CASE REPORT

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Nephrogenic diabetes insipidus associated with tenofovir administration: report of a paediatric case

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ABSTRACT

Tenofovir renal toxicity, particularly when associated with other antiretrovirals, has been reported in the adult HIV-positive population. Reports in HIV-positive children are very rare. The authors report a paediatric case of nephrotoxicity associated with tenofovir and didanosine, emtricitabine and lopinavir-ritonavir coadministration.

A 12-year-old girl with AIDS (clinical stage C) with a multidrug-resistant virus and several treatment failures initiated emtricitabine, tenofovir, didanosine and lopinavir-ritonavir in 2008 with good tolerance. Her viral load became undetectable and CD_4 count normal. Two years later she presented generalised weakness, polydipsia and polyuria. On physical examination dehydration was evident. Her vital signs were stable. She had lost 5% of her body weight in the previous week. Urinalysis revealed a urine gravity of 1000, osmolality 150 mOsm/Kg and no proteinuria or glucosuria. Blood analysis showed osmolality 289 mOsm/Kg, normal values of glucose, creatinine, urea, sodium, potassium, chloride and calcium. A water restriction test followed by desmopressin administration confirmed the diagnosis of nephrogenic diabetes insipidus. Tenofovir and didanosine were stopped and abacavir was added. The patient was treated with a thiazide diuretic and salt restriction. There was good clinical evolution and no relapses.

This case highlights important possible side effects of tenofovir and emphasises the need for further studies into the renal safety of this agent in paediatric patients.

Key-Words:
AIDS; HIV; nephrogenic diabetes insipidus; tenofovir.

INTRODUCTION

Tenofovir is a nucleotide reverse transcriptase inhibitor. While preclinical studies considered it to be effective and more secure than other members of this pharmacological class[1], recent years have seen reports of nephrotoxicity in the adult HIV-positive population[2,3] but very few in children[4,5]. In fact, there is little knowledge of its effects in the paediatric population. Two randomised studies suggested a safe profile[6,7] but, more recently, a multicentre cohort study with forty patients showed significant association between tenofovir and renal tubular dysfunction in HIV-infected paediatric patients[8].

The nephrotoxicity occurs as a result of tubular damage that can cause Fanconi Syndrome, renal failure and nephrogenic diabetes insipidus (NDI)[1-8]. We present the case of a female adolescent with AIDS who developed NDI while on rescue antiretroviral (ARV) regimen with lopinavir-ritonavir, didanosine and emtricitabine-tenofovir.

CASE REPORT

We report the case of a 12-year-old Caucasian female born from a pregnancy with no clinical surveillance. At the age of eight months she was admitted to our hospital with *Pneumocystis jiroveci* pneumonia and HIV1 infection was diagnosed (CDC category C3).

At fifteen months of age she had a disseminated BCG infection and systemic candidiasis, and at the age of eight had pulmonary tuberculosis. She also had HIV encephalopathy, spastic diplegia and epilepsy.

ARV treatment compliance was difficult, and the patient had a multidrug-resistant virus and several treatment failures. In May 2010 she began complaining of generalised weakness, polydipsia and polyuria (>5 ml/kg/h). The patient was since 2008 on rescue ARV regimen with lopinavir-ritonavir 200 + 50 mg twice daily; didanosine 125 mg twice daily and emtricitabine-tenofovir 200 + 300 mg once daily, with undetectable viral load and normal CD4 cell count.

On physical examination she had sunken eyes and dry mucous membranes. Her vital signs were stable (blood pressure 109/68 mm Hg; heart rate 90 beats per minute; temperature 37.1ºC; respiratory rate 14 cycles per minute). She had lost 5% of her body weight in the past week.

Urinalysis revealed a urine specific gravity of 1000, osmolality 150 mOsm/Kg, phosphaturia: reabsortion rate of phosphorus was 84.4% (N: 92.5±2.3 %) and no proteinuria or glucosuria. Blood analysis showed osmolality 289 mOsm/Kg, normal values of glucose (116 mg/dl), creatinine (0.56 mg/dl), urea (12 mg/dl), sodium (140 mmol/l), potassium (4.52 mmol/l) and calcium (2.22 mmol/l). She had hypophosphataemia (0.56 mmol/l) with PTH slightly decreased (9.9 pg/ml, N: 15-65).

The patient was admitted for a water restriction test followed by desmopressin administration (20µg intranasal) that confirmed the diagnosis of NDI:

- ADH levels before the test were slightly raised: 14.4 pmol/L (N: 2-13)
- There was elevation of blood osmolality (297 mOsm/Kg) without elevation of urine osmolality (194 mOsm/Kg), reflecting the inability to concentrate urine;
- Desmopressin administration caused no significant elevation of urine osmolality (219 mOsm/Kg).

Tenofovir and didanosine were stopped and abacavir was added. She also started a thiazide diuretic and salt restriction diet. There was good clinical evolution with progressive weight gain and symptoms resolution within a month. Her blood and urinary values of phosphorus also became normal and there were no relapses, with viral load remaining undetectable and normal CD4 count.

DISCUSSION

Toxicity can limit the use of successful antiretroviral regimens. Tenofovir has nephtotoxic potential, which has been related to dose and duration of therapy[5,8]. It should be used with great caution and the coadministration of didanosine avoided whenever possible. However, treatment options are frequently very scarce in antiretroviral experienced children with multidrug-resistant virus. They present complex therapeutical challenges that need a careful clinical and laboratory follow-up[5,8].

This case highlights important possible side effects of this agent and emphasises the need for further studies into the renal safety of tenofovir in paediatric patients. Renal complications of this drug should be anticipated by appropriate screening[8] and treatment discontinued if they are confirmed. Research is under way into new, structurally similar molecular derivatives which do not accumulate in proximal tubules[9].

Conflict of interest statement. None declared.

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