

Research Article**Comparison of normalization of serum alanine aminotransferase levels at 12th week and 24th week after start interferon therapy in cases of hepatitis C.**

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ABSTRACT

Objective: To compare serum alanine aminotransferase levels in term of normalization at 12th week versus 24th week after start of interferon treatment in patients with chronic hepatitis C.

Settings: This was a Quasi-experimental study was conducted at the Department of Medicine, Sheikh Zayed Hospital Rahim Yar Khan from March 2017 to September 2017. Total 250 patients were recruited to compare the serum ALT in term of normalization at 12th week versus 24th week after start of therapy with interferon and ribavirin in patients with chronic hepatitis C.

Results: Total 250 patients with HCV were recruited for this study. Mean age of the patients was 47.54 ± 6.74 years. Male were 136 (54%) and female were 114 (46%). Normal serum alanine aminotransferase levels were noted in 220 (88%) patients and 240 (96%) patients at 12th and 24th week respectively after the start of interferon treatment. Statistically significant ($P = 0.001$) difference in term of normalization of serum alanine aminotransferase level at 12th week and 24th week was noted.

Conclusion: Normalization of alanine aminotransferase is found significantly higher at 24 weeks of treatment as compared to 12 weeks of treatment.

Keywords: Serum level of alanine aminotransferase, hepatitis C, Ribavirin, interferon therapy

INTRODUCTION

About 180 million people globally infected by chronic hepatitis C virus. This infection is also a frequent cause of liver diseases including hepatocellular carcinoma and liver failure. Hepatitis C virus (HCV) is a RNA virus which belonged to Flaviviridae family with diameter of 40 nm to 50 nm approximately. It is a tremendous health problem in Pakistan and all over the world.¹ About 200 million individuals are suffered with HCV globally, which covers about 3.3% of the total population of world. Approximately 10 million individuals are infected with HCV in Pakistan.² There is wide variability in serum aminotransferase concentrations among

individuals patients with chronic HCV infection over time. Up to 1/3 of patients have a normal serum ALT. About 25 percent have a serum ALT concentration more than twice normal, and it is rare to find elevations more than 10 times normal. There is generally a poor correlation between aminotransferase levels and liver histology.³ It has also been suggested that serum ALT is an accurate marker of the response to interferon therapy. Interferon is widely used in treatment of HCV patients. According to some authors, the serum levels of ALT before the start of therapy should be at least 2 times the upper limit of its normal value. ALT levels decreases with the effective treatment

by interferon. We can measure ALT level to see the effectiveness of interferon therapy.⁴

Interferon is given subcutaneously at doses of 3 MIU 3 times a week for 24 weeks. INF alpha and ribavirin combination therapy has resulted 2 to 3 folds improvement in the virological response to disease.⁵ In Pakistan, chronic hepatitis C with genotype 2 and 3 are predominant and 80% to 85% response rates have been found in chronic hepatitis C patients. In Europe and America genotype 1 and 4 is prevalent; 60 % to 70% response rate was found with INF and Ribavirin combination treatment and it may require 48 weeks treatment. Treatment of chronic hepatitis C patients with interferon alpha has now replaced with pegylated interferon.⁶

Massive effort made worldwide in a search for adequate serum marker to monitor the effectiveness of interferon therapy that is cheap and easy to measure. The purpose of this study is to evaluate the changes in serum ALT at 12th week and 24th week of interferon treatment in viral hepatitis C positive patients so that some practical recommendations could be made for early monitoring of treatment response and to make decision about subsequent treatment to prevent morbidity and mortality in these patients.

MATERIAL AND METHODS

Settings: This was a Quasi-experimental study was conducted at the Department of Medicine, Sheikh Zayed Hospital Rahim Yar Khan from March 2017 to September 2017. An approval was taken from the institutional review committee and written informed consent was taken from all the patients. Total 250 patients of chronic hepatitis C for more than 6 months (positive HCV RNA by PCR and elevated alanine aminotransferase) with age range from 13 years to 80 years either male or female were recruited in this study. Patients with dual B and C viral hepatitis, patients with thyroid dysfunction before the initiation of treatment, Hepatocellular carcinoma, Decompensated-cirrhosis, previous treatment with IFN and/or ribavirin, autoimmune disease, pulmonary disease were excluded from the study.

These patients were selected from medical OPD of Sheikh Zayed Hospital Rahim Yar Khan who were under treatment for chronic hepatitis C. Base ALT level was performed along with HCV RNA by PCR. Included patients were treated with Interferon alpha 2b (INF) 3 million units subcutaneously 3 times a week and ribavirin 800-1200 mg orally daily 3 times a day for 6 months. Patients were followed up after 12 weeks and 24 weeks of starting treatment. Alanine aminotransferase tests were repeated at 12 weeks and 24 weeks. The collected data was entered on the pre-designed proforma and statistical analysis of the data was done. Mean and standard deviation was calculated for numerical data i.e. age and frequencies and percentages were calculated for categorical data. Normalization of ALT at 12 weeks versus 24 weeks was compared by chi square test. P value $\leq 5\%$ was taken as significant.

RESULTS

Total 250 patients with chronic hepatitis C were recruited for this study. Mean age of the patients was 47.54 ± 6.74 years. Comparison of serum ALT levels in term of normalization at 12th versus 24th weeks after start of interferon therapy was done. Out of 250 patients male were 136 (54%) and female were 114 (46%). (Fig. 1) Comparison of serum ALT levels in term of normalization at 12th week versus 24th week after start of interferon treatment in patients with chronic hepatitis C was done. Normal serum ALT levels were noted in 220 (88%) patients and 240 (96%) patients at 12th and 24th week respectively after the start of interferon therapy. Statistically significant ($P = 0.001$) difference in term of normalization of serum ALT level at 12th week and 24th week was noted. (Table 1) Patients were divided into 3 age groups, age group 15-30 years, age group 31-45 years, age group 46-60 years. Out of 8 (3.2%) patients of age group 15-30 years, normal alanine aminotransferase level was noted in 6 (71.43%) and 7 (87.5%) patients at 12th and 24th week respectively after the start of interferon therapy. Out of 73 (29.2%) patients of age group 31-45

years, normal alanine aminotransferase level was noted in 59 (80.82%) and 69 (94.52%) patients at 12th and 24th week respectively and 169 (67.6%) patients belongs to age group 46-60 years in which 156 (92.31%) patients had normal alanine aminotransferase level at 12th week and 164 (97.04%) patients at 24th week after the start of interferon therapy. (Table 2) After the gender distribution of patients, out of 136 (54.4%) male

patients, 118 (86.76%) and 134 (98.53%) had normal alanine aminotransferase level at 12th and 24th week after the start of interferon therapy. Among the 114 (45.6%) female patients, 102 (89.57%) and 106 (92.98%) female patients had normal alanine aminotransferase level at 12th and 24th week after the start of interferon therapy. (Table 3)

Fig. 1 Gender Distribution of the patients

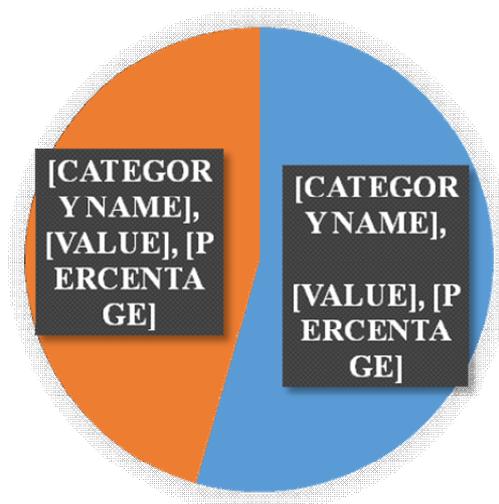


Table No. 1 Comparison of serum alanine aminotransferase level in terms of normalization at 12th and 24th weeks

Normalization	12 weeks (n= 250)		24 weeks (n=250)		P. Value
	No. of patients	%	No. of patients	%	
Yes	220	88	240	96	0.001
No	30	12	10	4	
Total	250	100	250	100	

Table No. 2 Age Distribution and Stratification Of The Patients (n=250)

Age(in years)	No. of patients	%	Normalization			
			12 weeks (n=220)		24 weeks (n=240)	
			No. of patients	%	No. of patients	%
15-30	8	3.2	6	71.43	7	87.5
31-45	73	29.2	59	80.82	69	94.52
46-60	169	67.6	156	92.31	164	97.04
Total	250	100	220(88%)		240(96%)	

Table No. 3 Stratification For Gender Of The Patients (n=250)

Gender	No. of patients	%	Normalization			
			12 weeks (n=220)		24 weeks (n=240)	
			No. of patients	%	No. of patients	%
Male	136	54.4	118	86.76	134	98.53
Female	114	45.6	102	89.57	106	92.98
Total	250	100	220(88%)		240(96%)	

DISCUSSION

Globally HCV infection is one of the leading cause of chronic liver disease (CLD). The frequency of new hepatitis C cases is growing and a number of patients are being identified with CLD and liver cirrhosis.^{8,9} INF-alpha in combination with ribavirin is the recommended treatment for HCV infection and is administered subcutaneously at a dose of 3 million units 3 times a week for 24 weeks.¹⁰ The response of therapy to INF mono for 6 months is 20% to 35% less as compared to INF and ribavirin combination therapy.¹¹

Massive effort made worldwide in a search for adequate serum marker to monitor the effectiveness of interferon therapy that is cheap and easy to measure. However, we planned to evaluate the changes in serum ALT at 12 weeks and 24 weeks of interferon therapy in viral hepatitis C positive patients so that some practical recommendations may be made for early monitoring of treatment response and to make decision about subsequent treatment to prevent morbidity and mortality in these patients.

In present study comparison of serum ALT levels in term of normalization at 12th week versus 24th week after start of interferon therapy in patients with chronic hepatitis C was done. Normal serum ALT levels were noted in 88% patients and 96% patients at 12th and 24th week respectively after the start of interferon and ribavirin therapy. Statistically significant ($P = 0.001$) difference in term of normalization of serum alanine aminotransferase level at 12th week and 24th week was noted. Similar findings were noted by Masood et al⁷, who showed that serum ALT became normal in 90.6% patients at 12 week and in 96.5% patients at 24 weeks. In one study, Nadeem et al¹³ reported treatment response at the end of 24 week as 86%. These findings are also in agreement with our study. Ashraf et al also reported treatment response rate as 79%¹⁴ while Wazir et al¹⁵ reported sustained virological response in 71.4% patients who were treated with INF alpha and ribavirin combination therapy.¹⁵ In another study Sarwar et al¹⁶ reported treatment response rate as 82%. Farooqi et al¹⁷ reported

treatment response rate as 87.3% in patients with HCV and Abbas et al¹⁸ reported treatment response rate as 90% and found normal serum ALT levels in 97% patients at 24 week of treatment. At 24 weeks of treatment of HCV with INF, Khokharet al¹⁹ noted treatment response rate as in 83% patients.

The better treatment response rate in our patients of HCV might be due to genotype 3, which is common in our country but definite evidence is not available being the limitation of the study. However, we recorded that treatment at 24 weeks is more responsive.

CONCLUSION

We concluded after comparison of serum ALT levels in term of normalization at 12th week versus 24th week after start of treatment with interferon in patients with chronic hepatitis C, normalization of serum ALT is significantly higher at 24 weeks of therapy.

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