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tk.phillips@uct.ac.za

Plasma efavirenz and tenofovir versus dried blood spot tenofovir-diphosphate, and self-reported adherence to predict virologic suppression in South African women

Tamsin K. Phillips[1,2], Phumla Sinxadi[3], Elaine J. Abrams[4,5], Allison Zerbe[4], Catherine Orrell[6], Nai-Chung Hu[2], Kirsty Brittain[1,2], Yolanda Gomba[2], Jennifer Norman[3], Lubbe Weisner[3], Landon Myer[1,2], Gary Maartens[3]

[1]Division of Epidemiology and Biostatistics, University of Cape Town, Cape Town, South Africa; [2]Centre for Infectious Disease Epidemiology & Research, University of Cape Town, Cape Town, South Africa, [3]Division of Clinical of Pharmacology, Department of Medicine, University of Cape Town, Cape Town, South Africa [4]ICAP at Columbia University, Mailman School of Public Health, New York, USA, [5]Vagelos College of Physicians & Surgeons, Columbia University, New York, USA, [6]Desmond Tutu HIV Centre, Institute of Infectious Disease and Molecular Medicine and Department of Medicine, University of Cape Town, Cape Town, South Africa.

Background

Tenofovir-diphosphate (TFV-DP) in dried blood spots (DBS) has been used as an objective adherence measure for pre-exposure prophylaxis but data are limited on its ability to predict virologic suppression (VS) in people on antiretroviral (ARV) treatment.

Aims:

- To compare DBS TFV-DP, plasma ARV concentrations and self-reported adherence as predictors of VS in an African cohort of women on antiretroviral therapy
- To examine viral load (VL) within existing thresholds of DBS TFV-DP in this population

Methods

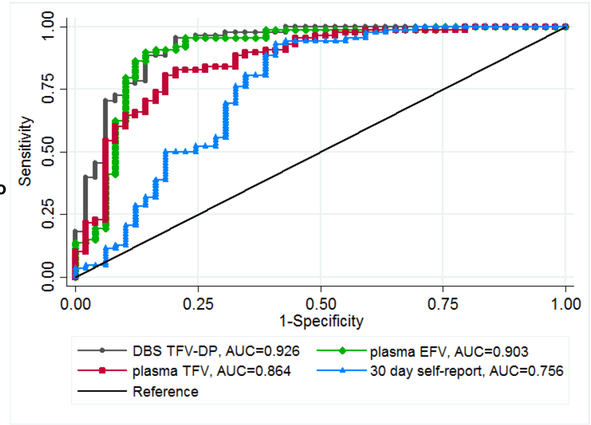
- Women participating in a larger cohort study in Gugulethu, South Africa, who were on a first-line regimen of tenofovir (TFV), emtricitabine, and efavirenz (EFV) were enrolled in a cross-sectional sub-study.
- 30-day self-reported adherence was measured using a three-item scale, venous EDTA blood samples were drawn for viral load and plasma ARV levels, and one DBS card was filled to measure TFV-DP concentrations; ARV concentrations were analysed with validated liquid chromatography tandem mass spectrometry assays.
- Plasma EFV and TFV, DBS TFV-DP assays, and 30-day self-reported adherence were evaluated as predictors of VS (<50 copies/mL) using area under the curve (AUC) of receiver operating characteristics (ROC) and logistic regression models.
- We also explored “white coat” adherence by comparing plasma TFV concentrations (half life ~14 hours[1]) with TFV-DP in DBS (half life up to 17 days[2]).

Results

- Among 137 women enrolled (mean age 33 years, median 3.9 years on ART).
- Overall, 88 women (64%) were VS.
- 84%, 76% and 86% of women had any detectable plasma EFV, plasma TFV and DBS TFV-DP, respectively (specimens taken median 15 hours after last dose [IQR 14-16]).

Results *(continued)*

Figure 1. Adjusted ROC curves of DBS TFV-DP, plasma EFV, plasma TFV, and self-reported adherence to predict VS; n=137 (adjusted for age and duration on ART)



- Self-reported adherence scores were high with 56% of women (n=77) reporting 100% adherence in the last 30 days on the three-item scale; 62 of whom were VS.
- TFV-DP in DBS had the highest AUC and this was significantly better than plasma TFV (p=0.006) but not different from plasma EFV (p=0.138).
- Having any detectable drug concentration on any of the three assays was highly predictive of virologic suppression; DBS TFV-DP, sensitivity 98%, specificity 74%

Table 1. Viral load characteristics within established DBS TFV-DP thresholds among 137 women

TFV-DP threshold (approximate doses per week*)	<350 (<2)	350-699 (2-3)	700-1249 (4-6)	≥1250 (7)
Total number of women	47	19	41	30
Median viral load $\log_{10}$ copies/mL (IQR)	3.7 (2.8-4.6)	1.3 (1.3-1.3)	1.3 (1.3-1.3)	1.3 (1.3-1.3)
Median viral load copies/mL (IQR)	12200 (618-40027)	20 (20-20)	20 (20-20)	20 (20-20)
Viral load <50 copies/mL				
Viral load <50 copies/mL, n (%)	7 (15)	16 (84)	36 (88)	29 (97)
aOR (95% CI)**	Ref	37 (8-178)	47 (13-175)	175 (20-1539)

*As previously described by Castillo-Mancilla et al [3], **Adjusted for age and duration on ART.

Results *(continued)*

- 97% of women who had a DBS TFV-DP concentration ≥1250 fmol/punch were VS (Table 1). This threshold also perfectly predicted viral loads <400 and <1000 copies/mL.
- A dose-response relationship was observed between VS and increasing concentrations of TFV-DP in DBS; this was not observed for increasing concentrations of plasma EFV or TFV.
- We compared plasma TFV concentrations (indicating recent dosing) with concentrations of TFV-DP in DBS (indicating consistent dosing in recent weeks) to assess “white coat” adherence.
- Four women with any detectable plasma TFV but DBS TFV-DP concentrations below 350 fmol/punch; all had detectable plasma EFV and only two were not VS.

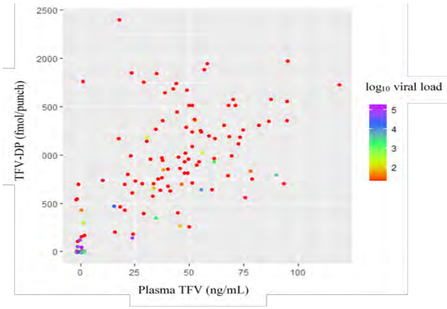


Figure 2. Scatter plot of DBS TFV-DP and TFV concentrations

Conclusions

- Plasma EFV, TFV and DBS TFV-DP were superior to self-reported adherence and were all strong predictors of VS.
- Unable to match TFV-DP concentrations in DBS to actual ARV dosing and further research is needed to establish optimal thresholds for adherence in African populations.
- Currently cost and logistical concerns limit use to research and high resource settings but EFV or TFV assays have potential for development as point-of-care assays that could be valuable objective adherence measures in resource-limited settings.

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