Journal of the International Association of Providers of AIDS Care
Volume 17: 1–3

DOI: 10.1177/2325958218760846
journals.sagepub.com/home/jia
SAGE

Acute Trigeminal Neuralgia Associated with Initiation of Emtricitabine/Tenofovir for HIV Pre-Exposure Prophylaxis

Loraine Van Slyke, FNP-C[1], and Mia Scott, DO[1]

Abstract

HIV pre-exposure prophylaxis (PrEP) with emtricitabine (FTC) and tenofovir disoproxil fumarate (TDF) fixed-dose combination (FTC/TDF) is undergoing rapid scale-up in the United States. While FTC/TDF is typically well tolerated, to our knowledge, cranial nerve pathology associated with FTC/TDF has not been previously described. We report the case of a 35-year-old patient who began FTC/TDF PrEP and developed acute trigeminal neuralgia. The neurologic symptoms resolved after treatment discontinuation and recurred upon rechallenge, resulting in permanent discontinuation of PrEP treatment.

Keywords

neuralgia, tenofovir/emtricitabine, PrEP

Introduction

Pre-exposure prophylaxis (PrEP) with emtricitabine (FTC)/tenofovir disoproxil fumarate (TDF) fixed-dose combination (FTC/TDF) is an effective and guideline-recommended intervention to prevent HIV infection in at-risk populations.[1-3] Emtricitabine/TDF PrEP is typically very well tolerated, though treatment-related adverse events have been reported, which include, but are not limited to, gastrointestinal upset (nausea, weight loss, abdominal pain), headaches, bone mineral density loss, and elevated serum creatinine levels.[4-6] Neurologic symptoms related to FTC/TDF, either for PrEP or treatment of chronic HIV infection, are rarely reported. Here, we describe acute and reversible trigeminal neuralgia associated with the initiation of FTC/TDF PrEP.

Case Report

A 35-year-old patient presented to our primary care clinic to establish care and discuss PrEP. The patient self-identified as a man who has sex with other men, who was HIV negative, who was in an open sexual relationship with a seroconcordant partner, and was naive to previous PrEP treatment. He had no significant past medical history and was not currently taking any medication. The patient's social history included use of tobacco (2 cigarettes/week), alcohol (approximately 10 drinks/week), and marijuana (infrequently). Per current clinical guidelines, the initial appointment for PrEP included a laboratory workup and evaluation of HIV risk prior to initiation. Further, wellness blood work was drawn as part of the scheduled physical examination. Laboratory test results for PrEP were as follows: negative HIV-1/2 fourth-generation antigen; complete metabolic panel revealed a serum creatinine 0.9 mg/dL, eGFR 110 mL/min/1.73; and reactive hepatitis B surface antibody/negative hepatitis B core antibody (immunity established to hepatitis B), negative hepatitis A total antibody, negative hepatitis C antibody. All other wellness laboratory test results (uric acid, alkaline phosphatase, thyroid-stimulating hormone, lipid profile, complete blood count, hepatic function panel) were normal. Increased risk of HIV exposure and laboratory assessment rendered the patient as an appropriate candidate for PrEP therapy.

With safe prescribing discussion and agreement reviewed with the patient (ie, side effects, dosing, routine HIV and renal function screening, etc), he initiated FTC/TDF once daily. The patient returned for complete physical examination 6 days after initiation. Examination findings proved to be benign, and the patient disclosed excellent tolerance to therapy. From a wellness standpoint, he also received hepatitis A (1 of 2 in the series) and tetanus-diphtheria-pertussis (TDaP) vaccinations without

[1] APEX Research/Family Medicine, Denver, CO, USA

Corresponding Authors:
Loraine Van Slyke and Mia Scott, APEX Family Medicine, 300 South Jackson Street, Suite 100, Denver, CO 80209, USA.
Emails: lorainegvs@gmail.com; mialscott@yahoo.com

complications. At that time, the patient was instructed to follow up in 1 month to repeat PrEP laboratory testing (HIV and complete metabolic panel) and discuss medication concerns, if any.

Eight days after therapy initiation, the patient returned with complaints of new-onset left-sided facial paresthesia exacerbated within hours after each oral dose of FTC/TDF. The patient described the sensation as profound "pins and needles," and he demonstrated that the distribution of the sensation extended from the left external ear structure, along mandible, to mental region, consistent with trigeminal neuralgia, involvement of the V3 branch. Patient denied systemic symptoms (weakness, malaise, upper/lower extremity neuropathy, balance disturbance, rashes, fever, joint pain, dizziness, change in appetite), dysphagia, dysarthria, and changes in vision, taste, or hearing. The patient self-discontinued FTC/TDF 1 day prior to follow-up encounter and reported gradual improvement in symptoms. A neurological examination with emphasis on cranial nerve evaluation was performed and yielded benign findings. The patient stated no other concerns during encounter; ENT, cardiac, and respiratory evaluations were unremarkable, and vital signs were normal. The patient was instructed to continue withholding therapy until resolution of symptoms and neurological baseline were achieved.

The patient was instructed to follow up with a medication challenge to determine whether a correlation between FTC/TDF initiation and neurological deficits could be confirmed, as confounding variables include immunizations received during the physical examination. He was instructed to return to clinic for reevaluation in 3 weeks. Unfortunately, recommended follow-up did not occur, and the patient did not present to clinic for 3 months. During the final encounter, the patient reported rechallenging the therapy after symptoms had resolved and the same clinical progression of facial sensory disturbance presented within days of second initiation of FTC/TDF. The patient reports that symptoms were intolerable, which resulted in discontinuation of the medication.

Discussion

We believe that this is the first report of adverse effects of FTC/TDF affecting cranial nerves. While peripheral sensory neuropathy has been reported as a side effect with both emtricitabine and TDF used as part of HIV treatment,[7,8] there are no reports of involvement of cranial nerves or its association with trigeminal neuralgia in use as HIV PrEP. A PubMed literature search revealed only 1 study that explored a potential cause and effect relationship between PrEP use and neurological deficits. In this publication, only upper limb symptoms of motor and sensory abnormalities were reported.[9] The investigators suggest that neuropathy from FTC/TDF may be related to previously studied mitochondrial toxicity (trigged by increased lactate levels) associated with its drug class (nucleoside reverse transcriptase inhibitors); however, even in these previous studies[10,11] deficits have never been explicitly reported within the cranial nerve pathways, which may suggest other etiologies to neuropathy associated with FTC/TDF are at play. Additionally, it should be noted that limitations in Owino and researcher's study,[9] as self-stated by authors, include inability to rule out differential neurological diagnoses (eg, multiple sclerosis and acute disseminated encephalomyelitis) and the study participant's low adherence during the therapy's rechallenge. Similar limitations also apply to this case study; confirmatory testing of neuropathy through electromyography and/or evaluation of inflammatory markers were not completed and presence of such evaluations may have strengthened the report.

HIV PrEP is being scaled up in the United States, select European countries, sub-Saharan Africa, and Brazil (Krakower & Mayer, 2016).[12] Since FTC/TDF is currently the only approved therapy for the PrEP, surveillance for neuralgias, specifically surrounding cranial nerve deficits, may define the adverse event profile of treatment and assist in clinical management.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010;363(27):2587–2599.
2. Centers for Disease Control and Prevention (CDC). *Preexposure Prophylaxis for the Prevention of HIV Infection in the United States—2014: A Clinical Practice Guideline*. 2014. https://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf. Accessed February 15, 2018.
3. World Health Organization. Guidance on oral pre-exposure prophylaxis (PrEP) for serodiscordant couples, men, and transgender women who have sex with men at high risk of HIV. http://www.who.int/hiv/pub/guidance_prep/en/. 2012. Accessed February 15, 2018.
4. Peterson L, Taylor D, Roddy R, et al. Tenofovir disoproxil fumarate for prevention of HIV infection in women: a phase 2, double-blind, randomized, placebo-controlled trial. *PLoS Clin Trials*. 2007;2(5):e27.
5. Spinner C, Boesecke C, Zink A, et al. HIV pre-exposure prophylaxis (PrEP): a review of current knowledge of oral systemic HIV PrEP in humans. *Infection*. 2016;44(2):151–158.
6. TRUVADA® (emtricitabine/tenofovir disoproxil fumarate) tablets, for oral use [prescribing information]. *Foster City*, CA: Gilead Sciences I; 2013.
7. Clay PG, Taylor A, Glaros A, et al. "One pill, once daily": what clinicians need to know about Atripla™. *Ther Clin Risk Manag*. 2008;4(2):291–302.
8. Fabbiani M, Mondi A, Colafigli M, et al. Safety and efficacy of treatment switch to raltegravir plus tenofovir/emtricitabine or abacavir/lamivudine in patients with optimal virological control: 48-week results from a randomized pilot study (Raltegravir Switch for Toxicity or Adverse Events, RASTA Study). *Scand J Infec Dis*. 2013;46(1):34–45.

9. Owino F, Mandala J, Amibia J, Agot K, Damme LV. Neurological syndrome in an HIV-prevention trial participant randomized to daily tenofovir disoproxil fumarate (300 mg) and emtricitabine (200 mg) in Bondo, Kenya. *Int Med Case Rep J*. 2013;6:91–93.
10. Osler M, Stead D, Rebe K, Meintjes G, Boulle A. Risk factors for and clinical characteristics of severe hyperlactataemia in patients receiving antiretroviral therapy: a case-control study. *HIV Med*. 2010;11(2):121–129.
11. Gerard Y, Maulin L, Yazdanpanah Y, et al. Symptomatic hyperlactataemia: an emerging complication of antiretroviral therapy. *AIDS*. 2000;14(17):2723–2730.
12. Krakower DS, Mayer KH. The role of healthcare providers in the roll-out of PrEP. *Curr Opin HIV AIDS*. 2016;11(1):41–48.