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Hypokalemia: A potentially life-threatening complication of tenofovir therapy

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Abstract

Tenofovir is a nucleotide analog reverse transcriptase inhibitor approved for the treatment of HIV and hepatitis B infections. It is widely prescribed and an integral part of the recommended regimens for the treatment of HIV infection in antiretroviral-naive patients. Tenofovir is implicated in renal proximal tubular dysfunction, which can be associated with Fanconi syndrome and hypokalemia. When the hypokalemia is severe, it can lead to life-threatening complications. We describe the case of a 59-year-old woman who suffered a cardiac arrest secondary to severe hypokalemia from tenofovir use.

Keywords

Hypokalemia, tenofovir, renal tubular acidosis

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Introduction

Tenofovir is a nucleotide reverse transcriptase inhibitor used for the treatment of HIV infection and is a key component of the commonly used anti-retroviral drug, Truvada®. Tenofovir-induced proximal tubulopathy and dyselectrolytemia with or without Fanconi syndrome have been documented in the literature.[1,2] However, in general practice, the severity of these electrolyte disorders is often underestimated. We recently cared for a patient with HIV who developed severe hypokalemia and renal tubular acidosis (RTA) from tenofovir that lead to cardiac arrest.

Case presentation

A 59-year-old White female presented to our institution for weakness, failure to thrive, and hypokalemia. She had a history of HIV for ~8 years, well controlled on tenofovir containing anti-retroviral therapy. Before 4 months to presentation, she suffered a sudden cardiac arrest after a diarrheal episode and required intensive care unit (ICU) stay at an outside facility where she was told that her serum potassium at admission was "almost zero." Cardiac catheterization did not reveal any ischemic etiology, and she was discharged with oral potassium supplementation 40 mEq twice a day. However, she was feeling sick with weakness, nausea, intermittent vomiting, and weight loss and thus came to us. At presentation, her serum potassium was 2.5 mmol/L (3.5–5.1), magnesium 1.9 mg/dL (1.5–2.8), phosphate 1.6 mg/dL (2.7–4.5), and bicarbonate 13 mmol/L (22–28) with an anion gap of 14. Her renal function was preserved and had a mild proteinuria of ~0.5 g/g creatinine. Initial workup was negative for malignancy. We noted that she had glycosuria with normal serum glucose and had a potassium–creatinine ratio of 250 mmol/g and fractional excretion of phosphate 65%. We diagnosed her with tenofovir-induced proximal RTA with Fanconi syndrome. Her anti-retroviral therapy was changed to non-tenofovir–based regimen. At 2-month follow-up visit, her serum potassium was stable at 4.1 mmol/L on 40 mEq/day oral potassium supplementation.

Discussion

Tenofovir is a known mitochondrial toxin and inhibits DNA polymerase gamma, the enzyme responsible for replication

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of mitochondrial DNA. With limited anaerobic adenosine triphosphate (ATP)-generating capacity, the proximal tubule is vulnerable to mitochondrial dysfunction and may manifest as RTA or full-blown Fanconi syndrome.[3] The latter is characterized by hyperphosphaturia, renal glycosuria, aminoaciduria, and tubular proteinuria in addition to proximal (type 2) RTA. Decreased proximal tubular bicarbonate excretion is the hallmark of type 2 RTA, which leads to renal bicarbonate wasting and fall in serum bicarbonate levels. This increased delivery of bicarbonate results in increased intraluminal negativity in the distal nephron resulting in potassium secretion and wasting.[4] Patients on tenofovir therapy are prone to developing severe hypokalemia, especially when combined with gastro-intestinal losses and/or poor eating. Severe hypokalemia can result in complications such as cardiac arrhythmias as in our case or spontaneous rhabdomyolysis,[5] which in turn can lead to acute renal failure. These patients should be frequently monitored with urinalysis and renal function panel while on therapy. Raising the awareness among clinicians with regard to this potential side effect is vital for early intervention and prevention of life-threatening complications.

Declaration of conflicting interests

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Ethical approval

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Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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