RESPONSE OF CHRONIC B AND C VIRAL HEPATITIS TO IFN - ALFA

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SUMMARY

To study the response to interferon Alfha in Chronic Hepatitis (Monotherapy) a long term follow up study in patients admitted with chronic hepatitis admitted in Medical A Unit Hayat Shaheed Teaching Hospital, Peshawar was conducted. Ten patients with chronic hepatitis were selected, six HBs Ag positive and four Anti HCV positive. The patients were put on different doses of IFN-Alfa HBsAg positive cases were put on 4.5 MIU thrice weekly and Anti HCV positive cases were put on 3 MIU thrice weekly. Both groups were treated for a period of six months. Main outcome measures: Histopathological improvement and ALT normalization in chronic hepatitis treated with IFN-Alfa for six months. The was a 50% response in anti HCV positive group and 50% response in HBsAg positive group. This study has got comparable results to contemporary studies. All patients with HBV or HCV infection, presenting with chronic hepatitis should be treated with IFN-Alfa, to avoid the long term sequel like cirrhosis, hepatic failure and hepatocellular carcinoma in a significant number of patients.

INTRODUCTION

Viral hepatitis has proved to be a major public health problem, occurring endemically in all areas of the world. The hepatitis viruses B and C (and occasionally D) may lead to chronicity and irreversible liver damage. Early treatment in the natural history of chronic viral hepatitis is most effective. Acute hepatitis is usually self limiting. It is therefore very important to identify patients with acute hepatitis who have a high risk of developing chronic hepatitis. Once chronic hepatitis supervenes, it must be trea-ted, the goal of treatment is early elimination of the virus, resolution of biochemical and histological signs. These changes must be sustained when therapy is stopped.

MATERIAL AND METHODS

Study was conducted at Hayat Shaheed Teaching Hospital Peshawar (Medical A Ward) on chronic HBV and chronic HCV hepatitis. The following exclusion and inclusion criteria was followed.

Inclusion criteria: Chronic hepatitis patients with:

1. Abnormal liver biochemistry
2. Anti HCV positively
3. HBs Ag and HBeAg positively
4. Abnormal liver histology.
5. Age between 20-50 years.

Exclusion Criteria:

1. Decompensated cirrhosis
2. Cardiac failure
3. Renal failure
4. Aplastic anemia or other myeloid dysfunction
5. Known psychiatric illness

All patients included were males. A thorough clinical history was taken with

emphasis upon previous history of jaundice, intravenous drug abuse, blood transfusion, sexual contact, HIV status, needle prick from a patient with jaundice, family history of hepatitis, drugs and other illnesses were also documented.

Clinical examination for signs and complications of chronic liver disease was methodically perfound. As a minimum, the following investigations were done in each patient. Haemoglobin, full blood count, Erythrocyte sedimentation rate, blood urea creatinine, liver function tests (including bilirubin, SGPT, ALT and total proteins) chest radiograph, ECG and an abdominal ultrasound. A prothrombin test was considered mandatory. Specific investigations to detect the virus were done, HBsAg, HBeAg and anti HCV were the important markers.

Evaluation of the response to therapy was based on two parameters: Biochemical and histological response. virological response could not be assessed because of the lack of facilities to do HBV-DNA and HCV-RNa by PCR at Peshawar. It is of notice that anti HCV does not necessarily show infectivity of immunity. However, patients having chronic hepatitis on other grounds, when found to have a positive anti HCV, could be safely assumed to be having chronic hepatitis due to HCV. These patients were subjected to liver biopsy and histological confirmation of chronic hepatitis was made.

After confirmation as chronic hepatitis, these patients were put on different doses of IFN-Alfa and treated for a fixed period of six months. HBsAg positive cases (total of six) received 4.5 million international units (MIU) thrice weekly and anti HCV positive cases received 3 MIU thrice week-ly. Biochemical and serological markers were observed during treatment, at the end of treatment and then after 6 months follow-up.

Liver biopsy was performed before treatment and 6 months after stopping the treatment. Histopathological sections were studied by a trained histopathologist.

RESULTS

For response see table-I and Figs.-I, II and III.

In chronic HBV patients (n=6), 2 patients (33.33%) had sustained response, one patients (16.66%) had a transient response while three did not respond at all (50%).

In chronic HCV patient (n=4), one patient had sustained response (25%), one patient had a transient response (25)%, two patients had no response (50) the results are shown graphically as:

TABLE - I

RESPONSIVENESS OF PATIENTS

I. Response pattern in ALT.

Complete response:	Normalization of ALT by the end of treatment and sustaining this response throughout follow up.
Transient response:	Normalization of ALT but relapse on stopping the treatment.
Relapse:	Increase in ALT>10 times the upper normal
No response:	Fluctuating ALT levels, above the upper limit of normal.

II. Other response patterns:

1. Loss of HBe Ag in HBV infection
2. Decrease in HBV-DNA and HCV-RNA on PCR
3. Decrease in 1gM-anti HBC to undetectable levels in the serum
4. Improvement in liver histology

Nonresponders	50%
Sustained Responders	25%
Transient Responders	25%

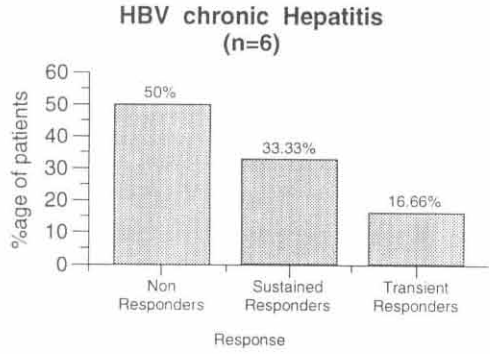

Fig. 1

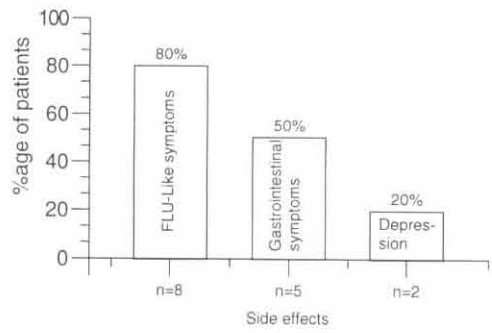

Fig. 3

Of the non responders 2 patients of the total ten; had cirrhosis liver (compensated) in each group.

Patients were scrutinized for side effects of IFN-Alfa, esp bone marrow depression. Only mild side effects were observed. None of them were serous enough to withdraw treatment. Flu like symptoms occurred in 8 patients (80%); Gastro intestinal symptoms were mild, like nausea and occasional loose motions occurring in only 5 patients and depression occurred in 2 patients (Graph-III)

DISCUSSION

The results of our study were based on two basic parameters, ALT normalization and histological improvement. In our study 50% of patients had responded (both for HCV and HBV) these results are comparable to contemporary studies of Causse-X et al 1991[1] and Iampertico et al 1994.[2] The response rate in HBV infection was 50% in our study based on ALT normalization and histological improvement, the results are equivalent to Braclay et al (IFN-Alfa in patients with chronic hepatitis B infection, New York 1994).

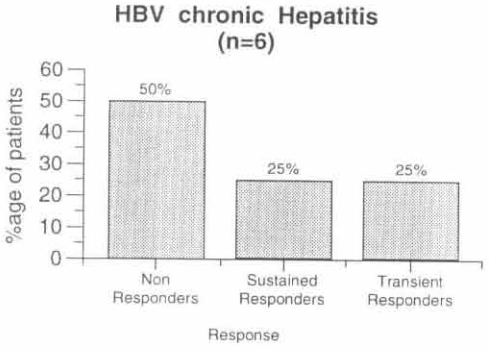

Fig. 2

The seroconversion of HBV infection with chronic hepatitis HBs Ag clearance rate was 33% in our study and of the non responders, two patients were compensated cirrhosis, one had simultaneous HBV/HCV infections. These are the cases which usually do not respond to treatment with conventional doses and needs higher dosage regimen e.g. 6-9 MIU/TIW.

Regarding the side effects they are usually trivial e.g. in our study like flu like symptoms in almost 80%, 50% patients got mild gastrointestinal disturbances like nausea, vomiting or loose motions, depression occurred in 20% people. These results are comparable to other studies in the international literature.

CONCLUSION

If we consider the effectiveness of IFN-Alfa as evidenced by most of the international studies and our own study. All those patients who have HBV or HCV chronic infection should be treated with IFN-Alfa to avoid the long term complications of infection, like cirrhosis, hepatic failure and hepatocellular carcinoma.

TABLE – II

Dose HBV	Patients	Schedule	Normalization in ALT level		Clearance of HBsAg		Clearance of HBsAg		Anti-HCV		Histological improvement		Response
			End of treatment	Follow up	End of treatment	Follow up	End of treatment	Follow up	End of treatment	Follow up	Pre-treatment	Follow up	
4.5 MIU	1	TIW 6 months	Yes	Yes	Yes	Yes	Yes	Yes	—	—	CAH	Yes	Sustained
4.5 MIU	2	TIW 6 months	Yes	Yes	No	No	Yes	Yes	—	—	CAH	Yes	–do–
4.5 MIU	3	TIW 6 months	Yes	No	No	No	No	No	—	—	CAH	No	Transient
4.5 MIU	4	TIW 6 months	No	No	No	No	No	No	+ve	+ve	Cirr	No	Non responder
4.5 MIU	5	TIW 6 months	No	No	No	No	No	No	—	—	CPH	No	–do–
4.5 MIU	6	TIW 6 months	No	No	No	No	No	No	—	—	CAH	No	–do–
HCV 3 MIU	1	TIW 6 months	Yes	Yes	No	No	No	No	+ve	+ve	CPH	Yes	Sustained
3 MIU	2	TIW 6 months	No	No	No	No	No	No	+ve	+ve	Cirr	No	Non responder
3 MIU	3	TIW 6 months	No	No	No	No	No	No	+ve	+ve	CAH	No	–do–
3 MIU	4	TIW 6 months	Yes	No	No	No	No	No	+ve	+ve	CAH	Yes	Transient

REFERENCES

1. Zuckerman AJ, Weatherall DJ, Ledingham JGG, Warrell DA.(eds) Hepatitis viruses. In: Oxford Textbook of Medicine. Oxford Medical Publications, Oxford, 1989; 5:139.
2. Zuckerman AJ. The Elusive hepatitis C virus. British Medical Journal 1989; 229: 871.
3. Shelock S, Dusheiko G. Hepatitis C virus updated. Gut 1991; 32: 965.
4. Caporaso N, Romano M, Marmo R et al. Hepatitis C infection is an additive risk factor for development of hepatocellular carcinoma. Journal of Hepatology 1991; 12: 367.
5. Hasan F, Jeffers LJ, De Madina M et al. Hepatitis C-associated hepatocellular carcinoma. Hepatology 1990; 12: 589.
6. Causse X, Godinot H, Chevalier M et al. Comparison of 1 or 3 MU of interferon alfa-2b and placebo in patients with chronic non-A, non-B hepatitis. Journal of Hepatology 1990; 11: S43.
7. Lampertico P, Rumi M, Raffaella R et al. A multicenter randomized controlled trial of recombinant interferon-alpha 2b in patients with acute
8. Alberti A, Chemello L, Bonetti P et al. Treatment with interferon(s) of community-acquired chronic hepatitis and cirrhosis type C. Journal of Hepatology 1993; 17(3): 123.
9. Alberti A, Chemello L, Diodati G et al. Treatment of chronic hepatitis C with different regimens of interferon alpha-2a (IFN-alpha 2a). Hepatology 1992; 16(2): 124.
10. Omata M, Imazeki F, Yokushuka O et al. Recombinant leucocyte A interferon treatment in patients with chronic hepatitis B virus infection in patients with chronic type B hepatitis Hepatology 1985; 5: 1033.
11. Dusheiko GM, Kassianides C, Song E et al. Loss of hepatitis B surface antigen in three controlled trials of recombinant alpha-interferon for treatment of chronic hepatitis B In: Viral Hepatitis and liver Disease. Alan R. Liss Inc., New York, 1988; 844.
12. Perrillo RP, Schiff ER, Davis GL et al. Hepatitis Interventional Therapy Group A randomized, controlled trial of interferon alfa-2B alone and after prednisolone withdrawal for the treatment of chronic hepatitis B. New England Journal of Medicine 1990; 323: 295.
13. McDonald JA, Caruso L, Karayiannis P et al. Diminished responsiveness of male homosexual chronic hepatitis B virus carriers with HTLV-III antibodies to recombinant alpha-interferon. Hepatology 1987; 7: 719.
14. Lok ASF, Lai CL, Wa PC, Leung EKY. A randomized controlled trial of recombinant alpha-2 interferon in chinese patients with chronic hepatitis B virus infection. In: Viral Hepatitis and liver Disease. Zuckerman Aj (ed. Alan R. Liss Inc., New York, 1988; 848.
15. Pastore G, Santantonio T, Milella M et al. Anti-HBe positive chronic hepatitis B with HBV-DNA in the serum: response to a 6 month course of lymphoblastoid interferon Journal of hepatology 1992; 14: 221.