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Tenofovir in Indian Children

We describe our experience with tenofovir-based antiretroviral therapy in seven HIV-infected children after failure of first line antiretroviral drugs, or due to adverse effects to other antiretrovirals. For follow-up period of average 3.4 years, none had adverse effects or failure of treatment, indicating that tenofovir has good renal and gastrointestinal safety profile in HIV-infected Indian children and adolescents.

Keywords: *Antiretroviral treatment, HIV infection, Renal dysfunction*.

Tenofovir Disoproxil Fumarate (TDF) is an orally bioavailable prodrug of tenofovir. In March 2010, the US FDA approved TDF for use in patients ≥12 years, and in January 2012, this approval was extended to children aged ≥2 years [1]. However response of TDF-based antiretroviral therapy (ART) in Indian children is not known.

Seven children (4 males) aged 6 to 16 years with mean (SD) age of 13.1 (3.5) years were started on TDF-based regimen. We used TDF, available as 300 mg tablet, in dosage of 8 mg/kg/dose once daily along with other antiretroviral drugs. At each visit, these children were evaluated for gastrointestinal symptoms and clinical evidence of rickets or pathological fractures. Serum creatinine, blood urea nitrogen, glomerular filtration rate, urinary proteins and blood gases were estimated trimonthly during the follow-up. Calcium and phosphorus levels in the serum were estimated trimonthly. Details of these patients are described in ***Table* I**.

Mean (SD) age for starting ART was 7.6 (4.2) years, and mean (SD) duration of for receiving TDF-based regimen was 3.4 (2.7) years. No patient suffered from renal dysfunction, urinary abnormalities or acidosis during the follow-up. Serum calcium and phosphorus levels in the serum remained normal. None of them had clinical evidence of gastrointestinal symptoms, rickets, or pathological fractures.

Adverse effects of TDF include lactic acidosis, besides nausea, diarrhea, vomiting, and flatulence [2]. While fatal lactic acidosis has been reported when TDF was added to a regimen that also contained didanosine, the effect was probably because TDF increases didanosine concentrations which causes significant mitochondrial toxicity [3]. None of our patients had lactic acidosis. Two small studies [4,5] in children reported reduction in bone mineral density (BMD) following TDF use. In these studies, BMD was measured by dual-energy *X*-ray absorptiometry (DEXA) scan. We could not do BMD in our patients on TDF-based regimen. A decrease in renal function and hypophosphataemia occur over time in HIV-infected children and adolescents on TDF-based ART [6]. Hypophosphatemia is significantly more common with recent TDF exposure, but is generally reversible if TDF is stopped [7]. A prospective study of 40 children, who had received at least six months of TDF, observed no change in creatinine clearance, but serum phosphate levels showed a significant decrease over the duration of follow-up [8]. Another study in 27 Italian children who received two years of TDF treatment found no evidence of impaired glomerular or tubular renal function [9]. We observed no adverse effect or failure of treatment in our case series, indicating that TDF has good renal and gastrointestinal safety profile in HIV-infected Indian children and adolescents. Reports based on larger number of patients are required to confirm our findings.

Contributors: JK: acquition, analysis of data and drafting of manuscript; IS: concept, design and critical manuscript revision for important intellectual content. The final version of the manuscript was approved by both authors.
Funding: None; *Competing interests*: None stated.

TABLE I DETAILS OF PATIENTS WHO RECEIVED TENOFOVIR-BASED REGIMEN

Case	*Patient 1*	*Patient 2*	*Patient 3*	*Patient 4*	*Patient 5*	*Patient 6*	*Patient 7*
Age at presentation (yr)	11	9	12.5	11	13	5	2.5
Reason for change to TDF	Treatment failure	Treatment failure	Treatment failure	Treatment failure	AZT induced anemia	Lactic acidosis and treatment failure	Treatment failure
Total (yr) on TDF	4	1	7	2	0.5	7	2
CD4 (cells/mm^3) at start of TDF	198 (18.9%)	70	88 (9%)	2637 (17%)	1022	388 (22.6%)	450 (20.5%)
Latest CD4 (cells/ mm^3)	499 (19%)	254 (31.4%)	432 (32.38%)	2793 (18%)	1144	517 (27%)	985 (36.8%)
Viral load (Copies/mL) at start of TDF	249098	20700	Not done	7161	Not done	19876	562000
Latest viral load (Copies/mL)	Undetectable	Not done	3986	Undetectable	3890	Not done	Undetectable
Side effects of TDF	No	No	No	No	No	No	No

TDF –Tenofovir Disoproxil Fumarate.

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