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ORAL COMMUNICATION

Critical clinical aspects underlining the control of viral hepatitis and emerging viral infections

OC 39 Chronic HDV coinfection (CHD) is characterized by a different HBsAg isoforms composition respect to HBV mono-infection with higher middle- and large-HBs levels paralleling the replicative and cytolytic activity of HDV

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ABSTRACT

Background: HBV surface proteins (HBsAg) facilitate HBV and HDV entry and morphogenesis. Total HBsAg comprises 3 different forms: Large- (L-HBs), Middle- (M-HBs) and Small-HBs (S-HBs) with L-HBs found in virions rather than subviral particles. Here, we investigate the levels of HBs forms in the setting of chronic HBV mono-infection (CHB) and HDV coinfection (CHD).

Method: 262 plasma samples from HBeAg-negative patients were included: 143 CHD and 119 CHB. Total HBsAg is measured by COBAS HBsAg II assays (Roche Diagnostics), HBs forms by ad hoc designed ELISAs (Beacle Inc) and HDV RNA by RoboGene HDV RNA Quantification Kit 2.0.

Results: CHD and CHB patients have a comparable age (median [IQR]: 54 [44-60] and 53 [39-64] years; P=0.8) and rate of NUC treatment (41.2% and 34.5%, P=0.3). CHD have lower HBV DNA (median [IQR]: 1.3 [0.0-2.3] vs 1.6 [1.2-3.4] logIU/ml, P=0.002) and higher ALT (median [IQR]: 79 [50-113] vs 36 [22-63] U/L, P<0.001) and total HBsAg levels (median [IQR]: 5206 [827-8555] vs

1776 [354-6936] IU/ml, P=0.008). Median (IQR) HDV RNA is 5.2 (3.4-6.0) logIU/ml. Notably, HBs forms composition varies between CHD and CHB with remarkably higher M-HBs and L-HBs in CHD (median [IQR]: 1127 [145-2301] vs 142 [25-707] and 2.0 [0.2-6.3] vs 0.06 [0.2-0.5] ng/ml), P<0.001) despite similar S-HBs levels in the two groups (median [IQR]: 3221 [587-6497] vs 1039 [239-5438] ng/ml). Multivariable analysis confirms CHD as an independent factor associated with higher levels of M-HBs and L-HBs (OR [95%CI]: 4.7 [1.7-12-4] and 6.2 [2.2-17.9], P<0.002 for both).
Among CHD, the HBs forms positively correlate with HDV RNA levels (Rho=0.48, 0.49 and 0.43 for S-, M- and L-HBs; P<0.001 for all) while, in CHB, milder correlation with HBV DNA levels is observed only for L-HBs (Rho=0.29, 0.02).
Furthermore, patients with highly-replicating HDV (HDV RNA >3log IU/ml) show significantly higher levels of all HBs forms than lowly-replicating HDV (median [IQR] ng/ml: 4431 [1251-6950] vs 274 [25-2640] for S-HBs; 1404 [191-2484] vs 127 [4-1242] for M-HBs; 3.3 [0.2-7.8] vs 0.3 [0.04-1.1] for L-HBs, P<0.001 for all).
Focusing on lowly-replicating HDV patients, 43.5% have altered ALT (median [IQR]: 75 [55-93] U/L). Notably, in this set of patients, M-HBs >200 ng/ml is the best cut-off predicting altered ALT (70% of patients with M-HBs >200 ng/ml vs 30% with M-HBs <200 ng/ml has ALT >40 U/L; PPV=70%, NPV=76.9%; P=0.04), supporting the role of M-HBs in reflecting cytolytic activity in the setting of low HDV replication.
Conclusion: The composition of HBs forms varies between CHD and CHB patients, with CHD characterized by higher M-HBs and L-HBs production along with HDV replicative activity. This may reflect a variation in the proportion of circulating viral and subviral particles for CHD and CHB.
Overall, HBs forms can help identifying patients more susceptible to liver disease progression, in whom treatment could be prioritized.