Antiviral efficacy of entecavir monotherapy in adefovir-resistant chronic hepatitis B: focus on genotypic mutation patterns

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Background/Aim: Entecavir (ETV) has been regarded as an effective agent to adefovir (ADV) resistance, but its antiviral efficacy, especially in terms of ADV signature mutation types, has not been elucidated so far. The purpose of this study is to assess the antiviral efficacy of ETV on multidrug-resistant mutation of A181V/T. Methods: We assessed consecutive 57 patients on ETV due to sequential lamivudine (LAM)- and ADV-resistant CHB. Antiviral efficacy was evaluated according to ADV resistant mutation patterns as following; A181V/T (n=33), N236T (n=9) and A181V/T+N236T (n=15). Results: The median age was 47.4 (range 24-66) years, 50 (86%) patients were males, and 45 (79%) patients were HBeAg positive. The median baseline viral load was 4.94 log 10 IU/ml (range 1.78-8.23) and the median duration of follow-up was 22 months (range 6-60). There was no significant difference in the baseline DNA levels among the three subgroups. A higher drop of HBV DNA level was achieved in A181V/T group at week 24 (-2.24±0.38 vs. -0.07±0.95 vs. -2.09±0.69 log10copies/ml, p=0.686). The mean reduction of HBV DNA level at week 48 was -1.57±0.34, -0.41±0.69, -2.24±0.61 log 10 IU/ml in A181V/T group, N236T group, A181V/T+N236T group, respectively (p=0.401). There were no significant differences in virologic breakthrough and virologic response and serologic response among the three subgroups at week 48. Serum alanine aminotransferase normalization was significantly higher in A181V/T subgroup at week 48 (44% vs. 0% vs. 14%, p=0.021). Conclusion: The response to ETV monotherapy was suboptimal in patients with previous sequential LAM-ADV therapy. The A181V/T mutation showed higher virologic response at week 24 and higher rate of ALT normalization at week 48 compared with other mutation types. Long-term therapy requires careful monitoring of viral load and genotypic resistance.