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Treatment of chronic hepatitis B patients with tyrosine-methionine-aspartate-aspartate mutations

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Abstract

Lamivudine is an antiviral used for the treatment of chronic hepatitis B. Several studies have reported various mutations that are induced by lamivudine therapy. These mutations in the tyrosine-methionine-aspartate-aspartate (YMDD) motif are necessary and sufficient to confer high-level lamivudine resistance. During treatment with lamivudine, mutations develop in the YMDD motif of the hepatitis B virus (HBV) polymerase gene and lamivudine cannot prevent the replication of the mutant form. The virulence strain of developed mutation in the polymerase gene is lower than the original virus and they are susceptible to treatment with some other nucleoside analogs except lamivudine. Entecavir and tenofovir are potent HBV inhibitors and they can be confidently used as first line monotherapies. We read the article written by Tan *et al* that lamivudine therapy improved the clinical course in HBV patients with natural YMDD mutations. We think that lamivudine use for this patient group is not appropriate. These patients should use YMDD mutant form-effective drugs such as adefovir, tenofovir.

Key words: Hepatitis B; Lamivudine; Tyrosine-methionine-aspartate-aspartate mutation; Drug resistance; Treatment

Core tip: Lamivudine is a nucleoside analogue that has been used in treatment of chronic hepatitis B. The only drawback of lamivudin is drug resistance during the treatment. Entecavir and tenofovir are potent hepatitis B virus inhibitors with a high barrier to resistance . They can used as first-line monotherapies. The main problem of lamivudine treatment is development of mutation in the tyrosine-methionine-aspartate-aspartate (YMDD) motif. Treatment with lamivudine may cause exacerbation of hepatitis in patients with YMDD mutation. These patients should use YMDD mutant form-effective drugs.

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TO THE EDITOR

We read the article entitled "Natural YMDD-motif mutants affect clinical course of lamivudine in chronic hepatitis B" by Tan *et al*[1] with great interest. However, we think that some points about the study need to be clarified. High resistance barrier drugs (*e.g.*, tenofovir, entecavir) are recommended in chronic viral hepatitis in many countries. The explanations of the authors about the reason of administering lamivudine to the patients under risk are necessary for readers, since administering lamivudine to patients with high viral load and possible tyrosine-methionine-aspartate-aspartate (YMDD) resistance mutation is risky. Therefore, we need to explain to such patients with high viral load (mean HBV-DNA: 6.67 ± 2.47 $\log_{10}$ genome equivalents) regarding the reason for the use of lamivudine. Current guidelines suggest that more potent drugs such as tenofovir or entecavir should be used in this patient group[2]. If a patient has YMDD mutation, we think that lamivudine use for this patient group is not appropriate. Use of lamivudine in these patients will select resistant mutants and treatment of the patient will be more difficult. Adefovir or tenofovir would be more appropriate in such a patient. If the viral load is low in the YMDD mutation patient group, interferon could be also used. We think that readers of this article will understand it more clearly were authors to explain this subject more fully.

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