ORIGINAL ARTICLE
TREATMENT OF CHRONIC HEPATITIS-C WITH STANDARD INTERFERON AND RIBAVIRIN

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Background: The prevalence of hepatitis-C is on the rise in Pakistan. Treatment of chronic hepatitis-C with pegylated interferon is expensive as compared to standard interferon. The objective of the study was to find out the end treatment response rate with standard interferon and ribavirin. **Methodology:** This case series study was conducted in Ayub Teaching Hospital Abbottabad and Orush General Hospital over a period of two years.170 patients were included in the study. These patients were HCV PCR positive either by qualitative or quantitative assay, had no other comorbidity or decompensated disease. The treatment started with standard interferon and ribavirin for six months. After the six months at the end of treatment again HCV PCR assay was done to detect hepatitis-C virus in the blood. Those who were PCR negative were responders and positive are non-responder. **Results:** The cumulative response rate was 73.5%, both sexes responded equally. Patients below 30years had the highest response rate and similarly patients having normal liver had better response than those having any degree of fibrosis. Baseline haemoglobin and ALT level did not have significant effect on treatment. **Conclusion:** Standard interferon is equally effective and comparable with the pegylated interferon which is costly and out of reach of many patients. It is therefore recommended, that combination of standard interferon and ribavirin may be the first line of treatment for chronic hepatitis-C treatment in Pakistan and pegylated interferon may be reserved for non-responders or relapsed cases

Keywords: Hepatitis-C, Interferon, Ribavirin, Cirrhosis, ALT
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INTRODUCTION

Hepatitis-C is becoming major public health problem in Pakistan, with 4.5% population infected with hepatitis-C virus (HCV).[1] WHO estimated, that 180 million people are infected with hepatitis-C and every year there is addition of three to four millions. Two third of these new infections will develop chronic disease.[2] Chronic hepatitis-C progresses into cirrhosis which is 18th largest cause of mortality.[3] HCV causative hepatocellular carcinoma is 8th largest cancer world wide[4].The globally reported prevalence of hepatitis is less than 3%, being 1.8% and 2.3% respectively in Europe and USA. The prevalence of hepatitis-C in Pakistan varies among different studies being more than 10 million people infected with hepatitis-C virus[5]. Pakistan is one of the two top countries only second to Egypt having 4.2% prevalence of chronic hepatitis-C[6]. In a recent survey world hepatitis alliance reported that 80% of the world countries have chronic hepatitis as an urgent public health issue[7]. In the light of these facts chronic hepatitis-C patients must receive urgent attention and treatment. The treatment of hepatitis-C improves liver histology, prevents liver cirrhosis and hepatocellular carcinoma. Treatment of chronic hepatitis-C, if successful will clear the virus from blood.[8] The successful treatment of hepatitis-C can help in prevention by eradicating the virus, so as reducing the reservoir. Most studies revealed that pegylated interferon and ribavirin are more effective than the standard interferon and ribavirin in obtaining sustained viral response.[9,10] In Pakistan since the burden of treatment falls on the patients himself, most of the patients are unable to get themselves treated with pegylated interferon which is costly. Since HCV genotype 3 is more prevalent in Pakistan.[11,12] The end treatment response of pegylated and standard interferon for genotype 3 are nearly the same with little differences.[13] The purpose of this study is to evaluate the effectiveness of end treatment response with standard interferon and ribavirin treated for 24 weeks

MATERIAL AND METHED

This case series study was conducted in Ayub teaching hospital Abbottabad and Orush general hospital over a period of two years .The population under study was the patients of Hepatitis-C presenting to the outdoor department of Ayub Teaching Hospital and Oursh General Hospital for the treatment of chronic hepatitis-C. Patients included in the study were HCV RNA PCR positive whether by qualitative or quantitate assay. Those had decompensated liver disease, comorbidity with reduced life expectancy or extreme of ages were excluded from the study. After selection of the patients the treatment started with standard interferon 3M units thrice weekly subcutaneously and ribavirin

400 mg three time daily with slight modification in accordance to body weight. These patients were followed up weekly for 4 weeks and then monthly for six months. During follow up period patients were examined for development of clinical symptoms like extreme depression hypothyroidism or hyperthyroidism. The laboratory investigations done were periodic measurement of complete blood counts to look for anaemia, neutropenia and thrombocytopenia. ALT levels were measured to observe the variation during treatment. After six months at the completion of treatment the HCV RNA PCR was done to detect its level in the blood. This was the end treatment response. Those patients who responded to the treatment were able to clear the virus from their blood. These patients were labelled responders, and those who could not clear the virus form their blood were non responders

RESULTS

A total of 170 patients, having hepatitis-C virus detected in their blood, whether by qualitative or quantitative assay were included in the study. Out of 170, 81 (47.6%) were male and 89 (52.4%) were female. The mean age of the patients was 40.3±10.934 years. The patients were divided into five groups each with interval of ten years. On ultrasound examination, liver was found normal in 104 (61.2%) patients, whereas fatty liver, chronic liver disease and cirrhosis was present in 28 (16.5%), 24 (14.1%) and 14 (8.2%) respectively. The mean baseline values for Haemoglobin, ALT, and TLC were 12.1053±1.55 gm/dl, 75.0295±63.584 U/ml, 6836.21±1542.689/ml respectively. The difference in these baseline values among male and female were found statistically significant *(p=0.000* for Hb, *p*=0.001 for ALT and *p*=0.002 for TLC).

After six months of treatment with standard interferon and ribavirin, 125 (73.5%) patients responded to the treatment, which was assessed by assaying PCR. Among total responders, 59 (47.2%) were males and 66 (52.8%) were females. The maximum response rate (89.5%) was observed in the age group below 30 years. The treatment response rate in other age groups is shown in table-1, and the difference in treatment response with respect to age groups is statistically significant (Pearson Chi-square=10.414 at 4df, *p=0.034)*. Baseline haemoglobin and ALT did not affect the final response rate (Table-2 and 3)

When compared with hepatic texture, the treatment response rate in patients with normal hepatic texture on ultrasonography was maximum (81.7%), whereas patients with fibrosis (altered echogenicity on ultrasound) had reduced response rate, lowest in cirrhosis (28.6%). The treatment response in patients with normal and abnormal hepatic texture was found to be statistically significant Table-4 (Pearson Chi-square=19.66 at 3 df, *p*=0.000).

Table-1: Treatment response with respect to age groups

Age groups		PCR-II (After completion of treatment)		Total
		Positive	Negative	
Below 30 years	% within Age groups	4 (10.5%)	34 (89.5%)	38 (100%)
	% of Total	2.4%	20.0%	22.4%
31–40 years	% within Age groups	17 (27.9%)	44 (72.1%)	61 (100%)
	% of Total	10.0%	25.9%	35.9%
41–50 years	% within Age groups	16 (32.7%)	33 (67.3%)	49 (100%)
	% of Total	9.4%	19.4%	28.8%
51–60 years	% within Age groups	8 (44.4%)	10 (55.6%)	18 (100%)
	% of Total	4.7%	5.9%	10.6%
Above 60 years	% within Age groups	0 (0.0%)	4 (100%)	4 (100%)
	% of Total	.0%	2.4%	2.4%
Total	% within Age groups	45 (26.5%)	125 (73.5%)	170 (100%)

Table-2: Treatment response with respect to ALT

Baseline ALT groups		PCR-II (After completion of treatment)		Total
		Positive	Negative	
Normal	% within ALT Groups	8 (23.5%)	26 (76.5%)	34 (100%)
	% of Total	4.7%	15.3%	20.0%
Up to two times	% within ALT Groups	27 (32.1%)	57 (67.9%)	84 (100%)
	% of Total	15.9%	33.5%	49.4%
Up to three time	% within ALT Groups	5 (17.9%)	23 (82.1%)	28 (100%)
	% of Total	2.9%	13.5%	16.5%
Up to four times	% within ALT Groups	4 (33.3%)	8 (66.7%)	12 (100%)
	% of Total	2.4%	4.7%	7.1%
Up to five & above times	% within ALT Groups	1 (8.3%)	11 (91.7%)	12 (100%)
	% of Total	0.6%	6.5%	7.1%
Total	% within ALT Groups	45 (26.5%)	125 (73.5%)	170 (100%)

Table-3: Treatment response with respect to Hb

Baseline Hb groups		PCR-II (After completion of treatment)		Total
		Positive	Negative	
Less than 10 gm/dl	% within Baseline Hb groups	4 (22.2%)	14 (77.8%)	18 (100%)
	% of Total	2.4%	8.2%	10.6%
10–11.9 gm/dl	% within Baseline Hb groups	19 (28.8%)	47 (71.2%)	66 (100%)
	% of Total	11.2%	27.6%	38.8%
12–13.9 gm/dl	% within Baseline Hb groups	15 (24.2%)	47 (75.8%)	62 (100%)
	% of Total	8.8%	27.6%	36.5%
14 gm/dl and above	% within Baseline Hb groups	7 (29.2%)	17 (70.8%)	24 (100%)
	% of Total	4.1%	10.0%	14.1%
Total	% within Baseline Hb groups	45 (26.5%)	125 (73.5%)	170 (100%)

Table-4: Treatment response with respect to liver texture

Ultrasound findings		PCR-II (After completion of treatment)		Total
		Positive	Negative	
Normal	% within Ultrasound Findings	19 (18.3%)	85 (81.7%)	104 (100%)
	% of Total	11.2%	50.0%	61.2%
Fatty Liver	% within Ultrasound Findings	7 (25.0%)	21 (75.0%)	28 (100%)
	% of Total	4.1%	12.4%	16.5%
Chronic liver disease	% within Ultrasound Findings	9 (37.5%)	15 (62.5%)	24 (100%)
	% of Total	5.3%	8.8%	14.1%
Cirrhosis	% within Ultrasound Findings	10 (71.4%)	4 (28.6%)	14 (100%)
	% of Total	5.9%	2.4%	8.2%
Total	% within Ultrasound Findings	45 (26.5%)	125 (73.5%)	170 (100%)

DISCUSSION

Pakistan is one of the few countries having highest prevalence of hepatitis-C in the world. These patients need treatment on urgent basis to reduce liver related mortality and morbidity. It will decrease prevalence by clearing the reservoir of the virus. Most of the studies done worldwide are on pegylated interferon and ribavirin, the response rate for genotype1 is 40–50% and for genotype 2 is 70–80%[14].which is comparable to the response rate in our study using standard interferon and ribavirin. Some studies indicated that prolonging the treatment can increase the response rate, especially for genotype 2, but it increases the cost of the treatment and adverse events.[15,16] The genotype 1 is the strongest viral factor influencing outcome.[17] This is also indicated by the results of our study, the good response is related to the genotype3a present in Pakistan.[11,12] The baseline viral load is inversely related to response.[18] In our country the patient has to bear the expenditures of treatment, so the treatment should be cheap and readily available. In this study the regimen given including standard interferon and ribavirin, had 73.5% end treatment response rate. There was no difference in response of male and female population. When we analysed the age of the patients, maximum numbers, responded were below 30 years. This finding has concordance with the reported studies, that older age has negative influence on response rate.[19]The baseline ALT and haemoglobin of the patients was also measured, both these factors did not affect the final outcome of the treatment. Patients having high ALT had equal response when compared with normal ALT levels. Similarly anaemic patient also had good response but recommendations for anaemic patients are a watchful follow up for decrease in Hb level. There is general consensus in multiple studies that normal liver has best response, and response rate decreases proportionately with the progressive fibrosis.[20] Initial abdominal ultrasound examination was done to define morphology. Patients in the study having normal liver had good response then those having fibrosis. The lowest response was observed in patients having cirrhosis. It is evident from the results of this study that the treatment implied including standard interferon is equally effective and comparable with the pegylated interferon which is costly and out of reach of many patients. It is therefore recommended on the basis of our study that, combination of standard interferon and ribavirin may be the first line treatment for chronic hepatitis-C treatment in Pakistan and pegylated interferon may be reserved for non-responders or relapsed cases. The drawback of regimen given in the study is, multiple weekly dosage resulting in more frequent flue like symptoms and fever, common side effect of interferon therapy. This opinion is further strengthened by the fact that hepatitis-C virus genotype 3a is more prevalent in Pakistan[11,12] which is equally responsive to both pegylated and standard interferon.

CONCLUSION

The conclusion of the study is, the combination of standard interferon and ribavirin is equally effective as pegylated interferon and ribavirin in treatment of chronic hepatitis-C

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