

Original Research Article**EVALUATION OF VIROLOGIC RESPONSE IN PATIENTS WITH HCV INFECTION AGAINST DIFFERENT TREATMENT REGIMENS**Sadia Qureshi^{1*}, M. H Qazi², Saba Khalid¹

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ABSTRACT

Hepatitis C is an infectious disease of the liver and remains to be the key cause of concern on public health worldwide and has acquired endemic proportions globally. Contrasting other chronic infectious diseases, people with hepatitis C can be cured. The therapy response is measured in expressions of Virologic response. Sustained virologic response (SVR) is taken to be viral cure and is when a person's hepatitis C continues to be undetectable six months after treatment is discontinued. A study was designed to assess the treatment efficacy when patients infected with HCV 3a genotype were treated either with Interferon (INF) + ribavirin (RV) or Pegylated Interferon (Peg INF) + RV. 84 patients were enrolled in the study after a written informed consent. Their periodic virologic response was measured in terms of viral load and was found that among patients treated with Peg INF+ ribavirin attained 90% sustained virologic response and hence were cured. Those treated with INF + RV either had breakthrough infection or relapsed and failed to attain SVR. Only 20.5% of the patients attained SVR. So concluded that Peg INF+ RV treatment regimen was more efficient.

Keywords: HCV, virologic response, sustained virologic response

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INTRODUCTION

Hepatitis C (HC) is an infectious disease and affects liver predominantly. Even after two decades since its discovery, Hepatitis C virus (HCV) remains to be a key cause of concern and a massive burden on public health systems globally. It has acquired endemic proportions in our population ^[1]. Frequency of HC in Pakistan is significantly higher (4.50%) ^[2]. Unlike other chronic infectious diseases, people infected with HC can be cured of the virus. There are seven

genotypes of HCV which differ by about 30 per cent in their nucleotide sequence and are known as genotypes one to seven ^[3]. Studies conducted in different parts of Pakistan have shown that there is a great diversity of subtypes in local population with considerable regional differences. HCV infections in hepatitis patients are attributed predominantly to viral genotype 3 in Pakistan with the rate of 68.94% in Punjab, 76.88% in Sindh, 58% in KPK and 60.71% in Baluchistan ^[1]. Understanding the virologic milestones measured during therapy, at the end of therapy, and post therapy is important in optimizing the treatment plan for the individual patient. All patients should have a baseline HCV RNA level obtained prior to starting treatment. The response to the therapy is measured in terms of Virologic response. SVR also known as viral cure – occurs when a person's HC remains undetectable six months after treatment is complete ^[4]. Progress toward the goal of viral cure is assessed by measuring the amount of HC virus in a person's blood (also called HCV RNA or viral load) at specific time like before treatment begins (at baseline) and at several key time points after treatment begins, including week 4, week 12, at the end of treatment (week 24 or 48), and 24 weeks after the end of treatment (week 48 or 72). Important treatment response terms include, baseline viral load (Amount of hepatitis C virus (HCV) RNA in the blood before treatment starts), Rapid Virologic Response (RVR) (untraceable HCV RNA at week four of treatment), Early Virologic Response (EVR) ^[5] an undetectable serum HCV RNA or a 2 log¹⁰ or greater drop in HCV RNA at week 12 of therapy is observed ^[6]. Failure to achieve an EVR is considered to be the most accurate negative predictor of SVR in dual therapy ^[5-6].

The term nonresponse refers to patients who do not achieve an undetectable HCV RNA during the first 24 weeks of treatment. There are two forms of Virologic non-response that are important to distinguish from each other: null response and partial response ^[5].

A study was designed to observe the virologic response in patients infected with HCV genotype 3a when treated with INF and Ribavirin or Peg INF+ Ribavirin therapy to assess the treatment efficacy.

METHODOLOGY

This was a prospective, cohort study, which was conducted at local general hospitals. Total 84 patients were enrolled in the study after written informed consent. A data collection sheet was developed according to the requirement of the study for recording the relevant information including patient demographic features and Serum HCV RNA levels at different time points of the treatment. Adult male / female patients, who were seropositive for HCV RNA on testing with the polymerase chain reaction, were included in the study. Patients with decompensated cirrhosis, anemia (hemoglobin concentration, less than 12g/dl in women and less than 13g/dl in men), pregnant women, men whose female partner is pregnant, not willing to take contraceptive measures and patients with human immunodeficiency virus infection, psychiatric conditions, seizure disorders, cardiovascular disease, hemophilia, poorly controlled diabetes mellitus, or autoimmune diseases were excluded. All patients were treated as per approved standard

guidelines of AASLD (American Association for the study of liver diseases) and IDSA (Infectious Disease Society of America), USA.

We divided our study group into two main groups. Group 1 included the patients who were infected with HCV Genotype 3a and were being treated with INF + RV. Group 2 included the patients who were infected with HCV Genotype 3a and were being treated with Peg INF + RV.

Different treatment regimens were evaluated in relation to serum HCV RNA level (initial viral load), and the virologic response.

The patient's Virologic response against standard therapy was evaluated by estimating HCV RNA levels at the start of the therapy labeled as week 0, then at week 4, week 12, week 24 and week 48 by real time PCR. As per their Virologic Response the patients were divided into different group's i.e.

- Early Virologic Responders
- Rapid Virologic Responders
- Sustained Virologic Responders
- Partial Responders
- Non Responders

Efficacy of treatment was evaluated by monitoring the Virologic Response in response to the prescribed regimens. Treatment showing early Virologic response and then SVR was considered to be the most efficient.

RESULTS AND DISCUSSION

To evaluate the treatment efficacy in our study group we monitored the Virologic response of the patients as per guideline of the EASL. As per guideline of the EASL, SVR is considered to be the actual cure.

The comparison of number and percentages of patients who have had attained RVR, EVR, DVR or not responded to the therapy at all, when treated with different regimens was done. We found that only 6 (13.6%) patients attained RVR, 32 (72.7%) attained EVR, none attained DVR and 6 (13.6%) proved to be non-responders when treated with a combination of INF+ RV while amongst those who were treated with PEG INF + RV 15 (37.5%) attained RVR, 17 (42.5%) attained EVR, 5 (12.5%) achieved DVR and 3 (7.5%) proved to be non-responders (see table 1).

When SVR against different treatment regimens was assessed, we found that 90% of the patients were successfully treated with Peg INF+ RV treatment regimen, 2.5% patients were relapsers and 7.5% of the patients were non responders. Amongst those who were treated with INF+ RV treatment regimen only 20.5% of the patients were successfully treated, 65.9% of the patients

had breakthrough infection when still were on treatment and 13.6% of these patients did not respond to the treatment at all (see table 2).

Table 1: Comparison of viral response against different treatment regimens

	Number	Viral Response			
Treatment Regimen	N (84)	RVR	EVR	DVR	NR
		n (%)	n (%)	n (%)	n (%)
INF + RV	44	6 (13.6)	32 (72.7)	0	6 (13.6)
Peg INF + RV	40	15 (37.5)	17 (42.5)	5 (12.5)	3 (7.5)

RVR=rapid viral response

EVR=early Viral response

DVR=delayed viral response

NR=non-responder

INF +RV= Interferon+ Ribavirin

Peg INF + RV = Pegylated Interferon+ Ribavirin

Table 2: Comparison of SVR against different treatment regimens

	Number (84)	SVR	Relapser	NR
Treatment Regimen		N (%)		
INF + RV	44	9 (20.5)	29 (65.9)	6 (13.6)
Peg INF + RV	40	36 (90.0)	1 (2.5)	3 (7.5)

SVR=Sustained viral response

NR=non- responder

INF +RV= Interferon+ Ribavirin

Peg INF + RV = Pegylated Interferon+ Ribavirin

The goal of the HCV therapy is to eradicate the infection completely so that the complications related to it like hepatic inflammation, fibrosis, cirrhosis; hepatocellular carcinoma and even death can be prevented. The end point of a therapy is the undetectable HCV RNA and achieving sustained Virologic response. Undetectable HCV RNA at 48 week after the therapy has been stopped is SVR 48. Long term follow-up studies have shown that an SVR corresponds to definite cure of HCV infection in more than 99% of the patients ^[3, 7].

Our results clearly suggested that the Peg INF + RV therapy was more efficient and effective. Although initially almost 90% of the patients treated with INF + RV responded to the therapy but 65.9% of them relapsed and only 20.5% of the patients attained SVR and it is recommended that the treatment efficacy is based on the percentage of the patients attaining SVR. On the other hand 90% of the patients treated with Peg + INF + RV therapy and only 2.5% of the patients relapsed.

It was observed that the patients who don't show any response till 12 weeks or after they proved to be non-responders and if there is detection of virus even at 24 week of therapy it suggests treatment failure. These findings were in agreement with the findings of the previous work done in other populations ^[8].

CONCLUSION

It is concluded that the patients infected with HCV genotype 3a can be treated well with combination of Peg INF + RV. Moreover INF + RV treatment should not be used to treat these patients as most of them ends up with relapse or break through infection.

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