Steady-state TDF/FTC in Genital, Rectal, and Blood Compartments in Males vs Females

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Abstract

Gaps in knowledge remain regarding the pharmacokinetics (PK) of the intracellular active moieties, tenofovir (TFV) and emtricitabine (FTC), at steady-state concentrations (Css) in different compartments in the body. The purpose of this study was to describe the steady-state PK of TDF/FTC and TDF in genital, rectal, and blood compartments in HIV positive and negative males and females. Methods

TFV positive and negative adults were enrolled in an intensive PK study of daily TDF/FTC for 30 days. Rectal, blood, and cervical mucosal cells (PBMC) were obtained at first dose, days 3, 7, 14, and 30. Rectal biopsies and genital samples were performed once each per subject at designated visits. Genital samples included cervicovaginal brush collection and made provided one semen sample. Cervical cells, seminal leukocytes, and rectal mononuclear cells were isolated, counted, assayed for viability, and stored. First order PK was used to determine average steady-state values (Css) in each compartment for TDF/FTC and FTC-TCP. Comparisons were made between the genders and according to HIV status using unpaired t tests, only for PBMC data given first on sample sizes.

Results

Thirteen females (10 HIV negative) and 24 males (11 HIV negative) were included. Available samples from female participants included 13 cervical cell, 12 rectal mononuclear cell, and 253 PBMC. Samples from males included 18 seminal leukocyte, 23 rectal mononuclear cell, and 414 PBMC. Steady-state was reached in all compartments for both TFV-TP and FTC-TP within 30 days.Css values are shown in the table. TDF-TP and FTC-TCP Cx in PBMC did not significantly by gender or HIV status, although females trended toward higher concentrations of TDF in PBMC (p=0.08). Females also appeared to have higher TDF-TP in rectal cells. Genital cell concentrations at steady state were ~10 fold higher in females compared with males for both TDF-TP and FTC-TP. Conclusions

These findings illustrate differential drug penetration at steady-state in genital, rectal, and blood compartments, which is relevant for prevention of HIV acquisition and suppression of HIV replication within potential reservoirs of the body. Females tended to have higher concentrations in these compartments compared with males. This information provide concentration ranges to help inform dose-response relationships for the prevention and treatment of HIV.

Background

Despite the widespread use of tenofovir disoproxil fumarate and emtricitabine/tenofovir (TDF/FTC) for treatment and prevention of HIV infection, gaps in knowledge remain regarding the pharmacokinetics (PK) of the intracellular active moieties, tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC). TDF and FTC-TCP concentrations are different in various compartments in the body. The purpose of this study was to describe the steady-state PK of TDF/FTC and TDF in genital, rectal, and blood compartments in HIV positive and negative males and females.

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