

Clinical Risk Factors of Kidney Tubular Dysfunction in HIV-Infected Thai Patients Treated with Tenofovir Disoproxil Fumarate

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Introduction

- Tenofovir disoproxil fumarate (TDF) is one of the widely use antiretroviral drugs.
- TDF-associated kidney tubular dysfunction (KTD) has been reported in a number of HIV-infected patients.
- We studied the association between clinical factors and KTD in HIV-infected Thai individuals receiving TDF.

Materials and Methods

- Blood and urine samples of 65 HIV-infected Thai patients receiving TDF-containing antivirals were collected between September 2012 and January 2013.
- KTD was diagnosed by the presence of ≥ 3 of the following abnormalities: $\beta 2$ -microglobulinuria, nondiabetic glucosuria, increased fractional excretion (FE) of uric acid, increased FE of phosphate, and renal tubular acidosis.
- Associations between clinical factors and KTD were tested by logistic regression analyses.

Results

- KTD was diagnosed in 13 of 65 (20%) patients.
- 33 patients (50.5%) were female.
- Median (interquartile range; IQR) age was 43.8 (40.4-50.9) years.

Table 1. Characteristics of 65 patients

Median (IQR)	Patients with KTD (n=13)	Patients without KTD (n=52)	P value
Age, years	42.7 (37.0-51.1)	43.9 (40.5-50.8)	0.422
Female, n (%)	7 (53.9)	26 (50.0)	0.804
CD4 cell count, cells/mm ³	589 (494-703)	548 (425-726)	0.461
Duration of receiving TDF, months	49.5 (35.3-59.0)	45.7 (27.2-54.0)	0.381
Weight, kg	48.5 (44.0-60.0)	55.7 (51.1-63.2)	0.093
Body mass index, kg/m ²	18.1 (16.9-21.9)	21.5 (19.6-23.9)	0.026
Serum creatinine, mg/dL	0.9 (0.7-1.1)	0.8 (0.7-0.9)	0.094
CrCl CG, mL/min	69.5 (50.6-83.0)	82.5 (74.2-99.8)	0.029
CrCl MDRD, mL/min	89.6 (60.3-98.9)	97.3 (85.7-109.3)	0.039

- Median CD4 cell counts (IQR) was 554 (437-716) cells/mm³.
- Median (IQR) duration of TDF use was 46.9 (31.5-54.1) months.
- Serum creatinine was comparable in patients with and without KTD.
- Creatinine clearance was lower in patients with KTD ($P = 0.029$).
- In multivariate model, body mass index (BMI), concomitant use of protease inhibitor (PI), and hyperlipidemia were independently associated with KTD in patients receiving TDF. (Table 2)

Table 2. Factors associated with kidney tubular dysfunction by multivariate analysis

Characteristics	OR (95% CI)	P value
BMI	0.76 (0.59-0.98)	0.037
Hyperlipidemia	8.59 (1.46-50.40)	0.017
Concomitant use of PI	11.39 (1.59- 81.56)	0.015

Discussion

- TFV-associated nephrotoxicity is multifactorial.
- Previous studies showed low BMI and concomitant use of PI as factors related to TFV-associated renal dysfunction.
- We revealed association between hyperlipidemia and KTD. Dyslipidemia is known to cause tubule-interstitial injury in cell culture model.

Conclusions

- KTD in HIV-infected Thai patients receiving TDF is not uncommon.
- Low BMI, concomitant use of PI and hyperlipidemia are associated with KTD in HIV-infected Thai patients receiving TDF.
- Closed monitoring of KTD should be warranted in patients who have these factors and receive TDF.