Original Article

Prevention of Mother to Child Transmission of HIV: Our Experience in South India

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Abstract :

Objectives: To determine the outcomes of various ARV (Anti-Retroviral) prophylactic regimes given to HIV positive pregnant mothers, based on time of presentation, for prevention of vertical transmission. **Methods:** During a four year period, 92 pregnant HIV positive women and their newborn infants received various ARV prophylactic regimes for prevention of vertical transmission. The outcome, in terms of presence of HIV infection in the infants born to these mothers was studied. **Results :** The prevalence of HIV infection in the antenatal group studied was 0.62%. Of the 92 HIV positive pregnant mothers who delivered live babies, 91.3% received ARV prophylaxis or HAART, and 95.6% of the 92 live infants received ARV prophylaxis. The risk of vertical transmission was only 3.3%. **Conclusions:** Judicious PMTCT regimes, even if they appear complex, are possible in the Indian setting, and can result in significant decline of HIV positive children. Duration of treatment and mode of delivery should be based on the time of presentation of the HIV positive pregnant mother.

Key Words: HIV, mother-to-child transmission, vertical transmission, zidovudine, nevirapine, ARV prophylaxis.

Introduction

In the last few years, the feminization of the HIV epidemic in India has resulted in increasing number of monogamous women becoming HIV positive and delivering infected babies. The percentage of HIV cases attributed to mother-to-child transmission had increased almost eightfold from 0.33% in 1999 to 2.8 % in 2004¹, and in 2006 accounts for around 4% of all HIV infections in our country².

Around 27 million births occur every year in India and the adult sero-prevalence of HIV is 0.36%. The risk of HIV transmission in India through vertical transmission is 20% to 45% and this is higher when compared to the Western world because women in underdeveloped and developing countries tend to breast feed their children for prolonged periods of time. Taking an average transmission rate of 30%, this will lead to the birth of around 30,000 HIV infected children every year. HIV infection in children is an important cause of morbidity and mortality. Over a period of time, this increase in mortality and morbidity in children would negate the progress that has been made as reflected by decrease in infant mortality and increase in child survival. It is therefore of paramount importance to integrate PMTCT services into routine antenatal care, as soon as possible.

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Following the efficacy of Zidovudine (ZDV)³, and later of Nevirapine (sd-NVP) in the HIVNET 012 study, in reducing vertical transmission, various combinations of ARV prophylaxis have been studied to further reduce this transmission. These include provision of long³ and short^{4,5,6} courses of Zidovudine for mother and child, single doses of Nevirapine⁴ for mother and child, combinations of ZDV and sd-NVP⁷, and HAART (Highly Active Anti-Retroviral Therapy) when the mothers require it for their own health.

In this study, a group of HIV positive pregnant women were provided with ARV tailored to their need, and the time of their presentation to the antenatal clinic, and the outcomes studied. Though studies using single drugs – ZDV^{1,8,9} or sd-NVP¹, or a combination of ZDV and sd-NVP¹ have been published in India, no studies using all of the combinations as recommended by the World Health Organisation have been published thus far.

Materials and Methods

One hundred and sixteen HIV positive pregnant women identified over a four-year period after voluntary counseling and testing in three urban and two semi-urban antenatal clinics in Bangalore (a high prevalence district), India, were included in this study. These women were given supportive counseling and were also counseled on ARV prophylaxis and mode of delivery. They made informed choices regarding infant feeding to prevent mother to child transmission. ARV prophylaxis was given free of cost to the mother according to the regimes that were recommended (and approved by WHO) at that period in time. These included single drug ZDV, long or short course, depending on whether the mother presented by the 28th week of pregnancy or later. The newborns received ZDV syrup for six weeks. The mother received sd-NVP if she presented after the 36th week of pregnancy or in labor, and so did the newborn. When studies using a combination of ZDV in ante-natal period and sd-NVP⁷ additionally in labor were published, mothers received this combination if they presented early enough, and the newborns were given a combination of sd-NVP and seven days of ZDV syrup as recommended. If the mother received ZDV for less than four weeks or received no drugs at all, the baby was given ZDV for four weeks along with sd-NVP. For mothers who came to labor room in active labor without any antenatal care, a rapid test was done to

detect their HIV status with oral consent and sd-NVP was given for HIV positive women followed by post-test counseling after delivery.

For those mothers who made an informed choice to give artificial formula to the newborn and had safe drinking water and adequate fuel for cooking, vessels needed for infant feeding were recommended and the method was demonstrated to the mother and attendants to ensure safe, hygienic methods of infant feeding. Bottle feeds were not advised. Pediatric HIV testing was done by HIV DNA testing at The Tamil Nadu Dr. M.G.R. Medical University in Chennai at six weeks and four months of age. The PCR tests were confirmed by an ELISA test at 15 months of age where possible.

Results

A total of 14,616 new antenatal women were registered in the participating institutions during the project period. All were counseled and 98% were willing to have the HIV test, of whom, 116 women were HIV positive. Of these, 87 (75%) women were booked (had two or more antenatal checkups) and the remaining 29 (25%) were unbooked (one or no antenatal checkups).

Out of the 116 women identified, 92 had live births. One mother had twins, the first one was a liveborn and the second was a stillbirth. The details of anti-retroviral therapy given to the 92 mothers are shown in Table 1. Five mothers were put on HAART for their own health, and seven women came too late to be given any treatment. This results in 92.4% of the mothers receiving treatment.

Among the 92 live births, 52 of the babies received sd-NVP with ZDV for one week or six weeks, 33 babies received ZDV monotherapy for six weeks, three babies received single dose NVP only and four babies received no treatment - Table 2.

After counseling regarding infant feeding all the mothers opted to give artificial feeds. One mother initially decided to give exclusive breast feeds for her baby, but changed her mind after two days and gave only artificial feeds thereafter.

For the PCR testing, this study has had one of the best follow-ups of 65.2% at six weeks, 40.2% at four months and for the ELISA at 15 months the followup was 25%. All the second PCRs were consistent with the first PCR results. Out of the 60 babies who had PCR testing only two were detected positive

Table 1.
Treatment given to mothers according to GA at registration

Treatment received by mother	Gestational age at registration										Total %	
	12-27 weeks	%	28-36 weeks	%	37 weeks & more	%	Term	%	Post delivery	%		
Sd-NVP Only	1	3.1	3	8.3	9	52.9	2	33.3	0	0	15	16.3
ZDV for less than 30 days	0	0	5	13.9	1	5.9	0	0	1	100.0	7	7.6
ZDV more than 30 days	11	34.4	11	30.6	1	5.9	0	0	0	0	23	25.0
ZDV for less than 30 days and sd-NVP	1	3.1	2	5.6	0	0	0	0	0	0	3	3.3
ZDV for more than 30 days and sd-NVP	18	56.3	13	36.1	1	5.9	0	0	0	0	32	34.8
HAART	1	3.1	1	2.8	2	11.8	1	16.7	0	0	5	5.4
No treatment	0	0	1	2.8	3	17.6	3	50.0	0	0	7	7.6
Total	32	100	36	100	17	100	6	100	1	100	92	100

(3.3% transmission).

The details of the two babies tested positive are presented in Table 3.

Both the mothers of these positive babies had treatment for less than one month in pregnancy. The first mother had 18 days of ZDV monotherapy and received sd-NVP during false labor, five days before delivery. The second mother received only sd-NVP. Both delivered by normal vaginal delivery. The babies received six weeks of treatment, the first baby with ZDV only and the second baby with both sd-NVP and ZDV.

Discussion

Several studies have been conducted to test the efficacy of single and combination drugs to reduce MTCT. Recommendations have kept changing over the last few years. According to the present WHO recommendations, ZDV only, or ZDV with sd-NVP are the two most efficacious drugs in reducing MTCT. ZDV reduces the viral load, and thereby

reduces MTCT3. This efficacy is extended to women with advanced HIV disease, low CD4 counts and prior ZDV therapy³.

The HIVNET 012 trial proved that sd-NVP given to the mother in labor and to the child within 72 hours of birth was also efficacious in reducing PMTCT because of its long half life, rapid oral absorption and rapid transplacental passage. The simplicity, efficacy and low cost make large scale implementation possible even in resource poor settings.

A study showing that a combination of ZDV and NVP was better in reducing transmission than either drug alone was published in 2004⁷. When it was established that single dose NVP resulted in development of resistance, a "tail" of ZDV and LMV for the mother for a week after delivery was found to decrease resistance according to papers presented at the XV International AIDS Conference.

The ideal regime at present is to give ZDV for the mother from 28 weeks of pregnancy, add NVP with

Table 2. Treatment given to babies compared to with mother's treatment

Treatment new born	Treatment received by mother						No treatment	Total
	Sd-NVP	ZDV only for less than 30 days	ZDV only for more than 30 days	Sd-NVP+ZDV for less than 30 days	Sd-NVP+ZDV for more than 30 days	HAART		
Sd- NVP only	3	0	0	0	0	0	0	3
Syr. ZDV only for 4 or 6 wks	2	5	20	1	2	2	1	33
Sd-NVP +syr.	9	1	2	2	30	3	5	52
ZDV for 4 or 6 wks	1	1	1	0	0	0	1	4
Nil	1	1	1	0	0	0	1	4
Total	15	7	23	3	32	5	7	92

Table 3.

Details of HIV positive babies

Characteristics	HIV positive baby 1	HIV positive baby 2
Husband's HIV Status	HIV positive	HIV positive
Registration (weeks)	34	36-38
Drugs (Mother)	ZDV x 18 days + sd-NVP five days prior to delivery (false labor)	sd-NVP only in labor
Drugs (Baby)	ZDV x six wks	sd-NVP+ZDV x six wks

the "tail" in labor and give single dose NVP to the baby along with one week of ZDV syrup. In addition, if the mother does not breast feed her baby, then the risk of transmission is reduced to less than 2%⁷.

Over the four-year period as each variation in regime was recommended, we altered our regimes accordingly so that the woman received the best treatment that was in vogue at the time. We also tailored the regime for each woman based on the time of her presentation and the need. Thus, five women were put on HAART for their own health. Others received short or long courses of ZDV based on the time of their presentation. Yet others received short or long courses of ZDV along with sd-NVP in

labor after 2004, and for mothers who presented later in pregnancy where a minimum of four weeks of ZDV could not be given, sd-NVP was given.

Studies have revealed that the greatest risk of vertical transmission is during labor (50%). Therefore, elective cesarean sections were advocated as a line of treatment to avoid labor and thereby reduce vertical transmission. However later studies revealed that if the mother was on HAART or she had received ZDV from the 28th week of pregnancy (i.e. if she had been on treatment for sufficiently long periods of time) then cesarean section was not absolutely necessary and she could have a normal vaginal delivery. In the study of 1844 HIV positive pregnant women⁷ only 20% of the deliveries were

by cesarean section, and of this 20%, only 28% had elective sections, the other 72% had cesarean section after the onset of labor for obstetric indications, yet the mother to child transmission was 1.9%.

In our study, of the babies who were HIV negative, 22 mothers had had normal vaginal deliveries and 38 had cesarean sections. Both the positive babies belonged to the mothers in the normal vaginal delivery group, and of these two mothers, one had received less than four weeks of ZDV and the other had not received ZDV at all, only sd-NVP in labor. If both these mothers had had elective cesarean sections, the outcomes in the babies may have been different as an elective cesarean section helps to reduce vertical transmission more in mothers who have not had treatment. This is demonstrated in a previous study which showed mother-to-child transmission in women who had ZDV during pregnancy with normal vaginal delivery was 3.3%, compared with transmission in women who had no treatment with an elective caesarean section, 6.8%⁴.

In tailoring our treatment for the pregnant HIV positive pregnant mother based on the time of presentation, mode of delivery should also be given due consideration, and if she is likely to receive less than four weeks of ZDV or only sd-NVP, then such a mother is likely to benefit from an elective cesarean section and should be given that option. Others, who have received four weeks or longer courses of ZDV, could have normal vaginal deliveries and also receive sd-NVP in labor, cesarean section in these cases being reserved only for obstetric indications.

Advocating only sd-NVP as the treatment for reducing vertical transmission has the disadvantage of a 15%-20% chance of mother-to-child transmission, and the possibility of inducing resistance even with a single dose. General seroprevalence of HIV infection in India is low. Pregnant mothers accessing health care services in our country are low. Pregnant HIV positive mothers accessing health care is even lower. Therefore, when a HIV positive pregnant mother does access the health care service, she should be given the best possible treatment available based on the time of her presentation, and every effort should be made to ensure that her child is born negative. Sd-NVP should be the minimum standard available.

This paper shows that complex regimes are feasible

in PMTCT in the Indian setting, and that treatment should be tailored according to the time of her presentation and her need.

Conclusion

Judicious PMTCT regimes, even if they appear complex, are possible in the Indian setting, and can result in significant decline of HIV positive children. Duration of treatment and mode of delivery should be based on the time of presentation of the HIV positive pregnant mother.

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