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• *LETTERS TO THE EDITOR* •

Erythropoietin in liver cirrhosis: Two questions without answers

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TO THE EDITOR

In a recent paper[1], and in a subsequent letter[2], Tacke *et al.* reported the investigation of plasma erythropoietin (Epo) levels in patients affected by chronic liver disease of various aetiologies. The authors also compared[2] their data to our previous work[3]. The results show a substantial agreement but also some important differences between the two works. We would like to highlight, from our point of view, this issue. Both the papers demonstrated increased Epo values in anaemic cirrhotic subjects when compared to healthy controls and non-anemic patients with liver disease. Conversely, a correlation between serum Epo and markers of liver dysfunction as well as between serum Epo and Child's stage of liver cirrhosis was shown by Tacke *et al.*[1], but not by our investigation[3]. Tacke *et al.*[2], suggest that these discordances could be due to different reasons: the population sizes, the diverse etiology of liver disease, the allocation of patients in subgroups, and the methods performed for statistical analysis. We appreciated and we agree with their considerations. In addition, diverse inclusion criteria (cirrhotic patients with iron-deficiency and renal impairment were excluded in our study) could contribute to these divergent outcomes. Considering the articles by Tacke *et al.*[1,2] and Pirisi *et al.*[4], we would like to underline the importance of a multifactorial regulation of Epo levels. Certainly, hemoglobin concentration, gastrointestinal bleeding, impaired pulmonary function and cytokine alterations can affect Epo levels in liver patients. Likely, the degree of liver dysfunction is also involved in the regulation of Epo values, even though our results do not support this hypothesis. Nevertheless, we would stress the importance of two questions. Firstly: is circulating Epo adequate to quantify the degree of anemia in cirrhotic patients? Since chronic anemia is a multifactorial complication of liver cirrhosis and hemoglobin concentration is inversely related to survivorship[5], this is not a secondary issue. To assess adequacy of Epo levels, the finding of higher levels than in normal individuals is not enough and values found must be evaluated in comparison to reference anemic patients[6]. In our study, we compared Epo levels observed in cirrhotics to those of patients with iron-deficiency[3]. Statistical analyses showed, in the former group, significantly lower values with regard to hemoglobin concentration. Besides ours, only one other paper[7] provided a reference anemic group and the results were similar. Secondly: independently of factors which are involved in regulating its levels, can the unsuitable concentration of Epo play a role in the persistence of anemic status, worsening the outcome of cirrhotic patients? To date, there is not really an answer. Therefore, cost-effectiveness of exogenous Epo administration in anemic cirrhotic patients could be attentively considered. In the near future, further investigations might be designed to answer these essential questions. From the answers will stem the assesibility of extending therapeutic options as well as improving the prognosis of these patients.

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