

Multidrug Regimens for PMTCT : Assessment of the Safety of First Line Antiretroviral Treatment in Pregnant Women and Newborns, Maseru, Lesotho

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BACKGROUND

In Lesotho 25.7% of pregnant women in antenatal clinics (ANC) are HIV infected. In 2007 the Ministry of Health and Social Welfare (MOHSW) introduced multidrug antiretroviral regimens for prevention of mother-to-child transmission (PMTCT):

- AZT at 28 weeks gestation + sd-NVP for CD4+ >350 cells/mm³ or;
- HAART for CD4+ ≤ 350mm³ or WHO stages III, IV
 - AZT + 3TC +Nevirapine (NVP), CD4+ ≤ 250 cells/mm³;
 - AZT +3TC + Efaviriz (EFV), CD4+ >250 cells/mm³ after 1st trimester;
 - AZT + sd-NVP for infants.



Kingdom of Lesotho

While evidence of efficacy for these regimens is accumulating in resource constrained countries, little is known about their safety in the context of limited laboratory monitoring and other maternal and infant health threats.

ICAP, with USAID support, and in collaboration with the Lesotho MOHSW, has been implementing a family centered MTCT-Plus program in health facilities in 4 Lesotho districts since 2005, including at Queen Elizabeth II (QEII), the national referral hospital where ANC HIV seroprevalence is 34.5%.

OBJECTIVES

To assess the safety of first line antiretroviral treatment in pregnant HIV-infected women and newborns at a national referral hospital in the Kingdom of Lesotho.

METHODS

A retrospective register and chart-review was done for 216 HIV-infected pregnant women who delivered with complete records initiating HAART from Nov 2007 - Sept 2008 at QEII hospital. Women were examined and laboratory tests were done at monthly clinic visits. Routine baseline and monthly follow up laboratory tests included full blood count and liver enzymes. Severe toxicities that warranted substitution or interruption of ARVs were reviewed. This includes severe anemia defined as Hgb < 8gm/dl, clinical signs and symptoms of hepatitis and/or liver enzymes elevated by ≥ 5 times the upper limit of normal, grade III or IV skin rash and severe neuropsychiatric manifestations.

Infant gestational age was estimated by midwives using maternal dates (preterm < 37 weeks); infants were examined for congenital malformations (CM). Low birth weight (LBW) was defined as < 2.5kg. Birth outcomes for women on HAART were compared to 216 HIV-uninfected (HIV-) women delivering during the same time period, randomly selected among 3308 mothers, from delivery registers. Odds Ratios (OR) with 95% confidence intervals (CI) were calculated.

RESULTS

216 pregnant women initiated HAART with AZT + 3TC + NVP (n=166) or EFV (n=50). There were no deaths or HAART terminations and all women continued HAART through delivery. Ten (5%) of 211 women developed severe anemia and switched to d4T; 2 (1%) of 166 on NVP developed severe rash requiring EFV substitution. There were no drug changes secondary to severe hepatic, gastrointestinal or neuropsychiatric events.

Overall, there was no significant association between HAART exposure during pregnancy and poor birth outcome. Nine (4%) of 216 births to women on HAART were stillborn vs. 7 (3%) of 216 infants of HIV negative women (OR = 1.3; 95% CI: 0.47, 3.55). Of 207 live births to HAART-treated women, 15 (7%) were preterm vs. 13(6%) of 209 HIV unexposed births (OR = 1.18; 95% CI: 0.55, 2.54). 32/207 (15%) after HAART exposure vs. 26/209 (12%) to HIV negative women were LBW (OR = 1.29; 95% CI: 0.74, 2.25). There were 3 (1%) and 5 (2%) reported CM in the HIV exposed and HIV negative groups respectively (OR = 0.59; 95% CI 0.14, 2.52). No infants exposed to EFV had CM.

Table 1: Side effects and toxicities of 1st line HAART in pregnant women

	Initial CD4 + ≤ 250	Initial CD4 + 250 - 350	Initial CD4 + > 350	Total
Total number of pregnant women	137 (62%)	76 (37%)	3 (1%)	216 (100%)
Regimen initiated				
AZT + 3TC + NVP	128/137 (93%)	34/76 (45%)	0	162/216 (75%)
AZT + 3TC + EFV	6/137 (4%)	42/76 (55%)	2/3 (66.6%)	50/216 (23%)
d4T + 3TC + NVP	3/137 (2%)	0	1/3 (33%)	4/216 (1.8%)
Initiated HAART :				
1 st trimester	18/137 (13%)	4/76 (5%)	0	22/216 (10%)
2 nd trimester	53/137 (39%)	33/76 (43%)	0	86/216 (40%)
3 rd trimester	66/137 (48%)	39/76 (51%)	3/3 (100%)	108/216 (50%)
Anemia (<8mg/dL) while on AZT based HAART	5/134 (4%)	5/76 (7%)	0	10/211 (5%)
Hepatotoxicity	0	0	0	0
NVP related grade 3 / 4 skin rash	1/131 (0.72%)	1/34 (2.9%)	0	2/166 (1%)

Table 2: Birth outcomes of pregnant women initiated on 1st line HAART

	Newborns of women initiated on 1 st line HAART during pregnancy	Newborns of HIV negative women	Odds Ratios (OR), 95% Confidence Interval (CI)
Number of women	216	216	
Live birth	207/216 (96%)	209/216 (97%)	
Preterm birth (<37 wks of gestational age)	15/207 (7%)	13/209 (6%)	OR: 1.18; 95% CI 0.55, 2.54
Stillbirth	9/216 (4%)	7/216 (3%)	OR: 1.3; 95% CI 0.47, 3.55
Low Birth Weight (LBW) (wt < 2.5 kg)	32/207 (15%)	26/209 (12%)	OR: 1.29; 95% CI 0.74, 2.25
Reported Congenital Malformation (CM)	3/216 (1%) (1 hypospadias, 1 spina bifida, 1 non-specified)	5/216 (2%) (1 spina bifida, 1 polydactyl, 3 non-specified)	OR: 0.59; 95% CI 0.14, 2.25

CONCLUSIONS

No profound drug-related toxicities were identified in this cohort of HAART-treated pregnant women and their infants. This simple, low-cost 1st line regimen is a suitable HAART in Lesotho and other resource-limited settings in the region to reduce the morbidity and mortality among pregnant women, and MTCT significantly. There is a need for continued vigilance as multidrug regimens become more widely used for PMTCT. Further studies are needed to assess the long term safety of HAART among women and infants.

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