Outcome of combination antiviral therapy in hepatitis C virus infected patients with sickle cell disease

To the Editor

We read with great interest the recent published outstanding article by Ayyub et al. on the treatment of chronic hepatitis C virus (HCV) infection with Peginterferon alpha-2a and ribavirin in patients with sickle cell disease (SCD). The authors treated 8 SCD patients with combination therapy for 48 weeks duration. All patients attained early viral response. One patients developed breakthrough, and 2 patients relapsed after cessation of combination therapy and ultimately 5 patients achieved a sustained virological response (SVR). The interesting aspect of this study was no treatment withdrawal and no need for transfusion in these patients. We want to address some points that merit more attention. As the authors have explained, hydroxyurea by increasing hemoglobin F can decrease transfusion need, resultant iron overloading, and chance of anemia in patients with congenital hemoglobinopathies. However in another comparative study on 6 SCD patients without oral hydroxyurea serum hemoglobin of patients did not also drop during treatment so, attribution of non-transfusion need in these patients to oral hydroxyurea administration is under-question. At present, there are evidences that intensive iron chelation and lowering of liver iron content such as administration of oral deferoxamine or phlebotomy can significantly enhance sustained viral response in hyper transfused patients however, the therapeutic role of hydroxyurea as adjuvant to ribavirin and interferon in polytransfused patients is not investigated yet. There are evidences that genotype 4 might be more responsive to combination anti-viral therapy than genotype 1 infection. Recently, Ferenci et al. has indicated that genotype 4 infected patients who are receiving 24 weeks of PEG-IFN alpha 2a plus ribavirin 1000-1200 mg/day after achieving a rapid virological response (RVR) had SVR rate as high as 86.7%. Hence, the patients in Ayyub et al.’s study had HCV RNA level $\leq 2 \times 10^6$ copy/ml and reasonable probability of attaining RVR the investigator could evaluate PCR results after 4 weeks of treatment and then adjust the treatment duration according to PCR results. Recently in a meta-analysis on 429 HCV infected thalassemic patients, we determined that ribavirin did not increase treatment discontinuation or major adverse events whereas increased transfusion needs by 30-50% that would return to pretreatment level during 2 months of post treatment cessation. We also indicated that genotype 1 infected thalassemic individuals significantly took benefit from ribavirin (OR 0.46, 95% CI 0.22-0.95 for monotherapy and OR 1.7, 95% CI 0.46-6.04 with combination therapy in genotype 1.
We are impressed by the meta-analysis results presented by Dr Alavian and Dr Tabatabaei. The results of this meta-analysis confirm our impression that ribavirin can be safely administered in patients with various hemoglobinopathies. This is particularly true in patients with SCD. In our series, none of the patients required transfusion, discontinuation or alteration of therapy due to any hematological side-effects. With the small number of patients we have studied, it is not possible for us to comment on the difference of response between HCV Genotype 1 and Genotype 4 patients with SCD. The study design in our case series did not include measurement of HCV PCR 4 weeks after initiation of therapy, primarily because the study was started in the year 2003 and at that time the concept of rapid virological response (RVR) had not been evolved. Hence, we are unable to comment on the issue of RVR and any possible adjustment of treatment duration that could have been made accordingly.

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References