HBV resistance frequency in nucleos(t)ide analogue-untreated patients from different Brazilian regions


Background - Presence of viral variants with drug-resistance mutations in drug-naive hepatitis B virus (HBV) infected patients can seriously compromise response to antiviral treatment. Therefore, our study aimed to determine the prevalence of HBV with drug-resistance in 557 untreated chronic hepatitis B (CHB) patients from five different geographic regions of Brazil. Methods – HBV reverse-transcriptase (RT) region was sequenced and mutations associated with resistance to NA inhibitors were analyzed. Amino acid changes potentially associated with resistance were also investigated. Furthermore, HBV genotypes and subgenotypes were determined by phylogenetic analysis of the sequences. Results – HBV genotypes A [A1 (66.8%), A2 (2.3%)] and D [D1 (0.5%), D2 (4.3%), D3 (11.8%), D4 (6.6%)] were the most prevalent in Brazil, but genotypes B1 (0.2%), B2 (0.2%), C2 (0.7%), E (0.7%), F2a (4.5%), F4 (0.4%) and G (0.5%) were also found. Overall, 1.8% (10/557) of the patients carried HBV variants with primary drug-resistance mutations [rtM204V/I (0.4%); rtM204V + rtS202G (0.4%); rtA181T (0.4%); rtM250I (0.2%); rtA194T (0.4%)]. The four strains with mutation at position 204 also had compensatory mutations [rtL180M (3/4); rtL180M + rtV207I (1/4). One patient was infected with HBV variant only with compensatory mutations (rtV173L + rtL180M). Thirty (5%) patients were infected with strain harboring some of that mutation potentially associated with Adefovir resistance [rtS85A (n=1), rtV214A (n=6), rtQ215S (n=14), rtI233V (n=6), rtN238T (n=4), rtN238D (n=5)]. Additionally, we observed in 18 (3.2%) patients the presence of variants with novel amino acid substitutions at positions reported to be potentially associated with Adefovir resistance: rtV214G (n=2), V214E (n=1), Q215P (n=1), E218D (n=2), I233L (n=1), T237A (n=1), N238H (n=3), N238A (n=1). Conclusions – HBV variability is high in Brazil, thirteen HBV subgenotypes were found. The rate of important drug resistance mutations was low (1.8%) among the drug-naive HBV infected patients studied, indicating the high potential to full efficacy of nucleos(t)ide analogue therapy in these patients. The high frequency of mutations potentially associated with Adefovir resistance among untreated patients suggests that these mutations are not really associated to resistance.