Executive summary

MSS 232 R - "Kidney tubular dysfunction in tenofovir-treated HIV-infected individuals in Hong Kong"

Aim and Objectives

Management of anti-retroviral adverse reactions remain an important component of current HIV management. Tenofovir disoproxil fumarate (TDF) is a recommended first-line nucleotide reverse transcriptase inhibitor, and is reported to be associated with nephrotoxicity, in particular kidney tubular dysfunction (KTD). In this study, we aim to (1) compare the prevalence of kidney tubular dysfunction and decreased renal function between HIV-infected individuals receiving TDF and those not receiving TDF in Hong Kong; (2) determine the accuracy of various urine biomarkers in diagnosing kidney tubular dysfunction, and (3) determine risk factors associated with the development of kidney tubular dysfunction in HIV-infected individuals in Hong Kong.

Project design and subjects

A cross-sectional case-control study was performed. One hundred forty HIV-infected individuals taking TDF and 53 HIV-infected individuals on combination anti-retroviral therapy but not exposed to TDF were recruited. Blood samples were taken to measure serum creatinine, phosphate, uric acid, and single nucleotide polymorphisms (SNPs) of ABCC2 gene. Paired urine samples were obtained to measure phosphate, uric acid, β2-microglobulin, α1-microglobulin, N-acetyl-β-D-glucosaminidase (NAG) and retinol-binding protein (RBP). KTD was defined as presence of three of the six abnormal urine biomarkers. The proportions of cases and controls with KTD and decreased eGFR were compared. The performance, including sensitivity, specificity, positive and negative predictive values, of each of the six criteria included in our definition of KTD was calculated. Receiver operating characteristic (ROC) curves were constructed for each of the above markers, and the areas under the curve (AUC) were estimated with 95 % confidence interval.

Main achievements

A total of 140 HIV-infected individuals taking TDF (cases) and 53 never exposed to TDF (controls) were recruited. Cases were younger (mean ± SD 46.2 ± 9.6 vs. 55.3 ± 12.9 years, $P<0.001$), had shorter duration of HIV infection [median (IQR) 7.0 (3.3, 13.0) vs. 11.3 (5.8, 16.4) years, $P=0.007$] and anti-retroviral treatment [median (IQR) 5.3 (2.6, 11.5) vs. 9.3 (4.8, 15.0) years, $P=0.005$], lower prevalence of hypertension (15.0% vs. 58.5%, $P<0.001$) and diabetes mellitus (7.9% vs. 54.7%, $P<0.001$), and higher prevalence of hepatitis B co-infection (22.9% vs. 1.9%, $P<0.001$).

Prevalence of KTD, was similar between cases and controls (20.7% vs. 17.0%, P=0.560). Impaired renal function (as defined by creatinine clearance <60mL/min//1.73m^2, as calculated by Cockroft Gault formula) was less prevalent in cases than controls (7.1% vs. 24.5%, P=0.001). β2-microglobulin showed the highest sensitivity of 92%. ROC analyses of various markers of KTD demonstrated best performance with retinol binding protein, β2-microglobulin, and α1-microglobulin.

Patients with KTD had more severe renal impairment [creatinine clearance 72 (IQR 61, 85) vs. 90 (72, 107) mL/min/1.73m^2, P<0.001; creatinine clearance <60mL/min/1.73m2: 23.7% vs. 9.0%, P=0.022]. KTD was associated with lower body weight, history of AIDS-defining illness, lower nadir CD4 count, diabetes mellitus, and duration of TDF therapy on univariate analysis (P<0.1). On multivariate logistic regression analysis, KTD was associated with lower body weight (OR 0.96, 95% CI 0.92-0.99, P=0.044), diabetes mellitus (OR 3.46, 95% CI 1.14-10.44, P=0.028), and duration of TDF therapy (OR 1.23, 95% CI 1.06-1.43), P=0.007).

Conclusions

In this study, 21% and 7% of HIV-infected individuals taking TDF had KTD and impaired renal function respectively. KTD was associated with lower body weight, diabetes and duration of TDF exposure.