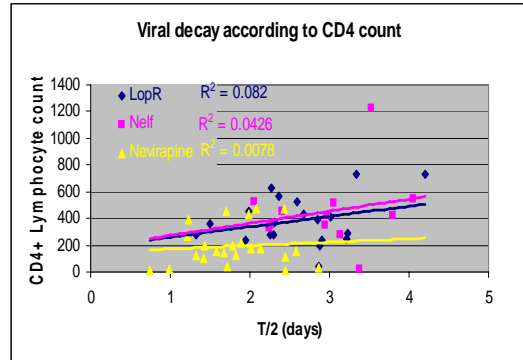


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Background. Optimal antiretroviral exposure during pregnancy is vital to prevent mother to child HIV transmission. Nevirapine (NVP) has been widely and effectively used but with concerns about toxicity. Consequently protease inhibitors are increasingly used in pregnancy despite reports that plasma concentrations may be sub-optimal^{1 2 3}. We therefore examined the rate of reduction of HIV viral load in plasma during the first 14 days of therapy in pregnant women starting a first antiretroviral combination of two nucleoside analogues (usually zidovudine plus lamivudine) plus either NVP or a protease inhibitor.

Methods. Three centre prospective data collection to study the change in viral load in consecutive pregnant women starting either NVP, nelfinavir or ritonavir boosted lopinavir. Change in viral load in non-pregnant women starting lopinavir/ ritonavir was also documented. HIV plasma RNA copies pre-treatment and at first routine review (usually 14 days) and baseline CD4 counts were collated. Data were entered into excel and the viral decay (T/2) over the 14 day period calculated. T/2 according to therapy were compared by T-test.

Results. HIV plasma half life during the first 14 days of therapy was shortest in women taking nevirapine whilst the tablet formulation of lopinavir/ ritonavir appears to out perform nelfinavir. Higher CD4 counts were associated with a slower viral load decline with the protease inhibitors but not with nevirapine, this data is represented in graph x. Viral decays with lopinavir/ ritonavir capsules in pregnant women were slower than in non-pregnant women but this did not reach statistical significance.



Conclusion These data support the continued use of nevirapine in pregnant women with CD4 counts < 250 cells/μl and may have implications for the type and timing of PI-based therapy in pregnancy.

	Nevirapine 200mg od	LPV/r Capsules 400mg/100mg bd	LPV/r Tablets 400mg/100mg bd	Nelfinavir 1250mg/bd	LPV/r capsules 400mg/100mg bd non-pregnant
No Subjects	25	20	9	12	10
Mean days on therapy (range)	12.7 (7 - 21)	13.3 (7 - 16)	13.8 (13-14)	15.4 (10-21)	13.8 (12-14)
Mean baseline CD4 cells/ml(range)	189.6 (10 - 470)	401 (40 - 730)	369 (20-650)	454 (16-1230)	162 (20 -300)
Mean baseline HIV RNA copies/ml	66,215 (4900-500000)	20,286 (751-121797)	10,542 (1531-24070)	14,773 (4580-36424)	176,745 (1443-500000)
Viral decay (T/2) days (range)	1.84 (0.74 - 2.86)	2.63 (1.5 - 4.2)	2.3 (1.93-2.83)	3.00 (2.24-4.06)	2.2 (1.43-3.43)

Discussion. Many physiological changes occur in pregnancy that can result in clinically significant changes in drug pharmacokinetics and dynamics. These changes occur from early in pregnancy, resolving in the post partum period. Pharmacokinetic studies have repeatedly demonstrated low plasma exposure to protease inhibitors during pregnancy. Plasma levels of nelfinavir were 34% lower in HIV positive pregnant women than in non pregnant women, however all but one of the pregnant women maintained a viral load below the level of detection and none of the babies were infected with HIV¹. Our data suggest that lower nelfinavir levels may be important as viral decay takes longer although causation is not shown.

Lopinavir exposure during late pregnancy has been found to be lower compared to the post partum period and compared to historic non-pregnant controls². Lopinavir is highly protein bound, with the unbound drug fraction in equilibrium with the site of action and remains so during pregnancy. There are limited data on the pharmacokinetics of Lopinavir in pregnancy especially with the new formulation, and a great deal of inter-patient variability, so therapeutic drug monitoring is recommended for pregnant taking protease inhibitors⁴. Placental transfer of lopinavir is minimal. Whilst not statistically significant the trend towards fast viral decay with lopinavir tablets compared with capsules is encouraging and may suggest that most pregnant women can be managed with standard doses.

	P values			
	Days	Decay	CD4	V/L
LPV/r Pregnant v Non-Pregnant	0.86	0.28	0.0008	0.014
Nevirapine v Nelfinavir	0.04	0.00004	0.01	0.04
Nevirapine v Lopinavir/ritonavir capsules	0.50	0.0002	0.0004	0.06
Lopinavir/ritonavir capsules v Nelfinavir	0.09	0.12	0.4	0.6
Lopinavir/ritonavir tablets v Nelfinavir	0.15	0.01	0.4	0.4
Lopinavir/ritonavir capsules v tablets	0.42	0.13	0.8	0.2

The main concerns with nevirapine relate to cutaneous and hepatic toxicity, especially in women with a CD4 greater than 250 cells/mm³, however the data vary between populations. There is a great amount of experience with nevirapine and it has been studied in widely pregnancy, plasma concentrations are similar to non-pregnant adults^{4,5}, with no dose adjustment required. In addition nevirapine crosses the placenta. This data helps to support the continued use of nevirapine in pregnant women who have a CD4 of less than 250.

References

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