Interferon treatment of chronic active hepatitis B: effect of a six month treatment regimen

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Abstract
In this study of 17 patients with chronic active hepatitis B, the loss of hepatitis B virus DNA, the return to normal of alanine aminotransferase activities, and histological improvement after six months’ treatment with 3 million units three times weekly with interferon alfa-2b, was achieved in 40% of hepatitis B e antigen (HBeAg) positive/anti HBe negative patients, and 41.66% of HBeAg negative/anti HBe positive patients. The reappearance of hepatitis B virus DNA was seen in most patients when treatment was stopped, although a higher percentage of HBeAg positive/anti HBe negative patients (20%) had a sustained loss of hepatitis B virus DNA, return to normal alanine aminotransferase activities, and histological improvement compared with HBeAg negative/anti HBe positive patients (8.3%).

We studied the response of patients with chronic active hepatitis B treated with low doses of interferon alfa-2b for six months and followed up for another six months.

Patients and methods
For inclusion in the study, patients were required to have serum alanine aminotransferase (ALT) activities at least 1.5 times the upper limit of normal for six months or more, together with histological evidence of chronic active hepatitis. They also had to be positive for serum hepatitis B virus (HBV) DNA.

Seventeen patients were included in the study (15 males and two females), with a mean age of 46 years (range 21-65). Twelve patients were hepatitis B e antigen (HBeAg) negative/anti-HBe positive and five were HBeAg positive/anti-HBe negative.

All patients were given interferon alfa-2b subcutaneously at a dose of 3 million units (MU) three times weekly for six months and were then followed up for a further six months without treatment. Estimations of serum ALT activities, liver function tests, and HBV DNA were performed every two months during the study. Liver biopsies were carried out before entering the study, at the end of treatment, and at the end of the follow up period.

Results
At the end of treatment, similar percentages of HBeAg positive/anti-HBe negative patients and HBeAg negative/anti-HBe positive patients had achieved negative HBV-DNA, normal ALT, and histological improvement (40% and 41.7%, respectively), but there were more patients who had less than a 50% reduction in HBV-DNA and ALT and no change in liver histology in the latter group (Fig 1). During follow up, 20% of the HBeAg

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**Figure 1** Response to treatment: (a) HBeAg positive/anti-HBe negative patients; (b) HBeAg negative/anti-HBe positive patients.
- HBV-DNA negative, normal ALT, histological improvement
- HBV-DNA and ALT reduced by at least 50%, with minor improvement in liver histology
- HBV-DNA and ALT reduced by less than 50% and no change in liver histology
positive patients sustained the negative HBV DNA, normal ALT, and histological improvement, compared with 8-3% of the HBeAg negative cases (Fig 2).

Influenza like symptoms occurred in 70-5% of patients and mild leukopenia in 29-4%. These side effects, however, did not necessitate withdrawal of treatment in any patients.

Conclusions
A beneficial response to six months' treatment with low doses of interferon alfa-2b was achieved in 40-41-7% of patients with either the 'wild type' virus (HBeAg positive/anti-HBe negative) or the mutant virus (HBeAg negative/anti-HBe positive). Although the reappearance of HBV-DNA was seen in most of those who had responded when treatment was stopped, a higher percentage of HBeAg positive patients had a sustained loss of HBV-DNA, return to normal of ALT, and histological improvement response (20%) compared with HBeAg negative patients (8-3%).

Treatment with interferon alfa-2b requires further investigation and the value of long term interferon treatment for patients in whom disease activity is only temporarily controlled during treatment should be reconsidered.
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