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Peripartum Hair Levels of Antiretrovirals Predict Viral Suppression in Ugandan Women

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Background

- Barriers to drug adherence and fluctuations in antiretroviral (ARV) pharmacokinetics during pregnancy and breastfeeding (BF) may reduce drug exposure and place women at risk for virologic failure and infants at risk for HIV acquisition[1-4]
- ARV hair concentrations
  - Pharmacologic (quantitative) measure of ARV exposure that integrate adherence and pharmacokinetics
  - Reflect uptake from circulation over weeks-months; less susceptible to transient improvements in adherence than plasma levels
  - Predict viral suppression in non-pregnant cohorts[5-7]
  - Not yet examined in pregnant and BF women

Methods

Objective: Evaluate ARV hair concentrations among pregnant and BF women in relation to virologic outcomes

Study Design

- Secondary analysis of PROMOTE-Pregnant Women and Infants Study (NCT00993031)
- Open-label, randomized trial conducted in Tororo, Uganda to test whether lopinavir reduces rates of placental malaria
- HIV-infected, ART-naïve pregnant women enrolled at 12-28 weeks gestation and randomized to LPV/r/AZT/3TC or EFV/AZT/3TC
  - LPV/r increased from 400/100 mg BID to 600/150 mg BID from 30 weeks gestation to delivery
- Infants received AZT or NVP prophylaxis during BF

Measurements

- HIV-1 RNA: screening, delivery, 24 weeks postpartum
- Adherence: self-reported recall over the 3 days prior to each study visit (every 4 weeks)
- Hair samples: collected at 30-34 weeks gestation (if on ARVs ≥4 weeks) and 10-25 weeks postpartum
- ARV hair concentrations measured via liquid chromatography/tandem mass spectrometry (LC/MS/MS)

Analysis

- Primary predictor: ARV hair concentrations
- Outcome: Viral suppression (HIV-1 RNA ≤400 c/ml) at delivery and 24 weeks postpartum
- Multivariate logistic regression models examined predictors of viral suppression at delivery (among women on ART ≥6 weeks) and 24 weeks postpartum

Results

Table 1. Characteristics of Study Participants

Enrollment	Efavirenz N = 162	Lopinavir N = 163
Maternal age, years, Mean (SD)	30.3 (5.5)	29.3 (5.3)
Gestational age, weeks, Median (min-max)	21.8 (13.6-28)	20.7 (13-29.3)
CD4 cell count, Median (min-max)	373 (14-1080)	358 (81-1030)
Log_{10} HIV-1 RNA, Median (min-max)	4.3 (2.6-5.9)	4.1 (2.6-5.9)
Delivery	**N = 162**	**N = 163**
HIV-1 RNA ≤400 c/ml	98.0% (149/152)	87.4% (139/159)
Self-reported adherence, Median (min-max)	100% (33.3-100)	100% (77.8-100)
ART duration, weeks, Median (min-max)	16.9 (4.6-27.9)	17.7 (3.9-27.1)
24 Weeks Postpartum	**N = 149**	**N = 151**
HIV-1 RNA ≤400 c/ml	92.5% (124/134)	90.6% (126/139)
Self-reported adherence, Median (min-max)	100% (80-100)	100% (80.6-100)

Table 2. Univariate Analysis of Predictors of Viral Suppression

	Delivery		24 weeks postpartum	
	Efavirenz OR (95% CI)	Lopinavir OR (95% CI)	Efavirenz OR (95% CI)	Lopinavir OR (95% CI)
ARV hair concentration, Per doubling	**1.86 (1.14-3.1)**	**1.62 (1.19-2.2)**	**1.58 (1.18-2.1)**	**1.51 (1.05-2.2)**
Pretreatment HV-1 RNA, Per 10-fold increase	0.54 (0.12-2.3)	**0.31 (0.16-0.62)**	0.46 (0.20-1.09)	0.70 (0.36-1.35)
Self-reported adherence, Per 10% of dose	1.17 (0.32-4.3)	**3.69 (1.10-12.4)**	*	3.1 (0.94-10.0)
Maternal age, Per decade	3.24 (0.34-31)	1.90 (0.75-4.8)	1.93 (0.55-6.7)	1.34 (0.49-3.7)
Gest. age at enrollment, Per week	0.89 (0.65-1.21)	0.94 (0.84-1.05)	1.01 (0.87-1.18)	1.04 (0.91-1.17)
ART duration, Per week	1.17 (0.89-1.53)	1.02 (0.93-1.12)	0.97 (0.85-1.11)	0.96 (0.86-1.07)

*Too little variation in self-reported adherence to permit a meaningful estimate.

Figure 1. Distribution of Efavirenz and Lopinavir Hair Concentrations in Virologic Failures/Successes

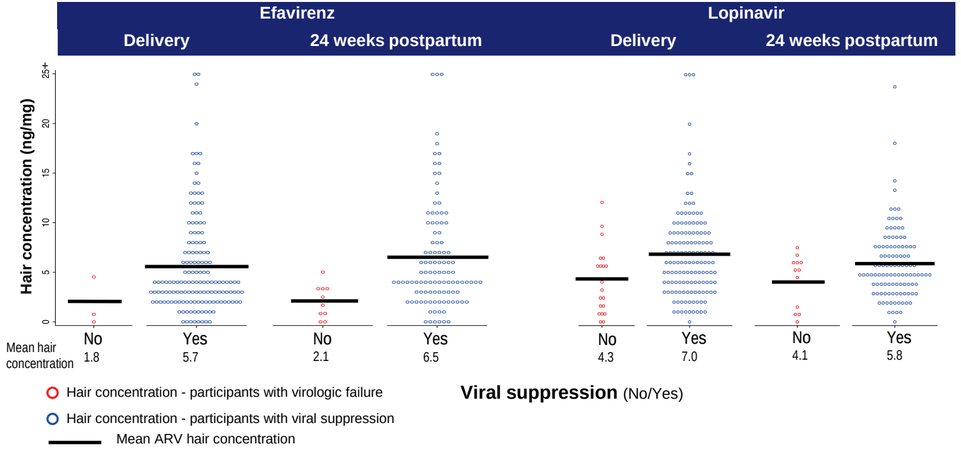
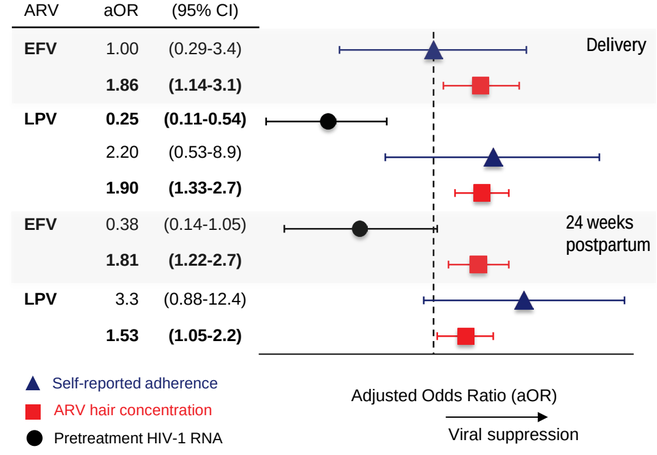


Figure 2. Multivariate Analysis of Predictors of Viral Suppression



Discussion

- Hair concentrations of efavirenz and lopinavir predicted viral suppression at delivery and 24 weeks postpartum
- ARV hair concentrations were more strongly associated with viral suppression than self-reported adherence
- Hair collection highly acceptable (84%)
- Hair concentrations of ARVs could serve as innovative tool to explain virologic outcomes in research studies
- Widespread applicability in clinical settings will depend on
  - defining thresholds for ARV hair concentrations associated with failure in larger cohorts
  - availability of lower-cost assays, currently under development

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