

LETTER to the EDITOR

Prevalence of Common YMDD Motif Mutations in Long Term Treated Chronic HBV Infections in a Turkish Population

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Dear Editor

We read the article published by Alagozlu et al. (2013) with interest. The authors found that 100% of chronic HBV patients who underwent antiviral therapy using either lamivudine/adefovir alone or in combination, contained either silent (24.4%) or missense (75.6%) mutations in their YMDD motif of HBV polymerase proteins. A variety of unusual silent mutations were found in the former group. Authors did not present the details for treatment regimen for patients group. Therefore, the mutation profiles in the text cannot be assigned to the type of drug-used. However, some comments deserve to mention. Interestingly, authors found a population of transitions/transversion nucleotide substitutions that might have some impacts on HBV combination therapy. Our unpublished data on Iranian genotype D patients (the same main genotype circulating in Turkey) confirms such hypothesis. We investigated the mutational profile for 3 similar groups as Alagozlu et al's study (Mahabadi et al., 2013). In Lamivudine-only group, we found F221Y/S and L229G which are related to adefovir (ADV) resistancy. W153Q, I169T, A200V and S202G which are related to Lamivudine-resistancy were found in ADV-only group. Finally, highest frequency of substitutions for residues L180M (43.7%) and M204I/V (68.7%) were found for Lamivudine/ADV combination group than all other groups. L217R and L229M/W were found in combination group. All of these patients showed partial resistance to these drugs, thus, they switched to other new anti-HBV nucleoside analogues regimen. Among 100 treatment-naïve patients (control group), we found a variety of above mono/combo mutations in an average of 1-8%. Similarly, in another national-based retrospective study, 2.4 to 17.3% of treatment naïve patients contained a cocktail of either mono- or combination related mutations; *ii*) Therefore the silent mutations found in Alagozlu study, highlights significant concerns about the potential role of such mutations on the evolution of HBV in patients under therapy.

Finding of 58.5% wild type genotype instead of mutations in YMDD in Alagozlu's study in some patients is not surprising, as direct sequencing usually fails to detect about 25% of exact mutational patterns of the samples studied. Thus, the existence of other mutational profile in a viral pool quasi-species with wild type dominance cannot be ruled out.

Taken together, we believe that a genotypic and/or phenotypic assay (s) should be performed before starting treatment for the chronic HBV patients who are candidate for therapy to identify the mutational profile of patients to avoid partial/typical resistance occurrence.

References

- Alagozlu H, Ozdemir O, Koksall B, Yilmaz A, Coskun M (2013). Prevalence of common YMDD motif mutations in long term treated chronic HBV infections in a Turkish population. *Asian Pac J Cancer Prev*, **14**, 5489-94.
- Mahabadi M, Norouzi M, Alavian SM, et al (2013). Drug-related mutational patterns in hepatitis B virus (HBV) reverse transcriptase proteins from Iranian treatment-naïve chronic HBV patients. *Hepat Mon*, **13**, 6712.

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