

Single dose Nevirapine to the mother and baby in the prevention of perinatal transmission of HIV infection



Medical Science

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Dr.B.K.Srikanth	Assistant Professor, Department of Paediatrics, VIMS, Bellary, Karnataka, India
Dr.Rajesh.D	Assistant Professor, Department of Paediatrics, VIMS, Bellary, Karnataka, India
Dr.Sanjay Sajjan	Senior Resident, Department of Paediatrics, VIMS, Bellary, Karnataka, India
Dr.Ramesh.K	Associate Professor, Department of Community Medicine, VIMS, Bellary, Karnataka, India

ABSTRACT

In India, perinatal HIV transmission, even after treatment, accounts for 5.4 per cent of HIV cases. This study was conducted in the 3 hospitals attached to J.J.M medical college, Davangere to know the vertical transmission rate of infection among neonates born to HIV positive mothers after giving single dose 200 mg Nevirapine tablet to the mother during labour and 2mg/kg body weight to the baby within 72 hours of life. This intervention was done with fond hope and good intension that vertical transmission rate would come down. Further babies were advised appropriate artificial feeds to reduce further risk due to breast feeds. These neonates were followed up periodically for clinical and virologic evaluation and to know the mortality and morbidity. 11 out of 30 babies at 3 months of age were found seropositive. Contradictory to earlier report of effectiveness of Nevirapine, we found in our study that vertical transmission is significantly high.

Introduction:

Human immunodeficiency virus (HIV) may be transmitted from mother to infant during the antepartum, intrapartum, or postpartum period. More than 3,70,000 children were newly infected with HIV in 2009, predominantly through mother-to-child transmission (MTCT) and an estimated 42,000-60,000 pregnant women died because of HIV1

Among the infected children nine out of ten children were infected either during pregnancy, labour and delivery or during breast-feeding. Without treatment, 15-30 per cent children become infected during pregnancy and delivery. India is the third largest population with HIV/AIDS with 2.39 million people living with HIV (adult HIV prevalence 0.31%). Parent-to-child transmission accounts for 5.4 per cent of the newly infected cases³

Pediatric HIV infection has emerged as an important public health problem in industrialized and developing nations. The first children with AIDS were described in 1983. Less than 2 decades later, the global HIV epidemic is having a profound effect on the health and survival of children. Almost all HIV infections among young children are caused by mother-to-child transmission.

Major advance in the understanding of the timing and pathogenesis of perinatal HIV infection have occurred in recent years, raising a new hope for prevention of perinatally acquired HIV infections.

The most dramatic prevention breakthrough occurred in Feb 1994, where the result of pediatric AIDS clinical trials group (PACTG) protocol 076 demonstrated that the risk for MCT could be decreased from 25.5% to 8.3% by treating mothers and neonates with ZDV4.

Most HIV – infected children are born in the developing world, and a crucial challenge is to identify safe and effective interventions that are feasible in countries with the most significant HIV burden.

Because of its high complexity and cost, the 076 regimen has not been implemented in most developing countries. Wide spread implementation of a short – course anti-retroviral drug regimens in the developing world, where most women present late for prenatal care, have limited access to HIV testing and counseling, and depend on breast-feeding to protect infants from early mor-

tality, provides a formidable challenge and a unique opportunity to protect future generations of children from the burden of HIV.

One such short-course anti-retroviral regimen is where nevirapine, a non-nucleoside reverse transcriptase inhibitor, is used which is safe and easy to administer. In addition to its potent antiviral properties, nevirapine remains active in the body for a long time (61-66 hrs half life in the pregnant women and 45-54 hrs in the babies) and is rapidly absorbed and transferred to the fetus in the womb. These properties make it an excellent candidate for therapy to interrupt HIV transmission in intrapartum period. A single dose 200mg PO of nevirapine to the mother during active phase of labour and a single dose 2 mg/kg body wt. nevirapine suspension (50mg/5ml) to the baby within 72 hours has shown MCT rates of 13.1% by 14-16 wks of age⁵.

Methodology:

All the mothers who were admitted for delivery underwent voluntary counselling and after taking the consent from the mother, blood for HIV serology was sent. Our institution, J.J.M. Medical college is recognized by the government for PMTCT (Prevention of Mother to Child Transmission) programme and all the antenatal mothers are counselled by the staff of PMTCT cell who are appointed by the government.

After testing, if the mother is found to be positive, post test one to one counselling was done and after taking the consent, a single dose of 200mg tab of nevirapine is given to the mother during labour which is given under direct observation and to ensure that she does not vomit, the mother was under supervision for an hour. After the delivery of the baby, the baby was resuscitated with universal precautions and a single dose nevirapine suspension in a dose of 2mg/kg body wt. was given to the baby (50mg / 5ml) and the baby was also observed for an hour, to ensure that the baby did not vomit, however in our study none of the babies vomited. The babies were observed till they were discharged from hospital to look for adverse effects of nevirapine, the most common being skin rashes. During the start of our study, there was some difficulty in getting nevirapine suspension and giving nevirapine to the baby was difficult. The hospital pharmacy helped us in preparing appropriate dose for the baby.

The relation between Gravida status, mode of delivery, SES, regional distribution and birth weight of baby with HIV infection was also studied.

All the mothers were asked not to breast feed their babies as it is well known that breast feeding carries an independent risk (15%) of transmission. By asking them not to breast feed, we took an additional responsibility by counseling them regarding maintenance of hygiene and feeding practices. After counseling them to give top feeds, we advised the mother's to feed the child with Clean, undiluted cow's milk with sugar, Clean cup and spoon and Clean hands. We emphasized the point that before every feed, hands should be washed with soap and water. To ensure that the mothers won't breast feed, house visits were made almost every fortnightly.

Regular followup of babies born to HIV seropositive women was done with special emphasis on nutritional status, opportunistic infections and psychosocial aspects.

Initially during the start of our study, we wanted to followup the babies regularly upto 18 months of age and the find out the HIV state of the baby by doing serology. But with the timely help and support from Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore, we were able to get HIV DNA PCR done any time after 3 months of age for the diagnosis of HIV infection in babies. Infants with one positive DNA PCR result were classified as infected.

All the babies were put on syrup co-trimoxazole as chemoprophylaxis against PCP starting from 4 weeks of life to 1 year of age.

During the duration of study which extended from march 2001 to December 2002, complete professional confidentiality was maintained.

Results:

Out of 36 cases which were recruited for the study, 3 babies died in the neonatal period, 2 babies died of gastroenteritis and one case was lost to follow up.

Of the remaining 30 infants followed, 6 completed 18 months, 16 completed 12 months and 8 completed 6 months.

Table.no1: Follow up of 30 HIV Positive (PCR) newborns born to HIV-1 infected mothers

Duration of follow up	No.of cases followed	Seropositivity at the end of follow up
6 months	08	04 (50%)
12 months	16	05 (31.25%)
18 months	06	02 (33.3%)

At the end of the study, 11 (36.6%) babies were infected.

Table no.2: Positivity by virologic assay (PCR) of infants at follow up in relation to maternal obstetric history

Obstetric history	Number of cases	HIV+	HIV-
Gravid I	19	07 (37%)	12 (63%)
Gravid II	07	03 (42%)	04 (58%)
Gravid III	03	01 (33%)	02 (67%)
Gravid IV	01	--	01 (100%)
Total	30	11	19

Seropositivity was high among primigravida mothers and more babies born to primigravida mothers were HIV negative compared to babies to multigravida mothers

Discussion:

HIV-1 transmission from an infected mother to her baby is estimated to be 21-43% in less developed countries, with more than half of transmission probably occurring late in pregnancy or during labour and delivery⁶.

All babies born to HIV seropositive mothers will be seropositive at birth as was the case in our study. This is because maternal IgG antibodies are actively transported across the placenta and may persist for as long as 15-18 months⁷. To confirm the diagnosis below 18 months of age one or more virologic assays which were mentioned earlier should be obtained. One such virologic assay is HIV DNA PCR, which was done in our study. It has a sensitivity of 38% if carried out within 48 hours of life, 93% by 14 days of age, 96% by 4 weeks of age and almost 100% by 6 weeks⁸. If PCR is positive within 48 hours of life then infants are considered to have inutero infection and if PCR test is negative within 48 hours of life but additional virologic testing after 1 week of life is positive then intrapartum HIV infection is considered⁹.

A perinatally HIV exposed infant is determined to be infected with the presence of 2 positive results of HIV virologic assays i.e. PCR/culture from the infants blood at 2 different times¹⁰. In our study babies with one positive HIV DNA PCR any time after three months of age were classified as infected. Overall, PCR assays have the advantage of high sensitivity and specificity because the method involves the amplification of the target gene rather than of the probe signal¹¹, but PCR is highly prone to contamination with nucleic acids, which may cause false – positive reactions, so the performance of this assay requires technical expertise¹². More than half of transmission probably occurs late in pregnancy or during labour and deliver. 10-15% of transmission occurs through breast feeding^{13,14}.

Worldwide, nearly 5,00,000 infants, almost all born in developing countries, are peri-natally infected with HIV-1 each year¹⁵. A clinical trial in the USA and France (PACTG 076) showed that, in the absence of breast feeding, zidovudine given orally 5 times per day to HIV-1 infected pregnant women starting at 14-34 weeks gestation, intravenously during labour, and orally to babies for 6 weeks, lowered the risk for perinatal HIV-1 transmission by two thirds⁴⁴. However this regimen could not be implemented in developing countries like Africa and India, because of the cost and complexity. A number of studies were conducted from then on for developing countries using short course regimens. One such regimen is single dose 200mg tablet of nevirapine given to the mother during labour and single dose 2mg/kg body weight nevirapine suspension (50mg/5ml) to the baby within 72 hours which showed a 50% reduction in the transmission with breast feeding continued. This regimen was implemented in the present study but without breast feeding⁵.

The test was done any time after 3 months of age in all the babies included in the study and in them 11 (36.6%) were tested positive for HIV infection.

In our study, most of the mothers were malnourished and presumably have Vit A deficiency though Vit A levels could not be done because of lack of facility, so that might have influenced high transmission rate.

Previous studies have shown that Vit A deficiency in mothers has got some influence on increase in the transmission rates^{16,17}.

In our study, 6 mothers who were tested positive during labour, had children who were around 2 years of age and were tested negative, which means to say that these mothers have acquired HIV infection in the recent past. High viral load in the mothers could be one more possibility of high transmission rates especially if the mother has acquired infection in the recent past.

The probability of In-utero transmission cannot be ruled out. This was also noted in PACTG 316 regimen, where In-utero transmission rate was 53%¹⁸.

Going by our results as compared to the HIVNET 012 study, nevirapine has hardly made any difference in the transmission rates in our study. A serious question whether nevirapine has acted in our patients (mothers) in this part of the world arises out of this study or another question, has nevirapine developed resistance as seen in some earlier studies because of several possible mutations. Here the question of resistance does not arise at all as nevirapine has not been used earlier in this part of the world.

The question of compliance does not arise here at all as the drug was given under direct supervision and was ensured that the mother won't vomit and if she does so within ½ hr after given the drug, NVP tablet was again repeated. In our study no mother vomited after giving the tablet.

In our study, vertical transmission rate, with intervention was 36.6%. Which was quite high compared to the previous study conducted in our institution where the transmission rate was 22.2% and no intervention was made.

Conclusion:

This study indicates in our area HIV transmission probably occurs more often early in pregnancy as vertical transmission rate is 36.6% in spite of nevirapine administration and exclusion of breast feeding. Hence it needs to be tackled by another approach.

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