HIV transmission from mother to child – HAART compared with dual therapy

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To the Editor: There are increasing calls for the use of highly active antiretroviral therapy (HAART) for the prevention of perinatal mother-to-child transmission (PMTCT) of HIV.[1] This approach does not recognise the weaknesses in health systems to implement complex treatment protocols. In addition, the safety of HAART during pregnancy is uncertain and the consequences of stopping HAART if not required outside pregnancy are unknown. If the same PMTCT of HIV could be attained with a simple regimen with proven safety and known adverse drug effects, this would be a better option in most under-resourced countries.[2] The superiority of HAART compared with dual therapy according to World Health Organization (WHO) recommendations for immune-competent women to reduce PMTCT has not been proven.[3]

We aimed to determine whether there is a difference in perinatal HIV transmission on HAART therapy compared with the national dual-therapy regimen. In addition, the relation between CD4 counts and transmission in the dual-therapy group was investigated.

Method

A retrospective case control study was conducted. Files of all HIV-positive women with Delft and Mfuleni addresses, who delivered at Tygerberg Hospital (TBH) between January 2007 and April 2008, were obtained after discharge. The antiretroviral treatment, which could be either HAART or dual therapy, received during pregnancy was recorded, along with the date when dual therapy was commenced. HAART was only commenced if the CD4 count was <250 cells/µl and the gestational age <34 weeks according to the provincial PMTCT guideline used during the study period.[4] The first-line HAART regimen consists of stavudine (d4T), lamivudine (3TC) and nevirapine (NVP).[4,5] Adequate dual therapy was at least 2 weeks of antenatal zidovudine (AZT), intrapartum single-dose (sd) NVP and AZT (300 mg 3-hourly per mouth) as well as sd NVP and AZT for 1 week for the newborn baby.[4] The first CD4 count available was recorded and broken down into <250 and >250 cells/µl. Information regarding the type of delivery and the mother's infant feeding choice was also recorded. Babies of HIV-positive mothers were tested for HIV with DNA PCR (polymerase chain reaction) tests at 14 weeks of age.[4] Fisher's exact test was done to determine whether the difference in transmission between the two groups was significant. The study was approved by the ethics committee of the Faculty of Health Sciences.

Results

A total of 581 HIV-positive women from the defined geographical area delivered babies during the study period. The study group included 73 women on HAART; 508 women received dual therapy; of the latter, 257 (50.6%) were eligible because their dual therapy was regarded as adequate. A control group of 146 patients was randomly selected from the adequate dual therapy group. Of the study group, 62 babies were available for follow-up; 58 (80.8%) had PCRs, 4 mothers declined PCRs, and 11 (15.1%) babies could not be traced. In the control group, 124 newborn babies were available for follow-up; 119 (81.1%) had PCRs, 5 mothers declined PCRs, and 22 (15.1%) babies could not be traced.

The difference in transmission rates in the study (2/58 (3.4%)) and control groups (12/119 (10.1%)) is not significant (p=0.15). The CD4 count in the study group was <250 cells/µl in 56 women (76.7%) and >250 cells/µl in 17. Both women who transmitted HIV to their babies were in the <250 cells/µl group. In the control group, the CD4 count distribution is shown in Table I. The transmission rate of women (Table I) with a CD4 count >250 cells/µl was 6/98 (6.1%) and, if the CD4 count was <250 cells/µl, the transmission rate was 6/21 (28.6%). Transmission rates in the control group according to three CD4 count cut-off values are shown in Table I. The caesarean section rate in the study group was 32.9% (31/73), with 7 elective caesarean sections. In the control group, the rate was 33.3% (56/146) with 8 elective caesarean sections. There was no significant difference regarding elective caesarean sections between the two groups (p=0.3). One mother in the study group, and 3 mothers in the control group, chose exclusive breastfeeding. No information about infant feeding was available for 2 mothers in the study group and 1 in the control group. All the other mothers went home formula-feeding their babies.

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Table I. Transmission rate in the dual-therapy group according to various CD4 count (cells/µl) cut-off values

CD4 group*	*N* (%)	Tested PCR yes (%)	Positives	Transmission rates (%)
<250	21 (14.6)	21 (100)	6	28.6
≥250	123	98 (78)	6	6.1
<350	52 (36.1)	45 (87)	8	17.8
≥350	92	74 (80)	4	5.4
<500	93 (64.6)	77 (83)	10	13.0
≥500	51	42 (82)	2	4.8

*Two of the 146 CD4 counts could not be traced.

Discussion

The study was confined to two high-prevalence geographical areas whose clinics send their PCR tests on babies to the virology laboratory at the Faculty of Health Sciences at TBH. The numbers are small and the results need to be interpreted with the necessary caution. The provincial protocol used a CD4 cut-off for HAART of <200 cells/µl. This was changed to <250 cells/µl in October 2006 by clinicians working at TBH.[4] The proportion of women in the dual-therapy group with adequate therapy (50.6%) compares favourably with what was achieved with the PMTCT programme in the public health sector in Thailand (61.7%).[6] More strict criteria were applied for adequate dual therapy (at least 2 weeks of antenatal AZT) in the index study, according to the recommendation of the provincial health authority. The proportion of babies whose information was available for transmission rates to be determined (80.8% and 81.1% in the study and control group, respectively) is also in accordance with what was found in Thailand (75.8%).[6] Invariably, a proportion of women with CD4 counts of <250 cells/µl will be on dual therapy. The most common reasons are CD4 count results available with a gestational age >34 weeks (too late to commence HAART, according to the 2003 provincial PMTCT protocol), missing appointments at the ARV clinic, defaulting antenatal visits, first contact with health care when in labour, and failing the adherence programme.[4,7]

The high transmission rate (10.1%) in the adequate dual-therapy group is due to a very high transmission rate in the group, with a CD4 count <250 cells/µl (28.6%). A CD4 count of <250 cells/µl seems to be a reasonable cut-off for initiation of HAART as the transmission rates at higher counts do not improve markedly (Table I). The proportion of women who will require HAART with a CD4 cut-off of <350 cells/µl will be more than doubled in the adequate dual-therapy group (14.6 - 36.1%). This is important information to consider as the WHO suggests a 350 CD4 cut-off for HAART, and some countries in southern Africa are using the higher CD4 cut-off for commencing HAART.[1] Early first attendance at antenatal clinics is very important. CD4 counts of HIV-positive women need to be available within 1 week. Every effort should be made to initiate HAART if the CD4 count is <250 cells/µl. Earlier PCRs at 6 weeks according to the new policy and guidelines for the implementation of the PMTCT programme of the national Department of Health will improve baby follow-up.[5] A larger study is required to determine whether HAART and dual therapy have an equivalent transmission rate at a higher CD4 count cut-off than 250 cells/µl.

References

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