

Lamivudine Continuation/Tenofovir Add-on Adversely Affects Treatment Response among Lamivudine Non-Responder HIV-HBV Co-Infected Patients from Eastern India

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Abstract : Presently, tenofovir disoproxil fumarate (TDF) is the most effective anti-viral agent for the treatment of hepatitis B virus (HBV) in individuals co-infected with HIV and HBV as TDF has activity to suppress both wild-type and lamivudine (3TC)-resistant HBV. However, suboptimal response to TDF was reported in HIV-HBV co-infected individuals with prior 3TC therapy from different countries recently. The incidence of 3TC-resistant HBV strains is quite high in HIV-HBV co-infected patients experiencing long-term anti-retroviral therapy (ART) in eastern India. In spite of this risk, most of the patients with long-term 3TC treatment are continued with the same anti-viral agent in this country. Only a few have received TDF in addition to 3TC in the ART regimen since TDF has been available in India for the treatment of HIV-infected patients in 2012. In this preliminary study, we investigated the virologic and biochemical parameters among HIV-HBV co-infected patients who are non-responders to 3TC treatment during the continuation of 3TC or TDF add-on to 3TC in their ART regimen. Fifteen HIV-HBV co-infected patients who experienced long-term 3TC (mean duration months 36.87 ± 24.08 months) were identified with high HBV viremia ($> 20,000$ IU/ml) or harbouring 3TC-resistant HBV. These patients receiving ART from School of Tropical Medicine Kolkata, the main ART centre in eastern India were followed-up semi-annually for next three visits. Different virologic parameters including quantification of plasma HBV load by real-time PCR, detection of hepatitis B e antigen (HBeAg) by commercial ELISA and anti-viral resistant mutations by sequencing were studied. During three follow-up among study subjects, 86%, 47%, and 43% had 3TC-mono-therapy (mean treatment-duration 41.54 ± 18.84 , 49.67 ± 11.67 , 54.17 ± 12.37 months respectively) whereas 14%, 53%, and 57% experienced TDF in addition to 3TC (mean treatment duration 4.5 ± 2.12 , 16.56 ± 11.06 , and 23 ± 4.07 months respectively). Mean CD4 cell-count in patients receiving 3TC was tended to be lower during third follow-up as compared to the first and the second [520.67 ± 380.30 (1st), 454.8 ± 196.90 (2nd), and 397.5 ± 189.24 (3rd) cells/mm³] and similar trend was seen in patients experiencing TDF in addition to 3TC [334.5 ± 330.218 (1st), 476.5 ± 194.25 (2nd), and 461.17 ± 269.89 (3rd) cells/mm³]. Serum HBV load was increased during successive follow-up of patients with 3TC-mono-therapy. Initiation of TDF lowered serum HBV-load among 3TC-non-responders at the time of second visit ($< 2,000$ IU/ml), interestingly during third follow-up, mean HBV viremia increased > 1 log IU/ml (mean 3.56 ± 2.84 log IU/ml). Persistence of 3TC-resistant double and triple mutations was also observed in both the treatment regimens. Mean serum alanine aminotransferase remained elevated in these patients during this follow-up study. Persistence of high HBV viraemia and 3TC-resistant mutation in HBV during the continuation of 3TC might lead to major public health threat in India. The inclusion of TDF in the ART regimen of 3TC non-responder HIV-HBV co-infected patients showed adverse treatment response in terms of virologic and biochemical parameters. Therefore, serious attention is necessary for proper management of long-term 3TC experienced HIV-HBV co-infected patients with high HBV viraemia or 3TC-resistant HBV mutants in India.

Keywords : HBV, HIV, TDF, 3TC-resistant

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