CLINICAL VIGNETTE

Vertigo from tenofovir disoproxil fumarate for Pre-exposure Prophylaxis for HIV

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Introduction

Pre-exposure prophylaxis (PrEP) for prevention of HIV infection was approved by the US Food and Drug Administration in 2012.[1] It is recognized as a mainstay in the fight to end the worldwide HIV/AIDS pandemic. Side effects from the medications used for PrEP may impact adherence with the medication, and when severe or persistent may lead to discontinuation of therapy. This vignette highlights an uncommon side effect of PrEP and subsequent management.

Presentation

An asymptomatic 46-year-old man who has sex with men (MSM) with a past medical history significant for anxiety was seen following a change in his relationship status. He anticipated the likelihood of new sexual partners and requested to start PrEP to prevent HIV infection. His evaluation included: negative 4th generation HIV antigen/antibody testing; negative RPR; negative urine, oropharyngeal and rectal gonorrhea/ chlamydia PCR; confirmed hepatitis B vaccination status; normal serum creatinine and urinalysis. Following a discussion of risks and benefits, he was started on tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) fixed dose combination for PrEP and advised to continue condom usage for prevention of other sexually transmitted infections.

The patient returned with a new complaint of acute dizziness. The patient had taken a first dose of TDF/FTC the prior morning, without other new or changes in medication. Approximately 12 hours after taking TDF/FTC he had acute onset of dizziness, which was described as room spinning. Vertigo was associated with generalized sensation of pressure in the head as well as nausea and an episode of vomiting. He denied diarrhea and abdominal bloating. These symptoms improved with rest in a dark room and were exacerbated by movement. His symptoms worsened during the encounter and he received a bolus of parenteral normal saline and ondansetron, which provided relief. TDF/FTC was discontinued, and the patient was referred to an HIV medicine specialist for presumed adverse reaction and consideration of alternatives.

He was seen a week later and reported symptoms had slowly resolved over 3 days, without recurrence. The patient remained concerned about the possibility of future HIV infection and was interested in attempting tenofovir alafenamide/emtricitabine (TAF/FTC) as an alternative to TDF/FTC for PrEP. Telephone follow-up was completed one week after starting TAF/FTC, and the patient denied any side effects following the medication change.

Discussion

TDF/FTC for pre-exposure prophylaxis is highly effective in preventing the transmission of HIV. In cis-gendered MSM it is 96-99% effective in preventing HIV infection with good adherence and when protective levels are detectable in blood.[2,3] It is also effective in reducing HIV transmission in heterosexual men and women by 90% when the drug is detectable in blood.[4] Once daily administration of TDF/FTC for sexually active adults was approved by the FDA in 2012.[1] Since approval, there has been widespread uptake primarily among MSM, barriers in cost and insurance coverage limiting use in the 1.1 million estimated to be at risk of HIV infection in the United States.[5] In 2019, the United States Preventative Services Taskforce added the use of PrEP for individuals at high risk of HIV exposure as a class A recommendation.[6]

In general, TDF/FTC is well tolerated, and severe side effects are uncommon. The most common side effect of TDF/FTC in HIV uninfected people is nausea in approximately 9% and frequently resolves after the first month.[2] Other common side effects of TDF/FTC are diarrhea, headache and dizziness, but these are rarely significant enough to necessitate discontinuation of the drug.[7] More familiar to many providers is the risk of renal dysfunction including decreases in eGFR, proximal renal tubular dysfunction, and Fanconi Syndrome, which are caused by the TDF component of the fixed dose formulation.[8] TDF has also been shown to decrease bone mineral density in some patients, although degree of clinical relevance in patients taking it for PrEP is still unclear.

Concern for nephrotoxicity and decreased bone mineral density with TDF/FTC lead to the development of TAF/FTC. TAF is a novel prodrug of tenofovir that is metabolized into its active component intracellularly, thereby decreasing systemic exposure to the active drug.[9] This novel formulation shows statistically significant differences that favor TAF with respect to renal function and bone health. In a 96-week trial, TAF/FTC was found to be non-inferior to TDF/FTC for PrEP in MSM and transgender women.[10] It received FDA approval for this indication in fall of 2019.[11] Other adverse effects were similar between the two drugs although nausea was more common with

TAF/FTC and headache was more common with TDF/FTC. Dizziness was not reported as a side effect in this study.

Although both TDF and TAF are both pro-drugs of tenofovir, their respective adverse effect profiles are different. To date, large trials comparing these two drugs both for the treatment of HIV-1 as well as for HIV-1 prevention have focused primarily on adverse effects on renal function and bone mineral density. The same attention has not been applied to other adverse effects because they are less likely to rise to the level of clinical significance. TDF/FTC remains the preferred option for PrEP, but TAF/FTC is an alternative for those with renal dysfunction or decreased bone mineral density. It may be an alternative for MSM and transgender women who are unable to tolerate adverse effects of TDF/FTC. TAF/FTC for PrEP has not been studied in other populations.

Conclusion

PrEP with TDF/FTC is highly efficacious for the prevention of HIV transmission and is the preferred agent for PrEP based on efficacy, tolerability and years of experience. TAF/FTC is non-inferior to TDF/FTC for PrEP and is an alternative for those with or at risk for kidney disease, or osteoporosis/osteopenia. It is also an alternative for those with intolerable side effects to TDF/FTC.

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