a day x 6 weeks) and were not given breast feeds. These infants were monitored regularly and HIV ELISA tests were done at 18 months using 2 different ELISA kits (HIV DETECT-MC and HIV CheX). A definitive diagnosis of HIV infectivity was made if the infant test was positive on at least 2 occasions. Due to the high cost of HIV DNA PCR, parents who could afford the test or in infants with clinical suspicion of the disease, HIV DNA PCR was done at 1.5 months, 3 months, 5.5 months and/or 7 months of age and their HIV status was reconfirmed by an HIV ELISA test at 18 months of age. The overall sensitivity and specificity of HIV DNA PCR as compared to HIV ELISA test was determined. The efficiency of HIV DNA PCR at various age groups was determined using the ANALYSE-IT software (version 1.7).

Results

Sixteen infants born to HIV infected mothers in the perinatal prevention programme were enrolled in the study. Eight patients (50%) were negative for HIV infection by HIV DNA PCR and eight patients were positive by HIV DNA PCR. Two patients were positive for HIV by HIV ELISA tests and died due to AIDS subsequently. Six patients (75%) were false positive by HIV DNA PCR when subsequently tested and reconfirmed by HIV ELISA test at 18 months of age (Table 1). Thus, the overall sensitivity of HIV DNA PCR was 100% [95% CI = 15.8% to 100%] and specificity was 57.1% [95% CI = 28.9% to 82.3%] with a positive predictive value of 25% and negative predictive value of 100% and efficiency of 62.5%. The efficiency of HIV DNA PCR at 1.5 months, 3 months, 5.5 months and 7 months of age was 50%, 42.9%, 60% and 100% respectively as shown in Table 2.

Table 1. Efficiency of HIV DNA PCR as compared to HIV ELISA

HIV DNA PCR	HIV ELISA TETS		
	Positive	Negative	Total
Positive	2(25%)	6(75%)	8
Negative	0	8(100%)	8
Total	2	14	16

Table. 2 Efficiency of HIV DNA PCR at different age group

HIV DNA PCR	(n)	True +ve	True -ve	False +ve	False -ve	Sensitivity	Specificity	Efficiency
1.5 months	2	0	1	1	0	-	50% [95%CI= to 98.7%]	50%
3 months	7	1	2	4	0	100%	33.3%	42.9%
5.5 months	5	0	3	2	0	-	60%	60%
7 months	3	1	2	0	0	100% [95%CI= 2.5% to 100%]	100% [95%CI= 15.8 to 100%]	100%

Discussion

In our study we had a very high incidence of false positive HIV DNA PCR (75%) especially in younger infants though there were no patients with a false negative HIV DNA PCR. A meta-analysis by Owens *et al.* of 32 studies published between 1988 and 1994 to evaluate the sensitivity and specificity of DNA PCR for the diagnosis of vertical HIV infection supports that sensitivity and specificity are lower in neonates as compared to older infants (10). As also found in our study, they state that HIV DNA PCR has a low positive predictive value; however negative tests are informative. Thus a negative test may almost certainly rule out HIV infection in an infant born to an HIV infected mother but a positive test still does not confirm HIV infectivity in an infant. The use of quality-controlled commercial DNA PCR kits with a common algorithm for performing the procedure and interpreting the results, in conjunction with an external quality assurance program, can help to ensure accurate results (11,12). However, false positive and false negative results may occur. Infact Busch *et al* have

reported a very high rate (18.5%) of false positive detection by HIV DNA PCR in uninfected individuals (13). There have also been reports of clearance of HIV infection in perinatally infected children (14,15). In a study by Roques et al 12 patients (6.7%) cleared their HIV infection during first year of life. However 5 of these patients were determined to be HIV positive only by an HIV DNA PCR suggesting that though seroconversion may be a possibility, chances of false positive PCR are high. Bakshi SS et al have also reported 3 HIV-1 exposed infants who had HIV DNA PCR positive repeatedly and finally seroconverted to an HIV negative status (16). One of the reasons stated for the false positive results is contamination and strict quality control would increase the reliability of HIV DNA PCR.

Thus, one can conclude that though HIV DNA PCR is a very sensitive tool, it is not very specific for diagnosing HIV infection in infants born to HIV infected mothers and its result has to be interpreted with caution in vertical transmission of HIV.

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