Original Article

Hepatitis C

Response Rate of Standard Interferon Therapy in Chronic Hepatitis C

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ABSTRACT

Objectives: Interferon combination therapy is used to eradicate the Hepatitis C Virus from infected individuals. HCV (hepatitis C virus) infections respond to standard conventional interferon (INF) therapy along with ribavirin (RBA).The aim of study was to look for response of chronic HCV infections to standard conventional combination interferon therapy and ribavirin.

Study Design: Interventional non randomized trial

Place and duration of Study: This study was carried out at Azad Kashmir Combined Military Hospital (AK CMH)/Sheik Khalifa Bin Zyad (SKBZ) Muzaffarabad (MZD) from June 2009 to July 2012.

Materials and Method: A total of 210 patients were selected for interferon combination therapy. After confirmation of active HCV infection by PCR-RNA, conventional interferon alpha 2a with ribavirin (RBA) was given to patients for 6 months. After end of treatment (ETR), the efficacy was defined as sustained virological response (SVR) if HCV-RNA remained undetected 6 months after stoppage of combination interferon therapy.

Results: Out of total 210 patients, 144 (68.6%) showed SVR and 66 (31.4%) did not show SVR. Hence out of 68.6 % were negative and 31.4% were positive for HCV RNA after 6 months of therapy. The non parametric chi squared showed age (p=<0.001), (age category p=<0.001), gender (p=<0.006), and HCV PCR response (p=<0.001) had statistical significant association.

Conclusion: Conventional Interferon and ribavirin combination therapy (INF-RBA) remains effective in chronic hepatitis naïve patients. HCV-RNA qualitative PCR test at 6 month of ETR is important predictor of SVR. The response of antiviral therapy against HCV infection in chronic HCV patients is 68.6 %. The high response rate may be due to the prevalence of IFN-responsive HCV genotypes type 3 in our country.

Key Words: Sustained virological response; Conventional Interferon; Ribavirin; Chronic Hepatitis C

INTRODUCTION

The hepatitis C virus (HCV) is a global health problem and the leading cause of chronic liver disease in world. The HCV genome is single-stranded, RNA. HCV infection effect annually more than one million people in world.[1-3] the effective therapy and prevention of HCV infection is our ultimate goal. It is major economic and life threatening infection in underdeveloped and developed countries. In our country patients have financial problems for its treatment.

The primitive goal of hepatitis C treatment is eradication of the virus .The sustained virological response (SVR) is defined as absence of HCV RNA in serum after 6 months of treatment which is confirmed by absence of hepatitis C virus by Polymerase Chain Reaction (PCR).[2, 4-5].Hepatitis C therapy is started with ribavirin (RBA) and recombination interferon therapy.[6] Interferon is very active against HCV. It decreases the level of serum alanin aminotransferase (ALT) as well HCV RNA level. These effects led to a sustained absence of virus in a proportion of patients.[7-8] Ribavirin is nucleoside analogues has activity against several flaviviruses and lowers ALT level and improves histological abnormality of the liver. Ribavirin had little effects on serum HCV RNA levels. The combination therapy of ribavirin with interferon has been observed with increased SVR.[9] Interferon and ribavirin in combination has SVR of 40-50% and has been used as treatment in chronic HCV infection.[10] It has less good response as compared to Pegylated interferon with Ribavirin.[11] Combination interferon and ribavirin therapy has been recommended due to economic reasons, genotype 3 prevalence in our county[12] and provision of free of cost therapy by our AJK Government.

MATERIALS AND METHODS

This study included 210 consecutive Hepatitis C Virus (HCV) patients of either sex, 20 to 69 years referred to (CMH) /SKBZ Muzaffarabad. The patients who were HCV positive by ELISA (enzyme-linked immunosorbent assay) the PCR (polymerase chain reaction) qualitative test HCV- RNA assays (Amplicor HCV test,version2.0 Roche Diagnostics) was performed to confirm HCV positive RNA cases. An analysis of response of combinational interferon alpha 2a with ribavirin therapy against HCV PCR positive was conducted. Among the confirmed HCV patients, 210 naive patients with PCR –RNA positive, were selected for interferon therapy keeping in mind the

exclusion criteria. HCV-PCR positive patients were given standard interferon combination therapy, interferon alpha 2a (3 MIU, S/C thrice weekly) plus Ribavirin (1000-1200 mg/day) continuously for 6 months with repeated monitoring of Blood CP, ALT level and coagulation profiles. HCV-RNA PCR testing was done at the end and after 6 months of interferon therapy to look for ETR and SVR respectively.

The data entry and analyses were done on software statistical package SPSS 20. Chi square nonparametric test done to show statistical significance of response to therapy.

RESULTS

After completion of the 6 months interferon therapy, the result of SVR was observed. Out of total 210 patients, 144 (68.4%) were negatives for HCV- RNA PCR and showing SVR while 66 (31.4%) were positive for HCV- RNA PCR and did not show SVR. Demographics and therapeutic response to conventional combination interferon therapy (Tables 1, 2 and 3).

Table No.I: Response rate of Interferon Therapy in Chronic HCV infections according to SVR

No.	Age group	Gender		SVR+ (%)	SVR- (%)
		Male (%)	Female (%)		
210	20-65	125 (59.5)	85 (40.5)	144 (68.6)	66 (31.4)

Table No.2: Descriptive Statistics demographics

	N	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
Age	210	20	69	39.73	.814	11.800
Age category	210	1	6	3.56	.085	1.237
Gender	210	1	2	1.40	.034	.492
HCV PCR AFTER THERAPY RESPONSE	210	-1	1	.36	.064	.934
Valid N (listwise)	210					

Table No.3: Nonparametric Test Statistics according demographics & HCV PCR response

	Age	Age category	Gender	HCV PCR after therapy response
Chi-Square	83.752[a]	76.571[b]	7.619[c]	27.505[c]
df	43	5	1	1
Asymp. Sig.	.000	.000	.006	.000

a. 44 cells (100.0%) have expected frequencies less than 5. The minimum expected cell frequency is 4.8.
b. 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 35.0.
c. 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 105.0.

DISCUSSION

Hepatitis C Virus infection is global health problem and HCV prevalence is nearly 200 million people worldwide.[13] The seroprevalence of Hepatitis C virus in different parts of Pakistan has been reported from 2.2%-13.5%. The highest seroprevalence of hepatitis C has been reported from Lahore (13.5%) as compared to other part of cities.[14-16]

Pakistan has low literacy rate and the people have lack of information of virus transmission. The parenteral routes are common mode of spread .Hence HCV infection has become an economic burden in our country. SVR defined as the absence of HCV- RNA after 6 months of IFN therapy in chronic HCV patients.

The average response rate of combination of conventional INF therapy with ribavirin in chronic HCV patients in our study was 68.6% [Table]. The HCV response rate p=<0.001) was statistical significant in our study comparable to other studies conducted locally[17-19] and internationally[20-21]. In HCV RNA infection six genotypes subtypes have been recognized. These genotyping are important predictors for duration of interferon and SVR[22].Genotype 1 is the commonest in North, South America, Europe and Japan. In China genotype 4 and genotype 3 is predominant in Pakistan and is involved in 67% to 87% cases.[23-26] Due to high cost, genotyping was not performed in most ours cases and presumed the prevalence of genotype 3 as evidence based on from many studies of our county.

The different responses to INF in our country may be due to prevalence of different strain of genotypes of HCV RNA viruses. Besides this lower response rate in our country could be attributed to the prevalence of resistant HCV genotypes, non compliance to treatment, poor maintenance of colds chain, poor type and quality of therapy .The immigration of people from HCV resistant region like Central Asian Countries to this

region and their virus transmission can result poor response of viruses resistance to conventional combination INF RBA therapy.[27-30] This study has obvious limitations as HCV 'genotyping was not done because of overall poverty of many patients..

CONCLUSION

This study shows that combination antiviral therapy of conventional interferon alpha along with ribavirin is effective against chronic HCV infective patients. The high response rate may be due to prevalence of IFN-responsive HCV genotypes in our district..

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