Low dose alpha interferon treatment in chronic hepatitis B virus infection

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Abstract

Fifty eight patients with chronic viral hepatitis B (HBV) were randomised in a prospectively controlled trial. Thirty patients were treated with 3 million units (MU) of interferon alfa-2b subcutaneously thrice weekly for four months. Twenty eight controls received no treatment. The follow up period after treatment was six months. Twenty eight treated patients and 27 controls completed the protocol. One woman in the treatment group showed a complete response, and eight other treated patients (32%) showed a partial response. Three patients in the control group (11%) lost hepatitis B e antigen and HBV-DNA spontaneously. This finding is statistically significant ($p<0.05$). The elimination of HBV markers from the serum was associated with a return to normal of serum aminotransferase activities. Reactivation of hepatitis was not observed after seroconversion.

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The objective of this study was to investigate the efficacy of low dose alpha interferon treatment in patients with chronic hepatitis B (HBV) infection.

Patients and methods

A total of 58 patients (46 men, 12 women; mean age 41 years (range 18-65 years)) were randomised to receive either interferon ($n=30$) or no treatment ($n=28$). These patients showed histological evidence of chronic hepatitis and had been seropositive for hepatitis B surface antigen (HBsAg) and HBV-DNA for more than six months. Patients with hepatitis delta virus and HIV infections, decompensated cirrhosis, chronic renal insufficiency, or those requiring haemodialysis or immunosuppressive therapy, as well as patients with previous organ transplantations or considered to be of poor general condition, were excluded. The presence of antibodies to hepatitis B e antigen (anti-HBe) in the serum was not considered an exclusion criterion. Twenty seven patients had chronic persistent hepatitis, 28 had chronic active hepatitis, and three showed early onset of cirrhosis. There were no significant differences between the groups in terms of sex and age of the patients, duration of disease, aminotransferase activity, serum concentration of HBV-DNA and histological findings.

Twenty eight treated patients and 27 controls completed the protocol. One patient in the treatment group and one patient in the control group were withdrawn from the study because of lack of compliance. One female patient developed a psychosis while being treated with interferon, which necessitated stopping treatment.

Serum analysis, including liver function tests and transaminase activities, was carried out at monthly intervals three months before starting treatment, then during treatment and six months after study completion. HBsAg and HBeAg values were determined by radioimmunoassay test kits (AUSRIA II, AUSAB, Abbott-HBe Abbott Laboratories, Chicago, IL, USA), and HBV-DNA by Hep-Probe (GIBCO/BRL), Life Technologies, Eggenstein-Leopoldshafen, Germany).

The therapeutic response to interferon was assessed according to the following criteria:

Complete response: elimination of HBsAg, HBeAg and HBV-DNA from the serum and return to normal of alanine aminotransferase (ALT) activity, at least until completion of the follow up period (six months).

Partial response: elimination of HBeAg and HBV-DNA, while HBsAg persisted, and return to normal of ALT activity at least until completion of the follow up period (six months).

No response: no change or transient loss of HBV-DNA and decrease in HBeAg titre.

STATISTICAL ANALYSIS

The therapeutic response was evaluated by the χ^2 test ($p<0.05$). The biochemical and virological results were analysed by the Wilcoxon's rank sum test.

Results

In the treatment group, one patient showed a complete response and eight patients a partial response (Table I). Three patients in the control group spontaneously lost HBeAg and

TABLE 1 Response rates in the control and treatment groups

	Interferon*	Control
No	28	27
Complete responders	1 (3.6%)	0
Partial responders	8 (28.6%)†	3 (11.1%)
Total	9 (32.2%)	3 (11.1%)

*INTRON A, 3 MU three times weekly for four months.

† $p<0.05$, difference between groups.

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TABLE II Comparison of baseline hepatitis B virus (HBV)-DNA serum concentrations (mean values, three months before starting treatment) in responders and non-responders to treatment with recombinant interferon alfa-2b

	No	HBV-DNA (genomes/ml $\times 10^8$) (Mean (SEM))
Complete and partial response	9	1.17 (0.19)*
No response	19	1.91 (0.22)*

* $p < 0.05$.

HBV-DNA and seroconverted to anti-HBe. The difference between the groups was significant at the $p < 0.05$ level.

The baseline HBV-DNA serum values in the group of patients who successfully responded to treatment ($n=9$) were significantly lower than in non-responders (Table II). There was no correlation between therapeutic response and the following parameters: age, enzyme activities of aspartate aminotransferase (AST), ALT, γ -glutamyltransferase (GGT), alkaline phosphatase (ALP), glutamate dehydrogenase (GLDH), cholinesterase (CHE), concentrations of bilirubin and immunoglobulins, electrophoresis, duration of disease, and the patients' recollection of their acute viral hepatitis.

The loss of HBV-DNA was associated with a return to normal of serum transaminase activity. Reactivation of liver inflammation after seroconversion was not observed during 24 months of follow up.

The interferon was generally well tolerated. Initially, all treated patients showed mild flu

like symptoms but, in most, these symptoms disappeared after the third injection of interferon.

Conclusions

The results show that 3 MU of interferon three times weekly over a period of four months can produce a positive response in 32% of patients with chronic HBV, compared with a spontaneous remission rate of 11% in untreated controls. These response rates are comparable with the results of other studies, which have been performed with various types of interferon in different dose regimens and with different treatment durations.¹⁻⁵

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