MedCrave
Step into the World of Research

Journal of Liver Research, Disorders & Therapy

Case Report

Open Access

CrossMark

First report of primary tenofovir resistance in a hepatitis b viral hepatitis patient from India without human immunodeficiency virus co-infection

Abstract

Tenofovir confers potent and durable HBV-DNA suppression; we do not know the best strategy in case of resistance of HBV to reverse transcriptase inhibitor Tenofovir. Levels of Tenofovir resistance in individuals with viral failure ranged from 20% in Europe to more than 50% in sub-Saharan Africa. Here we are doing case reporting of a rare case of resistance to Tenofovir in a patient with Hepatitis B related hepatitis without HIV co-infection. No past history of exposure, strict compliance was there, HIV and HCV were negative. Any systemic diseases that might have been able to explain the drug inefficacy and pharmacological history excluded a possible drug-drug interaction.

Keywords: virus, hepatitis, tenofovir resistance, mutation, nucleos(t)ide analogue

Volume 2 Issue 5 - 2016

Vijay Sharma,[1] Sharma R,[2] Gaurav G[3]

[1]Department of Gastroenterology, Manipal Hospital, India
[2]Department of Public health, Regional institute of Health medicine and research, India
[3]Department of Gastroenterology, Medipulse Hospital, India

Correspondence: Vijay Sharma, Department of Gastroenterology, Manipal Hospital, Vidhyadhar Nagar, Sikar Road, Jaipur, Rajassthan, India, Tel +9199 2801 5254, +9 1401 9159, Email vijaysadashiv@gmail.com

Received: August 17, 2016 | **Published:** December 02, 2016

Abbreviations: HBV, hepatitis b virus; HIV, human immunodeficiency virus

Introduction

Nucleos(t)ide analogs such as Tenofovir, Lamivudine or Emtricitabine work well against both HBV and HIV. Tenofovir confers potent and durable HBV-DNA suppression but the best strategy in case of resistance of HBV to reverse transcriptase inhibitor Tenofovir remains unknown. New tests are being developed to study HBV resistance.[1,2] Levels of Tenofovir resistance in individuals with viral failure ranged from 20% in Europe to more than 50% in sub-Saharan Africa.[3,4] it is likely that 7·5-17·5% of individuals given Tenofovir plus cytosine analogue plus Efavirenz will develop Tenofovir resistance within 1 year of treatment initiation under present practices in sub-Saharan Africa. One study has reported HBV genotypes quasi species diversity and drug resistance mutations in antiretroviral treatment naive and treatment experienced HBV-HIV co-infected patients[5,6] apart from case reports of prolonged and intermittent treatment of HIV with Lamivudine and Tenofovir and development of resistant to Lamivudine and Tenofovir, while HIV-RNA remained constantly suppressed. Here we are reporting a case of resistance to Tenofovir in a patient with Hepatitis B virus related hepatitis without HIV co-infection.

Patient and method

Patients were 59years old female, which consulted Gastroenterologist, baseline Hepatitis B Viral DNA level was 5,49,1000IU/ml and transaminase were more than two times normal. *Fibroscan* was done to grade and stage fibrosis, her kPa score was 8.6, Alpha fetoprotein level was 3.79IU/ml and HBeAg level was 111.64. Patient was started on Tenofovir disoproxil fumarate 300mg, one tablet daily (Brand Name Tanvir, Cipla Limited, which is one of the largest pharmaceutical companies in India, well known for cost effective high efficacy antiviral and other medicines). After one month of Tenofovir treatment first HBV DNA level was 3210 IU/ml. Patient continued same treatment and was on regular follow up at outpatient department. After 6months HBV DNA level was 674000IU/ml, on further history taking patient was on regular follow up, patient regularly purchased medicine from hospital pharmacy, patient confirmed that she took medicine regularly every single day, no history of any other medicine intake which could decrease efficacy of Tenofovir or increase its metabolism or we excluded any drug-drug interaction thoroughly. Clinical evaluation and laboratory findings excluded the presence of systemic diseases that might have been able to explain the drug inefficacy, resistance to medicine and/or rapid loss of medicine from body, there was no past history of exposure to Tenofovir, as patient was highly motivated, educated, college professor she was having all the records of regular visits, pharmacy shop purchase record were also available. On testing HIV and HCV were negative. We suspected possible resistance to Tenofovir. Patient consented for further high cost testing. First patients serum sample was sent for mutation study and genotyping and tablet Tenofovir was stopped, Tablet Entecavir (Brand name Entavir from Cipla Limited) 1mg once daily was started, which was well-tolerated. Report of mutation study and genotyping revealed A181T/V mutation with A194T and M204V/I, these mutations are associated with resistant to Lamivudine, Adefovir, Tenofovir and there was no reported resistance to Entecavir and Telbivudine. After one month, 3month and 6month treatment with Entecavir 1mg daily, HBV DNA level decreased to 3600IU/ml, transaminase level normalized on follow up. This unique mutation has been reported from different centers as case reports, mostly in HIV HBV co-infected cases with virological failure. Possible our patient acquired drug resistant Hepatitis B virus from some patient with HIV-HBV co-infection, another patient was taking antiretroviral, she did not get infected with HIV but developed Hepatitis B hepatitis possibly due to low inoculums size, possible she acquired infection from healthcare worker, this healthcare worker got HIV. possibly patient saved himself after exposure to blood product or body fluid of HIV infected patient took antiretroviral prophylaxis but did not take precaution for HBV, may be patient was in window period that time so HBV was negative, only HIV prophylaxis was taken care

off. Replacing Entecavir to failed therapy with Tenofovir is feasible, well-tolerated and results in virological success. Various studies have shown that Tenofovir is a drug of choice as a drug of choice apart from Entecavir for YMDD motif mutation and resistance to Lamivudine,[7,8] now multidrug resistant mutants are developing, future of HBV and HIV control seems difficult. In other reports Hepatologists have used Entecavir plus Tenofovir combination therapy for chronic hepatitis B in patients with previous nucleos(t)ide treatment failure.[9]

Conclusion

This is a First report from India of occurrence of Tenofovir mutation A181T/V, A194T and M204V/I in a non HIV infected patient with HBV hepatitis, without any prior irregular Tenofovir treatment and without drug-drug interaction.

Acknowledgements

None.

Conflict of interest

Author declares that there is no conflict of interest.

References

1. Chantratita W, Song KS, Pongthanapisith V, et al. HBV/4DR 9G tests and its Comparison with INNO-LiPA HBV Multi-DR test for the detection of drug-resistant Hepatitis B Virus. *J Virol Methods*. 2016;237:58–63.
2. Jiang B, Dai CY, Li XM, et al. [Drug-resistant mutations in hepatitis B virus found in chronic HBV carriers using PCR sequencing technology]. *Zhonghua Gan Zang Bing Za Zhi*. 2016;24(1):36–39.
3. Ford N, Vitoria M, Doherty M, et al. Tenofovir resistance and first-line antiretroviral therapy. *Lancet Infect Dis*. 2016;16(8):890–891.
4. TenoRes Study Group. Global epidemiology of drug resistance after failure of WHO recommended first-line regimens for adult HIV-1 infection: a multicentre retrospective cohort study. *Lancet Infect Dis*. 2016;16(5):565–575.
5. Archampong TN, Boyce CL, Lartey M, Sagoe KW, Obo-Akwa A, et al. HBV genotypes and drug resistance mutations in antiretroviral treatment-naive and treatment-experienced HBV-HIV coinfected patients. *Antivir Ther*. 2017;22(1):13–20.
6. Audsley J, Bent SJ, Littlejohn M, et al. Effects of long-term Tenofovir-based combination antiretroviral therapy in HIV-hepatitis B virus coinfection on persistent hepatitis B virus viremia and the role of hepatitis B virus quasispecies diversity. *AIDS*. 2016;30(10):1597–1606.
7. Zoulim F, Warzecha JB, Diculescu MM, et al. Entecavir plus Tenofovir combination therapy for chronic hepatitis B in patients with previous nucleos(t)ide treatment failure. *Hepatol Int*. 2016;10(5):779–788.
8. Utku AC, Karabay O. Treatment of chronic hepatitis B patients with tyrosine-methionine-aspartate-aspartate mutations. *World J Gastroenterol*. 2016;22(4):1727–1728.
9. Park JY, Kim CW, Bae SH, et al. Entecavir plus Tenofovir combination therapy in patients with multidrug-resistant chronic hepatitis B: results of a multicentre, prospective study. *Liver Int*. 2016;36(8):1108–1115.