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Improvement of serologic markers for liver function and fibrosis in HCV patients treated with DAA

가톨릭대학교 의과대학 내과학교실

*이응구, 이해림, 이승원, 한남익, 장정원, 배시현, 최종영, 윤승규

Introduction: The advent of direct-acting antiviral agents (DAA) has enabled high sustained viral response (SVR) rates in hepatitis C virus (HCV) infected patients. We aimed to evaluate longitudinal changes in liver function parameters and fibrosis scores in patients who achieved SVR. **Methods:** A total of 953 patients who received interferon free DAA combination±ribavirin for HCV infection between March 2015 and March 2017 at the liver unit of the Catholic University of Korea were consecutively recruited. Patients with hepatocellular carcinoma, other liver diseases, or those who received liver transplantation were excluded. 469 patients who achieved sustained viral response 12 weeks post treatment (SVR12) were analyzed and the parameters of liver function, AST to Platelet Index (APRI) and Fibrosis-4 (FIB-4) scores before treatment was compared to that of SVR12. **Results:** Of the 469 patients, 349 (74%) patients had chronic hepatitis and 120 (26%) patients had liver cirrhosis. In the total patients, aspartate aminotransferase were decreased from 60 and to 28 IU/L and alanine aminotransferase levels were decreased from 56 to 22 IU/L between baseline and 4 weeks post treatment ($p < 0.001$, both). In the patients with chronic hepatitis, APRI and FIB-4 scores, platelet (PLT), albumin and prothrombin time international normalized ratio (PT INR) levels were all significantly improved; Also, in the patients with liver cirrhosis, these serologic parameters of liver function and non-invasive serum fibrosis scores were all significantly improved; PLT level was 115±53 and 128±71, $p < 0.001$, albumin level was 3.8±0.6 and 4.2±0.4, $p < 0.001$, PT INR level was 1.15±0.13 and 1.10±0.09, $p < 0.001$, APRI score was 2.1±1.6 and 0.8±0.5, $p < 0.001$, FIB-4 score was 7.5±5.5 and 4.2±2.3, $p < 0.001$, at baseline and SVR12, respectively (mean±SD). **Conclusions:** This study suggested that a significant improvement in serologic parameters of liver function and non-invasive serum fibrosis scores could be achieved through short-term use of DAA in HCV infected patients who achieved SVR.

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Decreased PD-1 and CTLA-4, But Sustained FoxP3 During DAA therapy in Patients with CHC

가톨릭의대 의정부성모병원

*나민정, 김진아, 김지영, 천미주, 김희언, 김창욱

Background: Immune regulatory molecules such as forkhead box P3 (FoxP3), programmed death-1 (PD-1) and cytotoxic T-lymphocyte-associated protein-4 (CTLA-4) on T cell are associated with antiviral effector T cell dysfunction, which influences on T cell exhaustion and persistent viral infection in patients with chronic hepatitis C (CHC) and chronic hepatitis B (CHB). These FoxP3, PD-1 and CTLA-4 are known to up-regulated in CHC and CHB but, there is few report about the phenotypic changes of these molecules during direct-acting antiviral (DAA) therapy, especially, Daclatasvir and asunaprevir (DCV+ASV) in genotype 1b CHC. We investigated the expression of FoxP3, PD-1 and CTLA-4 during 6 months DCV+ASV treatment in 19 patients with genotype 1b CHC. **Methods:** Nineteen patients with genotype 1b CHC under DCV+ASV treatment were enrolled for detection of intrinsic inhibitory molecules of T cell signals (PD-1, CTLA4) and extrinsic inhibitory molecule, FoxP3. Peripheral blood mononuclear cells (PBMC) were isolated from these subjects before treatment (T0), 1 month (T1), 3 month (T3), 6 month (T6) and 9 month (T9) during DCV+ASV treatment. The expressions of FoxP3, PD-1, CTLA-4, CD8, CD4 on T cells were monitored by flow cytometry. **Results:** T cells from patients with CHC before DCV+ASV treatment (T0) showed increased expression of FoxP3, PD-1 and CTLA-4 compared to healthy control. However, T cells from patients with CHC under DCV+ASV treatment showed decreased expression of PD1 and CTLA-4 at T6 compared to T0 significantly. Interestingly, the expression of Foxp3 was sustained at T6 through T0. **Conclusions:** In CHC, PD-1 and CTLA-4 as inhibitory T cell molecules were down-regulated during 6 months DCV+ASV therapy but, FoxP3 as regulatory T cell marker was sustained during DCV+ASV therapy. This phenomenon could be one of background mechanisms of post-DAA syndrome such as HCC development or reactivation of HBV coinfection after DAA therapy.