

RESPONSE OF HEPATITIS C PATIENTS TO ALPHA INTERFERON AND RIBAVIRIN COMBINATION THERAPY

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ABSTRACT

Background: Hepatitis C virus infection is the major cause of chronic hepatitis in Pakistan. The aim of this study was to determine the response of patients with chronic hepatitis C to interferon and ribavirin combination therapy as initial treatment in our setup.

Material & Methods: It was an experimental study conducted from January 1997 to December 2001 at Postgraduate Medical Institute, Hayatabad Medical Complex, Peshawar. Non-cirrhotic chronic hepatitis C adult patients having no evidence of decompensated cirrhosis were treated with interferon and ribavirin combination for 24 weeks. Eligible patients had abnormal serum aminotransferase concentrations for six months before the start of treatment and they were positive for HCV antibodies by third generation ELISA, with positive serum HCV RNA. Serum HCV RNA was performed before treatment, at 12 weeks, at the end of treatment and at 24 weeks after the end of treatment. Patients were assessed for efficacy and side effects of therapy.

Results: Three hundred and eighteen patients with chronic hepatitis C were treated during the study period with 229 (72%) males and 89 (28%) females of adult age group. Five (1.57%) patients lost follow up and three (0.94%) patients left treatment because of adverse effects of drugs. The serum HCV RNA became undetectable in 222 (71.62%) patients at 12 weeks (EVR). It was 267 (81.12%) at the end of 24 weeks (ETR) and 242 (78.06%) at 24 weeks after the completion of treatment (SVR). All the patients with negative serum HCV RNA at 12 weeks had also negative serum HCV RNA at the end of treatment as well. The ALT decreased during treatment, became normal at 12 weeks in those patients who had lost HCV RNA after 12 weeks of treatment and remained normal at the end of treatment. White cell count and hemoglobin decreased during treatment and became normal after the completion of treatment. Two patients stopped treatment because of decreased hemoglobin and one because of neutropenia. No other significant adverse effects were noted in our patients. In the rest of patients, the side effects were flue like symptoms, which occurred in all patients.

Conclusion: Treatment of hepatitis C by combination of interferon and ribavirin for 24 weeks has high-sustained virological response with fewer side effects in our set up.

Key words: Chronic hepatitis C, Interferon, Ribavirin.

INTRODUCTION

Hepatitis C virus infection is the major cause of chronic hepatitis in Pakistan.^{1,2} Chronic infection with hepatitis C virus (HCV) is estimated to affect 170 million individuals worldwide.^{3,4} HCV is one of the leading cause of liver failure and cancer and is the single most common indication for liver transplantation.⁵ The current prevalence in Pakistan varies from 3 to 7 percent in different parts of the country.⁶ Approximately 20-30% of individuals will eventually develop cirrhosis and its sequelae over 10 to 20 years of infection.⁷ It also increases the risk of hepatocellular carcinoma (HCC). It is estimated that 2-6.7% of all patients with HCV in-

duced cirrhosis will develop HCC over 10 years and the annual risk is 1 to 4 percent.⁸ Both HCV and hepatitis B virus (HBV) infections are the leading causes of HCC in Pakistan and co-infection with HCV and HBV account for 7% of HCC.⁸ Interferon Alfa 2 b monotherapy in chronic hepatitis C for 48 weeks results in initial response in about half of the patients, but a sustained biochemical and virological response with histological improvement in only 15 to 20% patients.⁹

The combination treatment with interferon Alfa and ribavirin for 6 to 12 months is the current treatment of choice for chronic hepatitis C infection.¹⁰⁻¹²

The aim of the study was to assess the therapeutic efficacy and safety of combination therapy given for 24 weeks as initial treatment in chronic hepatitis C patients in our set up.

PATIENTS AND METHODS

It was experimental study carried out at Post-graduate Medical Institute, Hayatabad Medical Complex Peshawar, from January 1997 to December 2001. Patients aged 18 years and older with chronic HCV infection not previously treated with interferon or ribavirin were included in the study. Eligible patients had abnormal serum aminotransferase concentrations for at least 6 months before the start of therapy with positive HCV antibodies by third generation ELISA and detectable HCV RNA in the serum. Liver biopsy was not mandatory. Patients with decompensated liver cirrhosis, were excluded from the study i.e., presence of ascites, bleeding varices, spontaneous bacterial peritonitis, hepatic encephalopathy. Patients having serum albumin lesser than 35g/l, prothrombin time exceeding the normal limits or significant cytopenia were excluded from the study. Entry hemoglobin values had to be at least 12g/dl for women and 13g/dl for men. Patients with any other cause of liver disease or other relevant disorders including HIV infection or co-infection with hepatitis B virus, previous organ transplantation, pre-existing psychiatric condition, seizure disorders, cardiovascular disease, haemoglobinopathies, hemophilia and patients with poorly controlled diabetes mellitus and auto-immune diseases were excluded from the study as well. Written informed consent was taken from all the patients.

Patients were given combination of interferon alfa 2 b plus ribavirin for 24 weeks. All patients received interferon Alfa 2 b at a dose of 3 mega units subcutaneously three times a week for 24 weeks. Ribavirin was given orally twice a day to a total dose of 1000mg (body weight lesser than 75 Kg) or 1200mg (body weight more than 75 Kg) per day.

All patients were assessed in out patients setting for safety, tolerance and efficacy at the end of weeks 1, 2, then every 4 weeks for 24 weeks. Biochemical and hematological profiles were checked initially fortnightly and then monthly for 24 weeks. Serum HCV RNA was done before treatment, at 12 weeks and 24 weeks of treatment and at 24 weeks after the end of treatment. The primary end point was an end of treatment response and sustained virological response defined as, the absence of serum HCV RNA at the end of treatment and 24 weeks after completion of therapy. Secondary end point was normalization of the serum ALT concentration.

RESULTS

Three hundred and eighteen patients with chronic hepatitis C were treated during the study period with 229 (72%) males and 89 (28%) females of adult age group. (Figure-1)

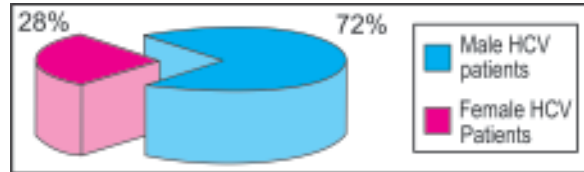


Fig. 1: Gender distribution of patients with chronic HCV.

Five (1.57%) patients lost follow up and three (0.94%) patients left treatment because of adverse effects of drugs. The serum HCV RNA became undetectable in 222 (71.62%) patients at 12 weeks (EVR). It was 267 (81.12%) at the end of 24 weeks (ETR) and 242 (78.06%) at 24 weeks after the completion of treatment (SVR). (Figure-2)

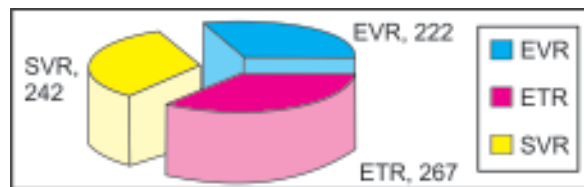


Fig. 2: Response to interferon plus ribavirin.

All the patients with negative serum HCV RNA at 12 weeks had also negative serum HCV RNA at the end of treatment as well.

The ALT decreased during treatment and it became normal at 12 weeks in those patients who had lost HCV RNA after 12 weeks of treatment and it remained normal at the end of treatment. The WBC count and hemoglobin decreased during treatment and became normal after the completion of treatment. Two patients stopped treatment because of decreased hemoglobin and one because of neutropenia. No other significant adverse effect noted in our patients. In the rest of patients, the side effects were mostly influenza like symptoms, which occurred in all patients.

DISCUSSION

The primary endpoint in this study was a sustained virological response (SVR) i.e. absence of serum HCV RNA at six months after stopping the treatment. The SVR substantially reduces the rate of HCC,¹³ leads to progressive histological improvement,¹⁴ and improved quality of life.¹⁵ The secondary endpoint was normalization of the serum ALT.

In our study the serum HCV RNA was cleared at 12 weeks in 222 (71.62%) and 267 (81.12%) at 24 weeks and remained negative at 6 months after stopping treatment in 242 (78.06%) patients. ALT levels decreased during treatment and it became normal at 12 weeks in those patients who had lost HCV RNA after 12 weeks of treatment and it remained normal at the end of treatment. The negative PCR results 24 weeks after stopping treatment is the most reliable marker of long term SVR.¹⁶

The monitoring of response to treatment is recommended with qualitative polymerase chain reaction (PCR), which is an important tool for detection of HCV RNA in hepatitis C Patients.¹⁷

In our study, the overall response rate to combination therapy is higher as compared to other international studies.^{18,19,20} But it was almost similar to the published data from Pakistan.^{21,22} The better response rate in our patients might be due to genotype 3, which is common in our set up.²³

CONCLUSION

Combination of interferon and ribavirin has high-sustained virological response with fewer side effects in our set up.

Keeping in view the low socio-economic background of our patients and the good response rate, we recommend the conventional combination therapy as the first line treatment for chronic hepatitis C patients in this part of the world.

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