



(CASE REPORT)



## A case report on tenofovir induced osteoporosis

Bhavani Dhomakonda <sup>1,\*</sup>, N. MSreeja <sup>1</sup>, Y. Vidhya Reddy <sup>1</sup>, Ankith Reddy <sup>1</sup> and Tadikonda Rama Rao <sup>2</sup>

<sup>1</sup> Department of Pharmacy Practice, CMR College of Pharmacy, Hyderabad, Telangana, India.

<sup>2</sup> Principal and Professor, CMR College of Pharmacy, Hyderabad, Telangana, India.

International Journal of Science and Research Archive, 2024, 11(02), 183–185

Publication history: Received on 15 January 2024; revised on 25 February 2024; accepted on 27 February 2024

Article DOI: <https://doi.org/10.30574/ijrsra.2024.11.2.0353>

### Abstract

The antiretroviral drug tenofovir, is a nucleotide analogue which is used in the treatment of HIV and hepatitis B infections. This drug works by inhibiting the HIV reverse transcriptase enzyme and prevent the synthesis of viral DNA. It is administered as a single 300 mg tablet once daily. This drug is mostly used in the combination with lamivudine, dolutegravir (TLD regimen). Although there has been success in the use of tenofovir in treating HIV infection, there have been some adverse effects associated with it. Multiple studies have implicated tenofovir associated bone loss and renal failure. In order to treat the adverse effects which are caused due to tenofovir, an alternate drug should be administered.

**Keywords:** Tenofovir; Reverse Transcriptase; TLD regimen; Bone loss

### 1. Introduction

Tenofovir disoproxil fumarate functions as a biologically available prodrug, converting to tenofovir, a potent nucleotide analogue reverse-transcriptase inhibitor effective against both human immunodeficiency virus (HIV) and hepatitis B virus. Approved by the US Food and Drug Administration (FDA) for HIV infection treatment since October 2001, this adenine 5' monophosphate analogue, tenofovir disoproxil fumarate, has rapidly become a prevalent element in antiretroviral treatment regimens. It is administered as a single 300-mg tablet once daily. Approved for HIV infection treatment based on clinical trial data showcasing its efficacy in treatment-experienced patients, it was later confirmed to be effective as part of initial therapy<sup>[1]</sup>. When administered without food, the oral bioavailability of tenofovir is 25%. With multiple doses of 300 mg tenofovir once daily, the median maximum serum concentration of 326 ng/ml at steady state is achieved approximately 2.3 hours after administration. Tenofovir exhibits a median serum terminal elimination half-life of 14.4 hours and is predominantly eliminated unchanged through the kidneys. Given its lack of inhibition on cytochrome P450 enzymes, it is anticipated to have minimal drug interactions with medications metabolized via this pathway<sup>[2]</sup>. Dolutegravir, in combination with tenofovir and lamivudine (TLD), is accessible for virologically-suppressed patients transitioning from NNRTI-based first-line regimens<sup>[3]</sup>.

Nucleoside reverse transcriptase inhibitors (NRTIs) serve as the fundamental component of highly active antiretroviral therapy (HAART) for effectively managing human immunodeficiency virus (HIV) infection clinically. NRTIs act on HIV reverse transcriptase, halting the production of viral DNA. Despite the significant effectiveness of tenofovir in HIV treatment, clinical observations have highlighted the occurrence of side effects linked to its use, with several studies indicating tenofovir-related bone loss as a notable concern. HIV infection has been identified as a risk factor for changes in bone mineral density, affecting both children and adults. Disruptions in growth factors and cytokines, along with the administration of HAART, may contribute to bone loss by elevating bone resorption<sup>[4]</sup>.

\*Corresponding author: Bhavani Dhomakonda

---

## 2. Case report

A 40 year old female patient is admitted in the general medicine department with a chief complaints of large joint pains associated with morning stiffness since 4 months, she is having difficulty in walking – walking with support since 2 months, patient is having a history of on and off fever, tingling sensation from calf to ankle, decreased sensation/ numbness over foot and burning sensation of B/L lower limbs since 6 months. Patient is a known case of RVD positive and on TLD regimen (tenofovir disoproxil, lamivudine, dolutegravir). On examination the patient is conscious and coherent, Afebrile, with a Blood pressure of 110/70 mm hg, Pulse rate – 88 bpm, CVS – S1 S2 Positive, RS – BAE Positive, P/A – soft. Laboratory investigations shows that complete blood picture was normal, serum calcium was found to be 9.8, vit b12 – 258, vit d – 23.7. The bone mass density test was performed and T- score was found to be -3.3 (t score - 2.5 and below indicates the patient is likely having osteoporosis), and z-score was -2.9 (a score below -2.0 indicates less bone mass). Alkaline phosphatase range is 257 which is higher than normal. Based on the subjective data and objective data the patient was diagnosed with Tenofovir induced osteoporosis due to long term use of TLD regimen. The physician changed the TLD regimen to ALD regimen (abacavir-lamivudine, dolutegravir) and physician prescribed Inj. Teriparatide 20 mcg s.c, Inj. Zoledronate IV to treat osteoporosis after checking the PTH levels. He also prescribed vit d 6000 iv weekly once as the vit d levels are lesser than normal, T. calcium 500 mg OD, inj. Multivitamin 1 ampule in 100 ml NS IV OD, T.IFA+VIT C OD, Cap collagen BD are prescribed.

---

## 3. Discussion

This case illustrates the adverse effect of the drug tenofovir. Tenofovir is a nucleotide analogue reverse transcriptase inhibitor, which block reverse transcriptase, an enzyme necessary for viral production in HIV and hepatitis B individuals<sup>[1]</sup>. This drug is used in the combination with lamivudine and dolutegravir (TLD regimen). While typically regarded as safe and well tolerated, there have been emerging concerns regarding potential long-term side effects linked to extended use, particularly focusing on the reported negative effects on bone mineral density (BMD). Diminished bone mineral density (BMD) frequently occurs among individuals living with HIV<sup>[5]</sup>. In the above case, the patient is RVD positive and is on TLD regimen, on prolonged use of TLD regimen, the patient developed osteoporosis. After the diagnosis, the TLD regimen (tenofovir disoproxil, lamivudine, dolutegravir) was changed to ALD regimen (abacavir-lamivudine, dolutegravir). Based on a conducted study, transitioning from tenofovir to abacavir appears to have a beneficial impact on bone tissue. This change also led to elevated levels of circulating sclerostin, a factor linked with enhancements in bone characteristics like density, microarchitecture, and strength, thereby reducing fracture risk<sup>[6]</sup>.

---

## 4. Conclusion

Long term use of the antiretroviral drug tenofovir is associated with the bone mineral density loss. However, the bone mineral density loss due to tenofovir is reversible. In this case, the TLD regimen (tenofovir disoproxil, lamivudine, dolutegravir) is changed to ALD regimen (abacavir-lamivudine, dolutegravir) and Inj. Teriparatide 20 mcg s.c, Inj. Zoledronate IV is given for the treatment of osteoporosis. Early diagnosis of this adverse effect and initiation of the alternate treatment will result in rapid recovery and good outcome as seen in our patient.

---

## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

---

## References

- [1] Joel E. Gallant, Stanley Deresinski, Tenofovir Disoproxil Fumarate, Clinical infectious diseases, 2003 Oct 1;37(7):944-50. <https://doi.org/10.1086/378068>.
- [2] Katherine A. Lyseng-Williamson, et al., Tenofovir Disoproxil Fumarate: A review of its use in the management of HIV infection, volume 65, 413-432, (2005). Doi: 10.2165/00003495-200565030-00006
- [3] Claire M Keene, et al., Virologic efficacy of tenofovir, lamivudine and dolutegravir as second-line antiretroviral therapy in adults failing a tenofovir-based first-line regimen: a prospective cohort study, AIDS.2021 Jul 15; 35(9): 1423-1432. Doi: 10.1097/QAD.0000000000002936

- [4] Iwen F Grigsby , et al., Tenofovir- associated bone density loss , 2010;6: 41-47.
- [5] Brown TT, Qaqish RB, et al., Antiretroviral therapy and the prevalence of osteopenia and osteoporosis: a meta-analytic review.AIDS.2006;20:2165-2174. Doi:10.1097/QAD.0b013e32801022eb.
- [6] EugeniaNegredo , et al., Switching from tenofovir to abacavir in HIV -1- infected patients with low bone mineral density: changes in bone turnover markers and circulating sclerostin levels , 2015 Jul;70(7):2104-7. <https://doi.org/10.1093/jac/dkv063>