Incidence of Tenofovir Disoproxil Fumarate Induced Proximal Tubulopathy in HIV-Infected Patients

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ABSTRACT

Background: Tenofovir disoproxil fumarate (TDF) is a highly effective antiretroviral agent, recommended for treating both HIV and hepatitis B virus infections. Although, TDF has a good safety profile, TDF has been most commonly associated with renal toxicity. TDF has been involved in proximal tubular toxicity with or without acute renal failure, and in severe cases, patients can develop Fanconi syndrome. However, the real incidence of TDF induced proximal tubular dysfunction in TDF-treated patients remains uncertain.

Objectives: The aims of the present study were to determine the incidence of TDF induced proximal tubulopathy and the risk factors among HIV-infected adult patients.

Methods: A prospective descriptive study of proximal tubulopathy due to TDF was conducted with 196 HIV-infected patients who attended the Infectious Diseases Clinic at Phramongkutklao Hospital, Bangkok, Thailand, between January 2015 and December 2015.

Results: Thirty-one (15.8%) patients had a TDF induced proximal tubulopathy with an incidence of 6.07 per 100 person-years (95%CI: 4.27-8.63). Among these 31 patients, most patients (77.42%) had proteinuria, followed by 12 (38.71%) patients having albuminuria, 4 (12.9%) had normal anion gap metabolic acidosis, 3 (9.68%) had hypophosphatemia, 2 (6.45%) had increased urinary uric acid excretion and 2 (6.45%) had glycosuria and a decrease in GFR (<60 mL/min/1.73 m²), respectively. The incidence rates of the laboratory markers of proximal tubulopathy, including proteinuria, albuminuria, normal anion gap metabolic acidosis, hypophosphatemia with increased urinary phosphorus excretion, increased urinary uric acid excretion and euglycemic glycosuria was 4.70, 3.92, 2.35, 0.78, 0.59 and 0.39 per 100 person-years, respectively. Two patients had eGFR <60 mL/min/1.73 m² at TDF induced proximal tubulopathy presentation with an incidence of 0.39 per 100 person-years. In addition, all patients with proximal tubulopathy had no hypokalemia, polyuria or bone pain. By univariate logistic regression, AIDS (OR 35.54, 95% CI 9.03-139.88, P <0.001), and concurrent TMP/SMX (80/400) 2 tabs per day (OR 8.8, 95% CI 2.42-31.98, P < 0.001) were a statistically significant association with a TDF induced proximal tubular toxicity. By multivariate logistic regression, there was no statistically significant association with a TDF induced proximal tubulopathy.

Conclusions: Both proportion and incidence rates of TDF-associated relevant proximal tubular toxicity are low. However, TDF use is associated with a risk of developing proximal tubular dysfunction in our HIV-infected patient population. Routine monitoring of proximal tubular function is essential for the prevention and early detection of proximal dysfunction that ameliorate the progression of kidney disease; especially among patients who had risk factors using creatinine-based eGFR, Na⁺, K⁺, Cl⁻, HCO³⁻, PO⁴³⁻ levels, uric acid, urinalysis, UPCR and UACR, although it may be a concern of infrastructure in resource limited settings. (J Infect Dis Antimicrob Agents 2016;33:33-55.)

Keywords: proximal tubular dysfunction, proximal tubulopathy, tenofovir disoproxil fumarate (TDF), incidence

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