Original Article

Response of Combined Antiviral Therapy in Chronic HCV Infection in Interior of Sindh

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ABSTRACT

Objective: To observe the treatment response and sustained response with combined antiviral therapy in patients of chronic hepatitis C in interior of Sindh.

Design: A prospective cross-sectional, observational study carried out from August 2006 to Dec. 2009.

Setting: Research Medical Center LUMHS Jamshoro, Departments of Pathology, Peoples Medical College Nawabshah and Department of Biotechnology University of Karachi.

Patients: A total of 344 HCV-PCR positive patients with persistent abnormal alanine aminotrasferase levels and histological evidence of chronic hepatitis with either fibrosis or inflammatory activity by biopsy were evaluated 239 men and 105 women with ages between 18-55 years of age were included in the study.

Methodology: All the patients went for ELISA test for the presence of HCV antibodies by ELISA kit of Biokit Spain, than all the patients were given Interferon alpha 3 mu subcutaneously on alternate days three times a week with Ribivirin 400mg three times a day as a combination therapy up to 6 to 12 months.. In order to see the treatment response, the presence of HCV RNA was checked after 6 months and 12 months.

Results: Out of 344 patients 276(80.23%) showed positive response (negative HCV-PCR at six months), while 68 (19.76%) cases showed no response (Positive HCV-PCR) after six months of combined antiviral therapy. 276 (80.23%) patients showed positive response (negative HCV-PCR) after 6 months to combined interferon alpha and ribazole therapy, while 214 (62.20%) causes showed sustained response (negative HCV-PCR at one year) after 6 months of stoppage of combined therapy.

Conclusion: The data in the current study shows that the treatment response and sustained response is different in comparison to other parts of the world. The long-term outcome of liver disease and the effectiveness of interferon with ribivirin therapy might be related with different genotypes of HCV, so further HCV genotype related studies are recommended.

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INTRODUCTION

HCV infection is worldwide health problem. HCV has a high propensity for inducing the life long persistent infections[1,2]. The clinical course of viral hepatitis is unpredictable. Patients may experience spontaneous remission or may have indolent disease without progression for many years, while some

have rapidly progressive disease and develop cirrhosis or even carcinomas within a few years, but which of the patients have a non-favourable evolution can not be predicted[3-5].

Although a certain degree of immunity appears to be induced following infection, it fails to control the infection. A number of possible reasons for the failure to mount a protective immune response are being studied and in particular, there is growing evidence that typically, HCV infections are associated with low viral titer which may account for low antigenic stimulus and rapid evolution of mutant viruses with altered B and T cell epitopes and also virus particles are closely associated with immunoglobin, thus could result in masking of antigenic determinants[6]. HCV as well as other members of Flaviviridae family might enter the cells by binding to low density lipoproteins (LDL) receptors[7]. HCV circulates in the sera of infected individuals with significantly lower concentration than HBV[8]. Thus there is a need for effective therapies to treat HCV infection[9].

The cost effective analysis indicates that antiviral therapy is economical beneficial[10,11]. Successful therapy is associated with clearance of serum HCV, RNA, normalization of serum ALT levels, and improvement in liver histology[12].

Keeping all these above facts in view, this study was conducted to observe the treatment response and sustained response with combined antiviral therapy in 344 HCV-PCR positive patients of chronic hepatitis C in interior of Sindh. This is first ever study in Pakistan which shows the data of whole interior of Sindh, as the cases were collected from all the teaching hospitals attached with all the medical colleges of Sindh. The information gained about response to therapy is showing its impact on progression of chronic hepatitis and treatment and is improving our understanding on HCV which is beneficiary for clinicians in treating these patients with precise therapy.

MATERIALS AND METHODS

This study was conducted at Research Medical Center LUMHS Jamshoro, Pathology Department Peoples Medical College for Girls Nawabshah and Department of Biotechnology University of Karachi, during August 2006 to Dec. 2009.

This study was a multi centric study covering all the interior of Sindh. The blood samples from 344 patients were collected from various medical wards of Liaquat University Hospital Jamshoro and Hyderabad, Nawabshah Medical College Hospital Nawabshah, Chandka Medical College Hospital Larkana, Civil Hospital Sukkur and Muhammad Medical College Hospital Mirpurkhas. The patients included in the study were having ages between 18-55 years, with persistent abnormal alanine aminotrasferase levels, of presence of HCV-RNA in serum of patient by PCR & histological evidence of chronic hepatitis with either fibrosis or inflammatory activity by biopsy

The suspected patients of chronic hepatitis were informed about the study, they signed a consent form and ELISA test for the presence of HCV antibodies was performed by ELISA kit of Biokit Spain.

Therapy:

All the patients were given Interferon alpha 3 mu subcutaneously on alternate days three times a week with Ribivirin 400mg three times a day as a combination therapy up to 6 to 12 months. In order to see the treatment response, the presence of HCV RNA was checked after 6 months and 12 months, so that in this way results were tabulated.

RESULTS:

In this prospective study (Table-1) a total

of 344 HCV-PCR positive patients were evaluated (239 men and 105 women). Their ages rang from 18-55 years with a mean age of 35.14 years. The duration of infection was evaluated in all the patients; it was below 2 years in 140 (40.69%), between 3 and 5 years in 196 (56.9%) and above five years in 8 patients (2.32%). The age at infection was below 20 years in 42 (12.20%) patients, between 21 & 40 years in 221 (64.25%) and above 40 years in 81 patients (23.55%).

Table-01

Characteristics of the study population

Variable	Number of Patients	%age
Gender		
• Male	239	69.47%
• Female	105	30.52%
Age of infection		
• ≤ 20 years	42	12.20%
• 21-40 years	221	64.25%
• > 40 years	81	23.55%
Duration of infection		
• ≤ 2 years	140	40.69%
• 3 -5 years	196	56.9%
• > 5 years	08	2.32%

Response to combined antiviral therapy:

The response to combined 6 months antiviral (interferon alpha + ribazole) therapy in patients with chronic hepatitis is presented in Table-02. Out of 344 patients 276 (80.23%) showed positive response (negative HCV-PCR at six months), while 68 (19.76%) cases showed no negative response (Positive HCV-PCR) after six months of combined antiviral therapy. While 214 (62.20%) cases showed sustained response (negative HCV-PCR at one year) after 6 months of stoppage of combined therapy.

Table-02

Response to combined six months therapy (interferon alpha + Ribazole) six months therapy in patients with chronic hepatitis-C

Variable	Number of Patients	%age
HCV-RNA PCR		
• No response (HCV-RNA PCR +ve)	68	19.76%
• Positive response (HCV-RNA PCR -ve)	276	80.23%
HCV-RNA PCR after Six Months of stoppage of therapy		
• Positive sustained response (HCV-RNA PCR -ve)	214	62.20%

DISCUSSION

The major goal in the treatment of HCV infection is to prevent the development of decompensated liver disease and death. This can be accomplished by preventing new infection, reducing the chance that acute infection will progress to chronic hepatitis, or effectively treating chronic infection. The goal in treating chronic hepatitis should include eradication or prolonged suppression of virus replication, reduction of hepatic inflammation, and ultimately, slowing of the rate of progressive liver injury. Not all these goals may be achievable in every patient. However, eradication of chronic HCV infection is now possible in half or more of treated patients[13].

The therapy for chronic hepatitis C has evolved steadily since alpha interferon was first approved for use in this disease in 1989[14,15]. Although the introduction of combination therapy

with interferon and ribivirin has markedly improved clinical outcomes, less than half of those with HCV infection can be expected to have favourable response to the agents that are currently available[16,17]. The success of these therapies can be measured in terms of biochemical response (Normalization of alanine aminotransferase levels), virological response (as defined by negative result on qualitative PCR assay for HCV RNA) and histological response, but in clinical practice there is little indication for post treatment biopsy[18]. The treatment success has been best evaluated in terms of response at the end of therapy (end of treatment response) and six months after cessation of treatment (sustained treatment response). Persons with a sustained virological response have a high probability having a durable biochemical, virologic and histologic response[19].

In our study 80.23% cases showed positive treatment response (negative HCV-PCR) after 6 months to combined interferon alpha & ribazole therapy, while 62.20% cases showed sustained response (negative HCV-PCR at one year) after 6 months of stoppage of combined therapy. This finding is contrary to studies conducted at other parts of the world, which show 53% positive treatment response and 17% sustained response[20], and some show 47% positive treatment response and 13% sustained response[21], in some other studies the efficacy of this combination therapy is reported to be around 20-40% [22,23] in some studies and another show 50%[24,25]. The differences in the response rate is quite low in other studies which may be related to HCV genotypes, as the prevalence of HCV genotypes is different in different parts of the world, & the above mentioned studies have been conducted in different parts of the world mostly in western world, where the HCV genotypes are different as that in Pakistan so the response of treatment is different.

CONCLUSION

The data in the current study shows that the treatment response and sustained response is different in comparison to other parts of the world. The long-term outcome of liver disease and the effectiveness of interferon with ribivirin therapy might be related with different genotypes of HCV, so further HCV genotypes related studies are recommended.

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