EDITORIAL

Simple predictor for anemia in chronic hepatitis C patients receiving peginterferon plus ribavirin

Combination therapy with pegylated interferon (Peg-IFN) and ribavirin can achieve a satisfactory sustained virologic response rate for the treatment of patients with chronic hepatitis C (CHC), and is still recommended in many countries including Taiwan in the era of directly acting antivirals (DAAs) [1–6]. This therapy is even more cost effective in the Asia-Pacific region because of a favorable IL28B genetic background. However, patients receiving Peg-IFN combination therapy may develop significant anemia, which may lead to dose reduction and treatment discontinuation, and therefore negatively influence the treatment outcomes [7–9]. The presence of severe anemia may also result in the development of cardiovascular complications.

A number of mechanisms have been proposed for the occurrence of anemia, such as dose-dependent ribavirin-induced hemolysis [10] and/or interferon-induced bone marrow suppression [10,11]. Clarification of the underlying mechanisms and identification of biomarkers for prediction of significant anemia would be of clinical significance.

Reticulocyte count is a useful clinical parameter of red blood cell production. After adjustment, reticulocyte production index (RPI) is derived and has been shown to reflect the bone marrow response to anemia [12]. Yan et al [13] thus aimed to examine the value of RPI as a biomarker for predicting clinically significant anemia in patients receiving Peg-IFN combination therapy in a prospective cohort of 69 patients with CHC. They found that clinically significant anemia was observed in 30 patients (43.5%). On multivariate analysis, older age > 60 years, low pretreatment hemoglobin level, and low RPI at Week 4 of the combination therapy were significantly associated with the development of anemia. Specifically, RPI < 0.9% at Week 4 had an odds ratio of 5.50 for the development of clinically significant anemia.

The merits of this manuscript include its novelty in the adoption of RPI as a biomarker for predicting anemia development. In addition, the prospective study design would avoid information and recall bias. The weaknesses of this manuscript include small case number, heterogeneity in the enrollment of both Genotype 1 and Genotype 2 patients with different treatment duration, and notably a lack of genetic information regarding inosine triphosphatase (ITPA) gene polymorphism. There is growing evidence that variations in the gene encoding inosine triphosphate pyrophosphohydrolase (ITPase), known as ITPA, are related to hemolytic anemia, which is frequently observed among CHC patients receiving ribavirin-containing therapy [14]. ITPA polymorphisms, particularly rs1127354 CC and rs7270101 AA genotypes, increase the likelihood of developing hemolytic anemia. Unfortunately, information on these gene polymorphisms was not available and not taken into consideration. Moreover, other potential causes of anemia were not investigated at the same time. For example, serum iron profile was not examined at all. Both reduced production and increased destruction of red blood cells are responsible for the development of anemia. The relative contribution of each pathogenetic process to the development of anemia has not yet been clarified. Serial and comprehensive examinations of all parameters relevant to the development of anemia including RPI through the course of treatment would help resolve this issue. Finally, ribavirin induced hemolysis has been proposed as a novel mechanism of action against chronic hepatitis C virus infection through anti-inflammatory/antiviral actions within the liver [15]. In the future, whether RPI could predict the treatment responses in addition to the development of hemolytic anemia should be clarified.

Overall, clinical applications of the current study findings can be expected. RPI is a routinely used laboratory test and is available in all medical centers or offices. Development of this predictive biomarker would help general practitioners to easily identify clinically significant anemia early during the course of Peg-IFN-based combination therapy for patients with CHC, and allow prompt management of anemia to avoid potential complications.
Conflicts of interest

The author declares no conflicts of interest.

References


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