REVIEW

Hepatitis C and Iron

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Abstract. Hepatitis C is the commonest form of chronic viral hepatitis in most western countries. A significant proportion of patients develop cirrhosis, hepatic failure and hepatocellular carcinoma. The results of controlled trials have shown that interferon α is an effective treatment for hepatitis C. Treatment results in normalization of elevated transaminase levels in up to 50% of patients, although only 15–25% of patients have a sustained response. Recent studies have shown that iron influences the response of chronic hepatitis C to treatment and the natural history of hepatitis C. The mechanisms responsible for the effects of iron are not clear but emerging data suggest that the cellular location of iron within the liver lobule and the subsequent effects on immune function are likely to be critical determinants for these effects. It is likely that therapies for chronic hepatitis C which either remove iron or interfere with the action of iron at the cellular level may not only prove useful clinically but may also elucidate further the mechanisms of cellular injury in this disease. (Keio J Med 48 (3): 124–131, September 1999)

Key words: hepatitis C virus, interferon, iron metabolism, ferritin

Introduction

Hepatitis C has emerged as the commonest form of chronic viral hepatitis in most developed countries and predisposes patients to the development of cirrhosis, hepatic failure and hepatocellular carcinoma. Clinical trials have shown that interferon α is an effective treatment for hepatitis C. Treatment results in normalization of elevated transaminase levels in up to 50% of patients, although only 15–25% of patients have a sustained response.[1–3] Furthermore, interferon α is costly with well-documented side effects. Thus, there is a need to identify alternative or complementary therapies which increase the proportion of patients who have a sustained response. Well characterized pretreatment characteristics of response include age, sex, duration of infection, mode of acquisition, liver histology, hepatitis C virus (HCV) RNA levels and genotype.[4–11] More recently, considerable interest has been generated regarding the role of iron in the pathogenesis of chronic hepatitis C and the role of de-ironing therapies as an adjunctive treatment for chronic liver disease which results from HCV infection. Whilst iron is an essential element for the survival of cells, excess amounts can result in tissue injury.[12] It is now apparent that iron can also modulate disease states and cellular function at levels much below those observed in classical iron overload. The aim of this article is to review the current state of knowledge pertaining to the role of iron in chronic hepatitis C.

Serum and Hepatic Iron Studies in Hepatitis C

The study of serum and hepatic iron parameters in chronic liver disease is readily achieved through the use of several standard methods. Serum transferrin saturation and ferritin levels, whilst useful in the assessment of iron overload in conditions such as hereditary hemochromatosis, are not as useful in the determination of iron status in chronic inflammatory liver diseases due to the effect of inflammation and pro-inflammatory mediators on serum iron levels and hepatic transferrin and ferritin synthesis.[13] The gold standard for defining hepatic iron content is biochemical measurement of the non-heme hepatic iron concentration (HIC).[14] The HIC can be determined from fresh or paraffin embedded

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