Efficacy of different regimens of interferon alfa-2b treatment in chronic hepatitis C

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Abstract

Four different dosage regimens of interferon (IFN) alfa-2b (3 million units (MU) three times weekly for three months, 3 MU three times weekly for six months, 6 MU two times weekly for six months, and 6 MU three times weekly for six months) were compared in patients with chronic hepatitis C. There was no significant difference measured by percentage of responders to treatment between the four groups, but the degree of response was inversely correlated with the severity of liver damage. Viraemia was undetectable in most (75%) of responders treated with interferon and also in 20% of those who did not respond to treatment.

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The aim of this study was to compare the effects of four different regimens of interferon alfa-2b (INTRON A) in patients with chronic active hepatitis C virus (HCV) liver disease proved by biopsy examination, with or without cirrhosis.

Patients and methods

Patients were required to have post transfusion or sporadic HCV infection, with serum aspartate/alanine aminotransferase (AST/ALT) activities greater than twice the upper limit of normal for at least 12 months, and histological features of chronic active hepatitis or cirrhosis (Table I) for inclusion in the study. Patients were excluded from the study if they were seropositive for hepatitis B surface antigen, hepatitis B virus DNA or HIV, or if they were drug addicts.

A total of 114 patients were randomised to four regimens of interferon alfa-2b treatment given intramuscularly: Group A (n=21): 3 million units (MU) three times weekly for three months; Group B (n=53): 3 MU three times weekly for six months; Group C (n=20): 6 MU two times weekly for six months; Group D

TABLE II Response to different interferon regimens

Group	n	Chronic active hepatitis 1	Chronic active hepatitis 2	Active cirrhosis	Total
A	21	7/12	5/6	0/3	12*
B	53	19/28	6/12	2/13	27*
C	20	6/10	5/8	0/2	11*
D	20	7/9	6/9	0/2	13*

*p=NS.

(n=20): 6 MU three times weekly for six months.

All patients were followed up for at least one year after the start of interferon treatment. Response was defined as a fall in serum AST/ALT activities to below the upper limit of normal by the end of interferon treatment.

Results

Overall, 55.3% of the 114 patients responded to interferon treatment. When comparing the different histological subtypes, 66.1% of 59 patients with chronic active hepatitis 1 (moderate to florid inflammation without fibrosis) responded, 62.8% of 35 with chronic active hepatitis 2 (moderate to florid inflammation with fibrosis (passive septa)), and 10% of those with active cirrhosis (p=0.0002 compared with chronic active hepatitis and 2; χ^2 test). There was no significant difference between any of the interferon regimens in terms of response rates (Table II). After one year, AST/ALT activities remained normal in only 18 patients, — that is, 28.5% of responders, or 15.8% of all treated patients.

Serum samples from 18 patients were tested for circulating HCV-RNA by nested polymerase chain reaction using two pairs of primers from the 5' non-coding region. HCV-RNA was found in baseline serum samples from eight of 13 responders (62%) and all of the five who did not respond to treatment (100%). At the end of treatment, HCV-RNA was still present in two responders and four of those who did not respond.

Conclusions

No significant difference was found between the four interferon groups with respect to percentage of responders, but the response rate was found to be inversely correlated with the severity of liver damage. HCV-RNA investigations indicated that interferon was capable of reducing viraemia to undetectable values in most of viraemic responders (75%), but also in 20% of those who did not respond.

TABLE I Patient characteristics

Men/women	70/44
Mean age (range)	46.8 (18–72)
Liver histology:	
Chronic active hepatitis 1*	59
Chronic active hepatitis 2†	35
Active cirrhosis	20

*CAH1: moderate to florid inflammation without fibrosis.

†CAH2: moderate to florid inflammation with fibrosis (passive septa).

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