CASE REPORT

TENOFOVIR INDUCED FANCONI SYNDROME: CASE REPORT OF A RARE CAUSE OF HYPOPHOSPHATEMIC SWAYING IN TERTIARY CARE HOSPITAL, KARNATAKA.

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Abstract:

A nucleotide reverse transcriptase inhibitor called tenofovir is used to treat human immunodeficiency virus (HIV) infection. Tenofovir disoproxil fumarate (TDF) is tenofovir's oral prodrug. Reports reveal that acute renal failure, fanconi's syndrome (FS), dysregulation of divalent ion metabolism, and diabetes insipidus linked with its use. Dysfunction of the renal proximal tubule is associated to fanconi syndrome. A generalised reabsorption defect, leading to the wasting of phosphate, amino acids, glucose, and bicarbonate is the primary pathologic characteristic. Therefore, it is crucial to understand the clinical characteristics and differential diagnosis of this syndrome. This is a case report of a 45-year-old female patient who presents with antiretroviral therapy (ART) induced fanconi syndrome.

Keywords: Antiretroviral therapy, Diabetes insipidus, Fanconi syndrome, Human immunodeficiency virus, Renal failure.

INTRODUCTION

The use of tenofovir disoproxil fumarate (TDF) is recommended as a component of all first-line treatment regimens in antiretroviral therapy (ART) in HIV-infected patients.[1] TDF has gained popularity because of its convenient dosing schedule, antiviral efficacy, and relatively favourable side-effect profile, making it one of the most widely prescribed antiretroviral drugs.[2] It is excreted through a combination of glomerular filtration and active tubular

secretion, with uptake in the proximal tubule and secretion into the tubular space.[3] Concerns regarding nephrotoxicity were initially raised by the structural similarity between tenofovir and the nephrotoxic acyclic nucleotide analogues adefovir and cidofovir.[4] The estimated incidence in decrease of CrCl to less than 50ml/min is 3-8% and to less than 30ml/min 0.2-1.6%.[5]

Post-marketing reports reveals that tenofovir results in fanconi syndrome (proximal tubulopathy) leading to glycosuria, phosphaturia, aminoaciduria and bicarbonate wasting. Subsequent studies have found that TDF use cause a small but big significant decrease in creatinine clearance (a surrogate for glomerular filtration) in both HIV positive and negative populations.[6] It is still widely used in developing countries due to low cost, efficacy and tolerability.[7] We describe a case of a patient on TDF who presented with PLHA (People living with HIV/AIDS), renovascular disease (RVD) and electrolyte imbalance compatible with fanconi syndrome. After stopping TDF, the patient's clinical condition improved along with her renal function and electrolyte abnormalities.

CASE REPORT

A 45-year-old HIV-positive woman was treated with stavudine, lamivudine, and nevirapine as per National AIDS Control Organization (NACO) guidelines for 24 months. She did not experience an improvement in her CD4 count (17 cells/L) or plasma viral load (1,27,734/mm of blood). As a result, the patient was instructed to undergo second-line antiretroviral medication, which consists of 150 mg of lamivudine and 150 mg of tenofovir twice daily. In addition, she was taking cotrimoxazole 960 mg once daily, along with multivitamins and folic acid. The patient complained of swaying, generalised weakness and urinary incontinence after receiving this treatment for a year. Investigation revealed that the random blood sugar (RBS)

was within the normal range and the serum creatinine had reduced. Albuminuria (1g/L) was detected in the urine sample on two further tests. Low serum phosphate (1.74, N: 2.7-4.5 mg/dL) was seen. Therefore, the patient was diagnosed as a case of fanconi syndrome considering the clinical presentation and time course of events .

On the suggestion of a nephrologist, tenofovir was discontinued as the likely causative medicine, and the patient was moved to an alternate regimen that included abacavir 300 mg, lamivudine 300 mg, dolutegravir 50 mg, and ganciclovir 450 mg twice daily for seven days. After 1 month, swaying, generalised weakness and urinary incontinence were resolved and serum phosphate returned to normal level (2.8 mg/dL). When the patient was last checked, there was no albuminuria. Using the Naranjo Scale and WHO-Uppsala Monitoring Center (UMC) standards, the causality of the adverse drug event was determined. Both the algorithms labelled tenofovir as "probable". According to a Hartwig scale analysis, ADR was of a severe degree. Additionally, the ADR was probably avoidable according to the preventability evaluation performed using the Modified Schumock and Thornton criterion.

DISCUSSION

Overall, tenofovir-related renal toxicity, particularly Fanconi syndrome (FS), is still quite uncommon.[8] It was approved by the US Food and Drug Administration in 2001. A generalised malfunction of the proximal renal tubule causes FS, which results in increased excretion of these solutes into the urine and decreased reabsorption of amino acids, glucose, urate, bicarbonate, and phosphate. Polyuria, dehydration, hypokalemia, hypophosphatemia, metabolic acidosis, rickets in children, or osteomalacia in adults, are some of the classical clinical signs of FS.[9] In this case, the patient developed albuminuria and hypophosphatemia after receiving tenofovir based antiretroviral therapy for 1 year. A possibility of primary fanconi syndrome was identified since the patient had no history suggestive of this condition

in the past. After receiving 12 months of drug therapy the signs and symptoms started to appear. Tenofovir was discontinued and a regimen consisting of abacavir 300 mg, lamivudine 300 mg, and dolutegravir 50 mg orally, once a day, along with ganciclovir 450 mg twice a day for seven days was started. Hence, the patient condition improved and renal functions returned to normal, suggesting the possibility of tenofovir induced fanconi syndrome.

Tenofovir-induced FS was initially documented in the year 2002.The first case of tenofovir-induced FS was reported in 2002. Later, Karras et al., Peyriere et al., reported similar cases. Most of these patients had HIV infection for several years, and renal dysfunction with classical signs of FS developed usually 6-12 months after starting tenofovir, just like our patient. However, in contrast, our patient presented with acute onset of hypophosphatemic swaying, which rapidly improved with treatment and after stopping tenofovir.[10] The multimodality of fanconi syndrome presentations challenges medical professionals. Since life-threatening situations can occur, therefore early diagnosis and management is a major concern. The preferred form of treatment is still symptomatic management. Thus, further research regarding etiology and therapy is needed, and this case report deserves discussion for future studies.

CONCLUSION

Fanconi syndrome is an uncommon complication of tenofovir therapy. FS presenting as hypophosphatemia along with swaying is rare. With the increasing use of tenofovir as first line-ART, clinicians must be aware of this complication. Baseline and annual monitoring of GFR is recommended for all patients on TDF. Moreover, patients on this medication should be screened for renal function and electrolyte balance from the start of therapy and periodically during the first year. This will ensure the early detection and management of the ADR.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest to disclose.

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