

Title	Tenofovir plasma concentrations in pregnant women: comparison of hepatitis B and HIV-infected patients
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Background

Tenofovir disoproxil fumarate (TDF) is one of the preferred drugs to prevent mother to child transmission in both hepatitis B (HBV)- and HIV-infected pregnant women. Previously we found decreased exposure of approximately 20% in HBV-mono-infected pregnant women and a similar decrease was observed in HIV-infected pregnant women. These results in HBV and HIV mono-infected women cannot be directly compared since HIV-patients may use co-medications such as ritonavir which increase tenofovir plasma concentrations. However, this comparison is interesting as infection itself could also have an effect on the drug exposure. For this reason, the aim of this study was to compare the effect of pregnancy on tenofovir exposure in women receiving TDF monotherapy for HBV mono-infection with tenofovir exposure in HIV-infected women on TDF with and without concomitant boosted protease inhibitors (b/Pis).

Methods

This is a retrospective data analysis using data from two clinical trials: iTAP and PANNA. iTAP studied HBV mono-infected women from Thailand which were randomized in pregnancy to receive TDF or placebo. Single random blood samples taken twice during pregnancy, at delivery and postpartum were used to estimate the area under the curve (AUC_{0-24}) and trough concentration (C_{trough}) with non-linear mixed effect modeling. The data of the first assessment in pregnancy (closest to PANNA) and postpartum (1 month) were used in this study. PANNA is a multicenter study in Europe which collects full pharmacokinetic curves of pregnant women on specific antiretroviral regimens in the third trimester (33 weeks) and postpartum (4-6 weeks after delivery). AUC_{0-24} and C_{trough} are obtained using non-compartmental analysis. Next to the previously published pharmacokinetic tenofovir data of PANNA, 30 additional curves (without boosters) were analyzed for this study. To compare the pregnancy effect on the pharmacokinetic parameters of HBV- and HIV-infected patients descriptive statistics are used.

Results

218 women were included of which 154 from the iTAP-study and 64 from PANNA (of which 34 using ritonavir boosted Pis). Although the age, weight and race differed between the two groups, the creatinine concentration was similar. Median (IQ range) was 53 $\mu\text{mol/L}$ (44-58) and 55 $\mu\text{mol/L}$ (50-60) for PANNA and iTAP respectively. In pregnancy the geometric mean (GM) with 95% confidence interval (95%CI) of the AUC_{0-24} was 2.44 $\mu\text{g}\cdot\text{hr/mL}$ (2.22-2.68) in HIV-infected patients on b/Pis, 1.92 $\mu\text{g}\cdot\text{hr/mL}$ (1.70-2.18) in HIV-infected patients without b/Pis and 1.84 $\mu\text{g}\cdot\text{hr/mL}$ (1.77-1.92) in HBV-patients. The geometric mean ratio (GMR) of 3rd trimester vs postpartum (with 90% confidence interval; 90%CI) of AUC_{0-24} was 0.75 (0.67-0.84), 0.74 (0.69-0.81) and 0.79 (0.78-0.80) for HIV patients with b/Pis, HIV patients without b/Pis and HBV patients, respectively. The GMR (90%CI) of the C_{trough} was 0.79 (0.72-0.86), 0.67 (0.61-0.73) and 0.69 (0.68-0.71), respectively.

Conclusions

The retrospective data analysis of these two different trials showed that pregnancy had a similar effect on tenofovir AUC in HIV-infected patients as in HBV-infected patients. The C_{trough} of TFV in HIV patients without b/Pis is similar to HBV patients.