



Management of Sequential Pregnancies in HIV Infected Women

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ABSTRACT

Background: Increasingly HIV infected women are embarking on more than one pregnancy. Cyclical use of antiretroviral therapy (ART) predisposes to viral resistance and failure. Optimum management of sequential pregnancies is uncertain.

Methods: HIV infected women with more than one pregnancy since 1998 were examined. According to protocol all women were offered antenatal ART and those with a pre-treatment CD4 >300x10⁶L discontinued therapy postpartum. When available genotypic resistance testing (HIV-1 TruGene) was performed after ART cessation postpartum.

Results: Since the introduction of antenatal screening (ANS) for HIV 53 women have had more than one pregnancy: 43=2, 9=3, 1=4 giving a total of 117 pregnancies. 49(90%) acquired HIV heterosexually. 47(87%) came from Sub-Saharan Africa, 37(79%) were originally diagnosed through ANS. Vertical transmission occurred in 1 pregnancy and this was a first pregnancy. 66(17.6%) started ART in pregnancy and stopped postpartum (median pretreatment CD4=474x10⁶L, viral load=2989cpm). Of these triple ART use increased with pregnancy number: 22(63%) of 1st; 24(96%) of 2nd and all of 3rd pregnancies. 36(55%) had postpartum genotypic data to guide subsequent ART prescribing; 20(55%) no mutations, 25(69%) primary reverse transcriptase mutations; 14(39%) unobtainable sequence or viral load <500cpm. Both mutations were seen after first pregnancies. Median pre-delivery viral load was 50cpm in the 1st pregnancy (n=35), 50cpm in the 2nd (n=25) and 147cpm in the 3rd (n=4). 20(67%) of 1st pregnancies and 16(64%) of 2nd had viral loads of <50cpm pre-delivery. In those with 3rd pregnancies (n=4) pre-delivery viral loads were 85cpm, 59000cpm (very late presentation), 50cpm and 230cpm. **Conclusion:** Vertical transmission of HIV did not increase with pregnancy number in this cohort. Despite stopping and starting ART the proportion with virological control increased between first and second pregnancy.

The data presented in this poster has been updated since the time of abstract submission

Background

In the developed world many HIV infected women are embarking on more than one pregnancy, prompted by a better life expectancy associated with HIV infection and the likelihood that their infant is unlikely to be HIV infected.

Many of these women do not meet criteria for commencement of antiretroviral therapy for their own health and therefore the need for antiretroviral therapy is only for the duration of the pregnancy.

Emergence of antiretroviral resistance has been demonstrated with temporary antiretroviral therapy use (1) and cyclical use of antiretroviral therapy in pregnancy may increase this risk.

The optimum management of sequential pregnancies is uncertain

Background (continued)

Routine antenatal screening for HIV infection was introduced in Ireland in 1998. Between 1998 and 2000 women not requiring antiretroviral therapy for their own health were offered dual nucleoside (usually zidovudine and lamivudine) or zidovudine monotherapy.

Since January 2002 all HIV-1 infected women attending the GUIDE Clinic, St. James's Hospital are offered triple antiretroviral therapy in pregnancy regardless of maternal need for therapy.

Methods

All women with more than one pregnancy from January 1998 to the present were identified from an ongoing database of pregnancies in HIV infected women attending our service.

According to protocol all women were offered antenatal antiretroviral therapy (ART) and for those with a CD4 count >300 x 10⁶L therapy was discontinued post partum.

From January 2002 all women that discontinued therapy post partum were asked to return within 6 weeks for genotypic resistance testing (TruGene HIV-1 Genotyping Kit, Visible Genetics).

Results

Between January 1998 and February 2005, 69 women have had 150 pregnancies: 58 women = 2 pregnancies; 10 women = 3 pregnancies and 1 woman has had 4 pregnancies.

The majority of the women came originally from Sub-Saharan Africa (60/69, 87%) and 9 (13%) are Irish. HIV infection was acquired heterosexually in 62 (90%), through injecting drug use in 5 (7%) and through contaminated blood products in 2 (3%), 54 (78%) were diagnosed with HIV through antenatal screening, 2 of these were tested in the post partum period.

Of these 150 pregnancies 4 are ongoing; 139 delivered at >28 weeks of pregnancy; 6 miscarried and there was 1 ectopic pregnancy. Of the 139 that delivered at >28 weeks there were 2 sets of twins and 2 intrauterine deaths. To date 1 infant has been documented as HIV infected, this was a first pregnancy.

Antiretroviral therapy

In 106/150 (71%) pregnancies ART was initiated during the pregnancy; 27 (18%) were on ART at the time of conception; 15 (10%) did not receive any and 2 (1%) have not yet started therapy. Of the 106 that initiated therapy in pregnancy 80 (75%) stopped in the post partum period; 25 (24%) remained on therapy post partum and 1 woman is still pregnant.

Where ART was discontinued post partum the proportion receiving triple ART increased with pregnancy number as shown in **Table 1**.

Results (continued)

Immunological and Virological parameters (n=80, with temporary ART)

The median pretreatment CD4 and HIV viral load in those women that stopped ART postpartum (n=80) were 462 x 10⁶L (174-1538) and 2771 copies/ml (50 – 31,1111) respectively. Two women that had pretreatment CD4 counts <200 x 10⁶L self-discontinued therapy postpartum.

The median pre-delivery viral load 50 copies/ml in the first pregnancy (n=42); 50 copies/ml in the second pregnancy (n=33) and 147 copies/ml in the 3rd pregnancy (n=4). The pre-delivery viral load was undetectable in 23/42 (55%) of first pregnancies; 20/33 (60%) of second pregnancies and the pre-delivery viral loads in the 3rd pregnancies were 50 copies/ml, 65 copies/ml, 230 copies/ml and 2307 copies/ml.

A summary of ART and outcomes in the woman with 4 pregnancies is shown in **Table 2**.

Genotypic resistance data

30 women had 37 post partum genotypic resistance tests performed. 20 tests were performed after the first pregnancy; 16 after the second and 1 after the third pregnancy. 18 (49%) sequences were "wild type" in both the RT and PI segments; 6 (16%) specimens demonstrated 8 mutations in the RT segment; 7 (19%) specimens demonstrated 11 PI polymorphisms. In 9 (24%) specimens either the postpartum viral load was too low to perform resistance testing or it was not possible to obtain a sequence, despite using additional primers.

Table 3 shows the antiretroviral regimen, on treatment viral load and mutations in the 6 women with mutations in the RT segment. Of note the V179E mutation was seen where there had been no NNRTI exposure. For 4 of the 6 women the mutations were seen after the first pregnancy and in the remaining 2 after the second (where specimen 2 and 6 in Table 3 are from the same woman).

Eleven PI polymorphisms were seen in 7 specimens: M36I =7; K20R =2; L63P =1 and L10I =1. In 3 of these protease inhibitors were included in the antiretroviral regimen (nelfinavir =2 and lopinavir/ritonavir =1). 2 of the 3 achieved virological control.

Conclusion

In this cohort, although numbers are small, sequential pregnancies were not associated with an increase in vertical transmission of HIV. Despite stopping and starting ART in pregnancy it was possible to achieve virological control in subsequent pregnancies. Postpartum genotypic resistance testing can provide important data to guide subsequent regimen choice.

As protease inhibitor use increases in pregnancy the impact of naturally occurring polymorphisms on viral response in sequential pregnancies remains to be seen and must be closely monitored.

Table 1: pregnancies where ART started and stopped (n=80)

	No. of drugs		
Pregnancy no.	1	2	3
1	2	14	26 (63%)
2	1	0	32 (97%)
3	0	0	4 (100%)
4	0	0	1 (100%)

Table 2: case summary of woman with 4 pregnancies and no transmissions

	Pre CD4	Pre VL	ART	Delivery VL
Pregnancy no.				
1	400	6676	ZDV/3TC	50
2	375	11093	ZDV/3TC/NVP	na*
3	488	23143	ZDV/DDI/NLF**	65
4	456	26399	ZDV/DDI/KAL	286

*delivered at 30 weeks **documented M184V mutation

Table 3: antiretroviral therapy, on treatment viral load and RT mutations

	ART	Del VL	Mutation
1	ZDV/3TC/NVP	1056	Y181C
2	ZDV/3TC/NVP	50	K101E*
3	ZDV/3TC	50	M184V
4	ZDV/3TC/NVP	400	G190A, T215S, Y181C
5	ZDV/3TC/NLF	50	V179E
6	ZDV/3TC/NLF	50	K101E*

*2 and 6 are the same woman in different pregnancies (no transmissions)

Reference

1. Lyons FE, Coughlan S, Byrne CM, Hopkins SM, Hall WW, Mulcahy FM. Emergence of antiretroviral resistance in HIV-positive women receiving combination antiretroviral therapy in pregnancy. AIDS 2005 Jan; 19(1):63-67