

# Assessment of Therapeutic Effects on Sustained Viral Response with Conventional Interferon and Ribavirin Therapy in Patients of Chronic Hepatitis C Virus

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## ABSTRACT

**Objective:** To achieve sustained viral response (SVR) with Conventional Interferon and Ribavirin therapy in a period of twenty four weeks an economical perspective for non-affording patients.

**Design:** An open labeled study

**Place and duration:** Sir Ganga Ram Hospital, Lahore and Sir Syed College of Medical Sciences Hospital Karachi from Dec. 2009 - Nov. 2012

**Methods:** Confirmed cases of Chronic Hepatitis C were selected, HCV- RNA was done by (Roche amplifier Switzerland). ALT double than (UNL) were given conventional Interferon and Ribavirin 800-1200mg according to body weight for 24 weeks.

**Results:** One hundred and sixty confirmed cases of chronic Hepatitis C were included in this study, male were 90(56.25%) and female 70(43.75%). Response to therapy was seen as after 12 weeks, early virological response (EVR) i.e., undetectable HCV-RNA among 135 patients (84.37%), end of treatment response (ETR) at week 24 were seen among 130 patients (81.25%) and non-responders with detectable HCV-RNA 30(18.75%). 5 patients (2.64%) who showed early virological response developed breakthrough i.e.; PCR was positive at week 24. Twenty two patients developed relapse after 6 month of stopping therapy. So overall sustained virological response (SVR) was 67.5%. Biochemical response among responder in the form of ALT/AST normalization was among 145 patients 90.63%. During the 24 weeks treatment adverse effects of the treatment were mainly fever, myalgia, fatigue (100%), epigastric discomfort was seen in 60(37.5%), and diarrhea was seen in 15 patients (9.37%). Mild anxiety and depression and irritable behavior along with insomnia were observed among 50 patients (31.25%). Hematological abnormalities seen were Hb<10gm% 37(23.13%), Leucocyte count <4000 105(62.6%) and Platelet count <100,000 28(17.5%).

**Conclusion:** This study supports that Interferon alpha with combination of Ribavirin has great efficacy and can achieve SVR in patients suffering from chronic hepatitis C virus.

**Keywords:** Hepatitis C, interferon, ribavirin, SVR.

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## INTRODUCTION

Hepatitis C is a chronic viral disease that varies in presentation from a silent disorder to a progressive inflammation of liver that may ultimately lead to premature death. In Pakistan it has become a great problem, its prevalence is very high despite the efforts to control viral infections. All over the world 130 million people are infected with Hepatitis C virus<sup>1</sup>. In Pakistan genotype 3 is common and response to conventional INF is about 68% to 70%<sup>2</sup>.

The first line treatments are based on interferon Alfa & ribavirin combination therapies which suppress the RNA (Hepatitis C) virus<sup>3</sup>. With conventional Interferon therapy sustained virological response can

be achieved about 53%<sup>4</sup>. Conventional Interferon and Ribavirin achieves good response and this combination is not costly<sup>5,6</sup>. Due to its cost effectiveness conventional Interferon is recommended by some research societies<sup>7</sup>. In certain regions of Pakistan the prevalence is as high as 16%<sup>8</sup>. About 3-4 million new cases are being reported every year<sup>9</sup>. 20% cases of chronic Hepatitis C may develop cirrhosis of liver if not treated<sup>10</sup>. Therefore, it is recommended that early treatment of Hepatitis C can prevent complications like cirrhosis, and hepatic failure, a small number of cases of cirrhosis with in the period of 20-25 years may develop Carcinoma of liver. Therefore eradication of virus may result in to clinical improvement and regression of fibrosis<sup>11,12</sup>. Late relapses may be due to presence of virus in the liver tissue and in the peripheral blood mononuclear cells (after achieving SVR). Only 20-55% patients are able to clear HCV virus without Interferon Therapy<sup>13</sup>.

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## PATIENTS AND METHODS

An open labeled study conducted from Dec. 2009 up to Nov. 2012 in the liver clinic/Department of Medicine at Sir Ganga ram hospital, Lahore and Sir Syed College of Medical Sciences for Girls Hospital Karachi. One hundred and sixty patients were enrolled in this study out of which 90 male and 70 female between the age of 40-60 years. All patients were informed about the therapy events, its side effects and outcome of therapy, a written consent was obtained from all patients. Pregnant ladies, renal compromised patients, cardiac patients and patients with low Hb and low platelets counts were excluded from the study.

HCV RNA was done by (Roche reverse transcriptase method). LFT was done and ALT of double (UNL) was considered to start the therapy. Before starting therapy all base line investigations CBC, LFT, serum Albumen, Urea, Creatinine, FBS, Lipid profile, Prothrombin Time (PT), APTT, TSH, Qualitative HCV-RNA and Genotype were done. An ultrasound of whole abdomen was done. All the patients were started Interferon Alpha 3 million units subcutaneously thrice a week with Ribavirin 800-1200mg according to body weight. Initially patients were reviewed fortnightly along with the CBC and ALT during first month and then monthly for follow up. Treatment was continued for 24 weeks. HCV-RNA was done at week 12 to see early virological response and at the end of therapy HCV-RNA Qualitative was done to assess the end of treatment response. HCV-RNA Qualitative was done again to see sustained virological response.

## RESULTS

One hundred and sixty confirmed cases of chronic Hepatitis C were included in this study, male were 90(56.25%) and female 70(43.75%) between the age group 40-60 years. Most frequent mode of transmission of HCV were from IV injections use / intravenous drug abuse 65(40.63%), different surgical/ dental interventions were 29(18.13%) blood transfusions 30(15.62%), transmission through sharp was seen in 12.5% patient and Intrafamilial transmission was seen among 6.88% patient. In many of these patients, however, more than one risk factor was present as shown in table 1.

Patients were given conventional Interferon 3million unit s/c thrice weekly and Ribavirin 800 - 1200 mg according to body weight for 24 weeks. During the 24 weeks treatment adverse effects of the treatment were mainly fever, myalgia and fatigue were observed in almost all patients along with headache 100(62.5%), and Gastrointestinal effects

such as epigastric discomfort was seen in 60(37.5%), anorexia 46(28.75%), Nausea 24(15%) and diarrhea was seen in 15 patients (9.37%). Mild anxiety and depression and irritable behavior along with insomnia were observed among 50 patients (31.25%). Hematological abnormalities seen were Hb<10gm% 37(23.13%), Leucocyte count <4000 105(62.6%) and Platelet count <100,000 28(17.5%). Three patients also developed hypothyroidism. All these abnormalities are shown in table 2.

Table 1: Mode of transmission

Risk Factors	=n	%age
I/V Injections/ I/V drug abuse	65	40.63
H/o surgery / dental procedure	29	18.14
Blood Transfusion	25	15.62
Transmission through sharp	20	12.5
Unknown case	10	6.25
unknown cause	11	6.88

Table 2: Adverse effects of treatment

Symptoms	=n	%age
Fever, fatigue and myalgia	160	100
Headache	100	100
Epigastric discomfort	60	37.5
Anorexia	46	28.75
Nausea	25	15
Diahroea	15	9.37
Hb< 10gm%	37	23.13
Leucocyte Count < 4000	105	62.6
Platelet Count < 100,000	28	17.5
Hypothyroidism	3	1.87

Response to therapy seen as after 12 weeks was recorded as early virological response (EVR) undetectable HCV-RNA 135(84.37%), end of treatment response (ETR) at week 24 were seen among 130 patients (81.25%) and non responders with detectable HCV-RNA 30(18.75%). 5 patients (2.64%) who showed early virological response developed breakthrough i.e., PCR was positive at week 24. Biochemical response among responder in the form of ALT/AST normalization was among 145 patients 90.63%. 22 patients developed relapse after 6 month of stopping therapy. So overall sustained virological response (SVR) was 67.5% (Table 3).

Table 3: Response to therapy

Investigation	=n	%age
HCV-RNA Undetectable at week 12	135	84.37
HCV-RNA Undetectable at week 24	130	81.25
Breakthrough	5	2.64
Sustained virological response	108	67.5
ALT normalization	145	90.63

## DISCUSSION

Hepatitis C Viral infection is among leading cause of chronic liver disease in Pakistan as well as worldwide. It is also the most common cause of transplantation of liver world wide. Due to chronic nature of this disease, these figures are expected to grow many folds in the next decade. It is difficult to study natural history of HCV infection because of multiple risk factors. Vast majority of patients Hepatitis C virus are asymptomatic and have slow progressive disease.

This study shows the adverse affect profile of antiviral therapy was comparable with previous studies<sup>14</sup>. These were mainly fever, myalgia, fatigue, epigastric discomfort, anorexia Nausea and diarrhea. Mild anxiety and depression and irritable behavior along with insomnia were also observed among significant number of patients. Hematological abnormalities seen were Hb<10gm% 37(23.13%), Leucocyte count <4000 105(62.6%) and Platelet count <100,000 28(17.5%). Three of our patients developed hypothyroidism.

As it is well known that hepatitis C virus in lymphocytes, hepatocytes, macrophages remain undetectable and it is possible that in some cases relapses may occur after some time. Some studies have supported that eradication of virus from the hepatocytes may results in to HCV-RNA undetectable up to 12 years<sup>15</sup>. In another cohort patients after the end of therapy were followed for 18 years. HCV-RNA remained undetectable in serum but was detectable in biopsies of liver<sup>16</sup>.

Patients treated with pagylated INF in these cases SVR was achieved in 78% as reported in some studies and with conventional INF only 53%<sup>17</sup>. Our study showed that SVR can be maintained in majority of cases (67.5%). In our country the genotype 3 is more common and is found to be highly sensitive and responsive to conventional INF<sup>18</sup>, so standard treatment duration is 24 week for genotype 2 and 3. However in patient with High pretreatment RNA > 600,000 IU/ml or steatosis, treatment beyond 24 week may improve response. Many researchers are of opinion that yet optimal treatment of hepatitis C is not available<sup>19</sup>. It is the need of time that some other economical modalities should be introduced which should be economical to those patients who are not affording.

## CONCLUSION

This study supports that those patients who cannot afford pagylated INF treatment for those patients Interferon Alpha with the combination of Ribavirin has

great efficacy and can achieve SVR after 6 months therapy.

## REFERENCES

1. Global Burdon of disease (GBD) for hepatitis C. *J Clin Pharmacol* 2004, 44: 20-29
2. Ahmed N, Asgher M, Shafique M, Qureshi JA. An evidence of high prevalence of hepatitis C virus in Faisalabad, Pakistan. *Saudi Med J* 2007, 28:390-395
3. Poynard T, Marcellin P, Lee S. et al. randomized trial of alfa 2 b plus ribavirin for 48 weeks or for 24 weeks versus interferon alfa 2 b plus placebo for treatment of chronic hepatitis C virus. *International hepatitis therapies*, 1988; 352: 1431-62.
4. Crespo M, Estebin JI, Ribera E, Falco V, Sauced S, Buti M, Esteban R, Gaurdia J, Ocana I, Phissa A. Utility of week-4 viral response to tailor treatment duration in hepatitis C virus genotype 3/HIV co infected patients. *AIDS* 2007, 21: 477-481
5. Manns MP, Mc Hutchison JG, Gordon SC, Rustigi VK, Shiffman M, Reindollar R et al, Peg interferon alpha-2b plus Ribavirin compared with interferon alpha-2b for initial treatment of chronic hepatitis C randomized trial. *Lanced* 2001; 358: 958-65
6. Jamal IS, Yousaf S, Azhar M, Jamal S, is Pagylated interferon superior to interferon with ribavirin in chronic hepatitis C genotype 2/3. *Word J Gastroenterology* 2008; 14: 6627-31
7. NIH consensus statement on management of hepatitis C : 2002 NIH Consensus State Sci Statements 2002; 19: 1-46
8. Ahmed N, Asgher M, Shafique M, Qureshi JA. An evidence of high prevalence of hepatitis C virus in Faisalabad, Pakistan. *Saudi Med J* 2007; 28: 390-395
9. Pantazis KD, Brokalaki H, New Data concerning the epidemiology of hepatitis B virus infection in Greece. *Gastroenterol Res Pract* 2008; 2008: 580341
10. Thomas DL, Seeff LB, Natural history of hepatitis C. *Clin Liver DIS* 2005; 9: 383-98, Vi.
11. Scott JD, Mc Mahon BJ, Bruden D et al. High rate of spontaneous negativity for hepatitis C virus RNA after establishment of chronic infection in Alaska natives. *Clininfec Dis*, 2006; 42: 945-52
12. Santantonio T, Piccinino F, Andreone P et al. Sustained virological response to interferon alpha is associated with improved out come in HCV related Cirrhosis; a retrospective study. *Hepatology* 2007; 45: 579-87.
13. Dooly JS, Lok A, Burroughs A, Heathcote J, editors. *Sherlocks diseases of liver and biliary system*. London: John Willey and Sons; 2011
14. Bernstei n et al. relationship of health related quality of life to treatment adherence and sustained response in chronic hepatitis C patients. *Hepatology* 2002;; 35: 704-708.
15. Camma C, Guinta M, Pinzello G, Morabito A, Verderio P, Pagliaro L. Chronic hepatitis C and interferon alpha: Conventional and Cumulative meta-analysis of randomized controlled trials. *Am J Gastrienterol* 1999; 94: 581-94

16. Maylin S, Martinol-Peignoux M, Maccari R, et al. Eradication of hepatitis C virus in patients successfully treated for chronic hepatitis C. *Gastroenterology*. 2008; 135: 821-9
17. Crespo M, Esteban JI, Ribera E, Falco V, Sauleda S, Buti M, Esteban R, Guardio J, Occana I, Pahisa A. Utility of week-4 viral response to tailor treatment duration in hepatitis C virus genotype-3/ HIV co infected patients. *AIDS* 2007; 21: 477-481
18. Shash HA, Jafri W, Prescott L, Simmonds P. Hepatitis C virus (HCV) genotypes and chronic liver disease in Pakistan. *J GastroenterolHepatol* 1997; 12: 758-761
19. Jaeckel E, Cornberg M, Wedmeyer H, Santantonio T, Mayer J, Zankle m, Pastore G, Dietrich M, Trantwein C, Manns MP. Treatment of acute hepatitis C with interferon alpha-2b. *N Engl J Med* 2001; 345: 1452-1457.