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O0981 HCV clearance and prothrombotic shift in advanced liver disease

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Background:

Hepatitis C virus (HCV) infection is associated to an increased risk of cardiovascular disease (CVD) and thromboembolic events. Direct acting antiviral (DAA) agents have an excellent safety profile and induce HCV viral clearance in almost all treated patients, but their impact on CVD risk remains unclear. Platelet activation and oxidative stress play a crucial role on the onset of thrombosis and CVD. We investigated the levels of urinary thromboxane B2 (TxB2), a marker of platelet activation, and 8-iso-prostaglandin F2α (8-iso-PGF2α), a marker of oxidative stress, during and after DAA treatment in HCV patients with advanced liver disease.

Materials/methods:

We enrolled 90 consecutive HCV patients with advanced fibrosis (Metavir F3-F4) who achieved SVR after DAA treatment (65.6% with ribavirin,77.8% with sofosbuvir). Urinary levels of TxB2 and 8-iso-PGF2α were measured at baseline (T0), end-of-treatment (EOT) and after 12-weeks of follow-up (FU) by ELISA commercial kits. Statistical analysis was performed by IBM SPSS version 21.0.

Results:

The characteristics of enrolled patients were: age 59.3±10.8 years, 58.9% males, BMI 25.0±3.6, 75.6% HCV Gt-1, HCV viral load 6.1±0.8 Log10 IU/mL, platelet 156.0x10^6/mm^3, liver stiffness 19.7±12.7 KPa). Urinary TxB2 levels increased sharply and significantly during antiviral treatment (161.5 [150.0-188.5] vs 230.0 [185.0-265.0] ng/mg creatinine, p<0.001) with a small further increase during FU (242.5 [179.7-298.5] ng/mg creatinine, p=0.057). Conversely, urinary 8-iso-PGF2α levels increased steadily during therapy (150.0 [136.5-161.0] vs 165.0[151.5-210.0] pg/mg creatinine, p<0.001) and FU(210.0 [167.5-255.0] pg/mg creatinine, p<0.001). A significant correlation between TxB2 and 8-iso-PGF2α levels increase was observed during the study period (r=0.421,p<0.001) (Figure). Platelet levels modifications did not correlate neither with TxB2 (r=-0.043, p=0.48) nor with 8-iso-PGF2α increase (r=-0.027,p=0.66) and no clinical, biochemical, virological or treatment factors were found to correlate with TxB2 and 8-iso-PGF2α level changes.

Conclusions:

The fast and significant increase of TxB2 and 8-iso-PGF2α levels observed in patients with advanced fibrosis successfully treated with DAA might indicate a shift toward a pro-thrombotic profile concomitant with viral clearance. These findings support the potential need of an antithrombotic prophylaxis administration early on treatment with DAA therapy.