Could Chelation Therapy with Deferoxamine Enhance the Percentage of Responders to Interferon Therapy in Chronic Hepatitis C?

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It is known that there is a relationship between the activation of the immune system and modifications of iron status [1]. The hematological modifications typically consist of reduced iron level and high level of serum ferritin, and both of them seem to be related to a chronic macrophage stimulation [2] with a 'shifting' of iron toward the storage sites. The inhibitory effect of iron on the immune system has been demonstrated in vitro and it is fully reversed when iron is administered concomitantly with an iron che-lator such as deferoxamine [3]. Furthermore deferoxamine alone is even able to enhance the efficiency of the interferon-gamma signal [3]. It has also been demonstrated that deferoxamine inhibits the expression of the alpha chain of the interleukin-2 receptor on T lymphocytes, resulting in a significant immunosuppressive action [4]. On the basis of this evidence of a negative effect of iron on the immune system we might expect a poor efficacy of interferon therapy in thalassemic patients with viral hepatitis since they have high levels of both free and stored iron. However in our experience the use of an alpha re-combinant interferon (Roferon A, Roche) at a dosage of 5 MU/m² thrice weekly for 6 months, then 3 MU/m² thrice weekly for further 6 months in thalassemic patients with chronic hepatitis C (ELISA and RIBA 2 positive) showed quite encouraging results. In fact, according to our preliminary criteria of evaluation (ALT and ferritin value modifications), 57% of patients showed a normalization of ALT after interferon therapy although 33% of them had a

Table 1. Serum ferritin levels in thalassemic patients with hepatitis C during and after interferon therapy

Ferritin

therapy

follow-up after 12 months

before

12 months

Responders 3,392.7 (a) $\pm$ 1,643.8

2,387.6 (b) $\pm$ 966.2

2,189.5 (c)

$\pm$ 773.2

Nonresponders 4,752.5 (d) $\pm$ 2,939.0

3,656.5 (e) $\pm$ 1,957.2

2,864.6 (f) $\pm$ 1,444.0

avs. d:T = 1.10, p = 0.28. avs. b:T = 1.73, p = 0.09. avs. c:T = 2.23, p < 0.04.

relapse during follow-up. Moreover we observed a significant decrease in serum ferritin in responders (table 1). If it is true that deferoxamine interacts with interferon, we can suppose that the chelator has an immunomodulant action [5] also in chronic hepatitis C. This action is added to the direct anti-inflammatory activity of deferoxamine on lipid membrane peroxidation with reduction in hydroxyl radical formation [6, 7].

These observations may explain the high rate of responders and the lower rate of relapses after interferon

therapy among thalassemics compared with nonthalas-semic patients [8-10]. However future clinical trials in non-polytransfused patients are required to establish whether the chelator can really increase the number of responders in chronic hepatitis C and prevent the relapse after the cessation of therapy.

In conclusion, according to our data the efficacy of in-terferon therapy is confirmed also in thalassemic patients with chronic hepatitis C and we suggest that deferoxamine can contribute to the improvement of the response to in-terferon therapy because of its direct and iron chelating-mediated effect on the immune system.

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