エジプト人C型肝炎患者における貧血因子に対するイノシン三リン酸ピロフォスファターゼ遺伝子多型性前治療の働き

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ABSTRACT

AIM: To investigate and clarify for the first time, the role of inosine triphosphate pyrophosphatase (ITPA) polymorphism in Egyptian chronic hepatitis C virus (HCV) patients.

METHODS: The human genomic DNA of all patients was extracted from the peripheral blood cells in order to determine the single nucleotide polymorphism (SNP) of ITPA (rs1127354). SNP genotyping was performed by real time polymerase chain reaction (PCR, ABI TaqMan allelic discrimination kit) for 102 treatment-naive Egyptian patients with chronic HCV. All patients had no evidence of cardiovascular or renal diseases. They received a combination treatment of Pegylated interferon α (PEG-IFNα) as a weekly subcutaneous dose plus oral weight adjusted dose of ribavirin (RBV). The majority received PEG-IFNα 2a (70.6%) while 29.4% received PEG-IFNα2b. The planned duration of treatment was 24-48 wk according to the viral kinetics throughout the course of treatment. Pre-treatment liver biopsy was done for each patient for evaluation of fibrosis stage and liver disease activity. The basal viral load level was detected quantitatively by real time PCR while viral load throughout the treatment course was performed qualitatively by COBAS TaqMan assay.

RESULTS: Ninety three (91.2%) had ITPA SNP CC genotype and 9 (8.8%) had non-CC genotype (CA and AA). The percentage of hemoglobin (Hb) decline was higher for CC patients than for non-CC patients, particularly at weeks 4 and 8 (P = 0.047 and 0.034, respectively). During the first 12 wk of treatment, CC patients had significantly more hemoglobin decline > 3 g/dL than non-CC patients: 38.7% *vs* 0 and 64.5% *vs* 22.2% at weeks 8 and 12, respectively (P = 0.024 and 0.038). Reduction of the amount of the planned RBV dose was significantly higher for CC patients than non-CC patients during the first 12 wk (18 ± 12.1% *vs* 8.5 ± 10.2%, P = 0.021). The percentage of CC patients with RBV dose reduction was significantly greater than that of non-CC patients (77.4% *vs* 44.4%, P = 0.044). Multivariate analysis identified only the percentage of RBV dose. Platelet (plt) decline was significantly higher in non-CC patients than CC patients at weeks 12, 24 and 48 (P = 0.018, 0.009 and 0.026, respectively).

CONCLUSION: Rs1127354 ITPA polymorphism plays a decisive role in protecting against treatment induced anemia and the need for RBV dose reduction in Egyptian HCV patients.