ISSN NO. 2320-5407

Journal homepage: http://www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH

RESEARCH ARTICLE

Standred interferon therapy and its Response rates in Chronic HCV Patients in District Mardan, Khyber Pakhtunkhwa

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Manuscript Info

Manuscript History:

Received: 12 July 2013
Final Accepted: 25 July 2013
Published Online: August 2013

Key words:
Hepatitis C,
Interferon, Ribavirin,
Virologic response,
End of treatment,
District Mardan.

Abstract

To eradicate the Hepatitis C Virus from the bodies of the infected individuals Interferon and Ribavirin based therapy is used. HCV is highly prevalent in District Mardan Khyber Pakhtunkhwa that is why it is important to determine the response of standard interferon based therapy in Chronic HCV patients of this region. A total of 215 patients were selected for interferon based therapy. The patients were selected from three different Tehsil of District Mardan. After confirmation of active HCV infection by q-PCR, standard interferon with Ribavirin was given to patients for 6 months. After completion of therapy, end of treatment virologic response (ETR) was calculated. After completion of the 6 months long therapy, the results obtained were as. Out of total 215 patients, 168 (78.13%) were negative for HCV RNA and showing end of treatment response (ETR) while 47 (21.86%) were positive for HCV RNA and did not show ETR. In Tehsil Mardan, out of 102 patients who had completed therapy, 76 patients (74.51%) showed ETR and 26 (25.49%) did not show the ETR. In Tehsil Kattlang, we found that out of total 51 patients who had taken 6 months therapy, 41 (80.39%) were negative for HCV RNA and 10 (19.61%) were resistant to therapy while in Tehsil Tkhatbhai, out of 62, 50 (80.64%) were negative and 12 (19.35%) were positive. The above discussion shows that antiviral therapy against HCV infection in chronic HCV patients of District Mardan KPK province is 78.13%. The high response rate may be due to the prevalence of genotypes 2 and 3.

Introduction

Hepatitis C virus, most important public health problem and leading cause of liver infection and affected an estimated 180 million people worldwide (William, 2006). Its genome consists of a single stranded, positive-sense RNA which was of 9600 bp long and encoding single ploypeotein. Epidemiological studies showed that HCV infection increases annually more then one million new cases are reported. Among all type of Hepatitis, HCV is more than other type's infection i-e HBV (*Cooreman* and schoondermark, 1996). Their major associated problems are the leading cause of liver transplantation and organ storage. The introduction of effective therapy for the prevention of life threatening diseases is the vital target. Its especially most important in underdeveloped countries, Where HCV infection is more and most of the infected patients have financial problems for the treatment of HCV infection (Ahmad *et al.*, 2012).

Major purpose of Hepatitis treatment is to eradication the virus that is Sustained virologic response (SVR) Which is defined as absence of HCV in serum after six months of treatment completion and evidenced through polymerase chain reaction (PCR) tests, when treatment strategies have been shifted from interferon monotherapy to combined interferon plus Ribavirin a great improvement in the SVR rates have been observed by the past so many years (Muhutchison *et al.*, 1998; Poynardn *et al.*, 1998).

Hepatitis C therapy started almost 25 year ago with a small trial of recombinant human interferon Alfa (Hoofnagle *et al.,* 1986). Interferon has broad spectrum activities so that why it was selected against the viruses and it might also be active against still undiscovered non-A and non-B hepatitis. Interferon was found very active against HCV and resultant effects were decrease the level of ALT. Before the discovery of the HCV the effects of interferon was unknown but the result of using the interferon was the reduction in HCV RNA level. This led to SVR in patients of HCV (Hoofnagle and Seeff, 2006). Ribavirin a nucleoside analogue, known to have activity against a number of flaviviruses had strong effects in lowering the level of ALT and little effects on serum HCV RNA levels. Besides that when Ribavirin and interferon was given in combination for 48 weeks then it has increased sustained virologic response rate, then sustained virologic response rates was 40-50% which is two to three times more than that obtained with interferon alone (Dibiceglie *et al.,* 1995; Muhutchison *et al.,* 1998). When Ribavirin combined with Pegylated interferon it response rate has better than standard interferon (Fried *et al.,* 2002).

Standard interferon therapy is use in Pakistan, due to economic reasons and Pakistan Society of Gastroenterology and GI Endoscopy also favours the use of SdIF in genotype-3 (Hamid *et al.,* 2004). PgIF is out of reach for the majority of the patients because the Government of Pakistan is providing only SdIF via a special Prime Minister's initiative programme against hepatitis, thus. Response rates of standard interferon in chronic HCV patients have never been investigated in District Mardan, KPK. The study had focused on the effectiveness of standard interferon therapy as given in the case of chronic HCV patients in District Mardan, Khyber Pakhtunkhwa province of Pakistan.

Material and Methods

Present study was conducted at District Head Quarter Hospital, Mardan (DHQ) in collaboration with Provincial program for Hepatitis Control and Prevention.

To assess the response of standard interferon combination therapy against chronic HCV infection, we selected three different regions/Tehsil of District Mardan, KPK province. The regions were Tehsil Kattlang, Mardan and Tehsil Tkhatbhai. In present study, patients with suspected liver disease were included who were referred to Head Quarter Hospital, Mardan (DHQ) from three Tehsil of Mardan District during June 2012 to January 2013 in the Provincial Program for Control and Prevention of Hepatitis which provides molecular based diagnostic facility that general public sensitive, specific and more reliable diagnostic tests on the basis of utilizing PCR and real-time PCR methods and Hepatitis treatment (Standred interferon therapy). After initial screening with ICT (ACON, USA) and Elisa assay kit (Glibe Diagnostics, ITALY), PCR test was performed for each patient sample according to the instructions of the manufacturers (Gibco BRL, Life Technologies USA). Among the confirmed anti-HCV patients, only 215 patients whose PCR was positive, were selected for interferon therapy keeping in mind the exclusive therapy criteria that is, age of the selected personals (18-55 years), platelets and Hb levels within the accepted range, stage of cirrhosis, no co-infection associated and ALT level higher than normal. We selected 102 patients from Tehsil Mardan, 62 from Tehsil Tkhatbhai and 51 patients from Tehsil Kattlang. There was no need for separate written informed consent from subjects for this study, since this analysis was a part of the original protocol in a routine workup of Molecular Diagnosis and Treatment.

PCR positive patients were given standard interferon combination therapy i.e. interferon alpha 2a (3MIU thrice a week) plus Ribavirin (1000-1200 mg/day) continuously for 6 months with repeated testing of ALT level and HCV RNA during and after the interferon therapy.

Statistical Analysis & Graphical representation

Statistical Analysis for the calculation of percentage and distribution of the samples in different groups, Microsoft Excel 2007 was used. It was also used for graphical representation.

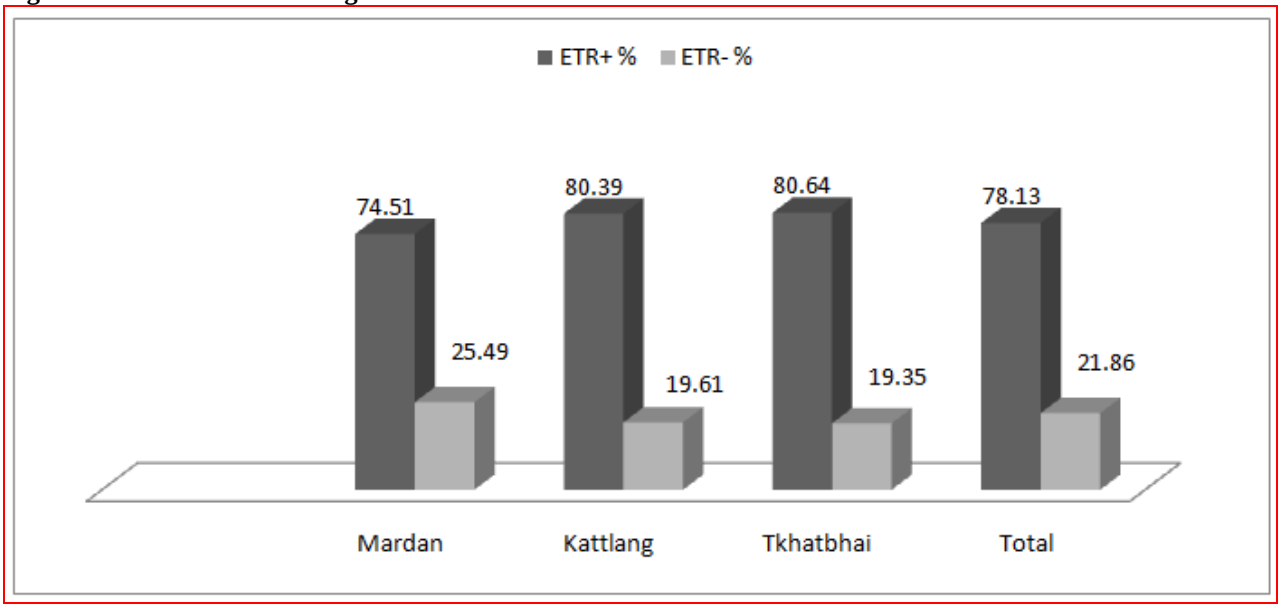
Results

After completion of the 6 months long therapy, the results obtained were as. Out of total 215 patients, 168 (78.13%) were negative for HCV RNA and showing end of treatment response (ETR) while 47 (21.86%) were positive for HCV RNA and did not show ETR. In Tehsil Mardan, out of 102 patients who had completed therapy, 76 patients (74.51%) showed ETR and 26 (25.49%) did not show the ETR. In Tehsil Kattlang, we found that out of total 51 patients who had taken 6 months therapy, 41 (80.39%) were negative for HCV RNA and 10 (19.61%) were resistant to therapy while in Tehsil Tkhatbhai, out of 62, 50 (80.64%) were negative and 12 (19.35%) were positive. (Table 1).

Table 1: Tehsil wise distribution of HCV positive sample and their respective ETR

Tehsil	T. sample	Age group	Sex		ETR^+	ETR^-	ETR^+ %	ETR^- %
			Male	Female				
Mardan	102	19-52	80	22	76	26	74.51	25.49
Kattlang	51	18-55	36	15	41	10	80.39	19.61
Tkhatbhai	62	21-54	51	11	50	12	80.64	19.35
Total	**215**		**167**	**48**	**167**	**48**	**78.13**	**21.86**

Figure 1. Tehsil wise Percentage of ETR Bar



Our study revealed that response rate of combination therapy was comparatively higher in Tehsil Tkhatbhai (89.64%), Tehsil Kattlang (89.39%) and than in Tehsil Mardan (74.51%). The percent response of overall therapy calculated was 78.13% (Figure 1).

Discussion

Hepatitis C Virus infection is scattering very speedily. HCV incidence is nearly 200 million people worldwide and each year infects 3-4 million new people (Yvan *et al.,* 2004). The seroprevalence of Hepatitis C virus reported from different parts of Pakistan, in last 5 years, is from 2.2%-13.5%. The highest seroprevalence of hepatitis C has been reported from Lahore (13.5%) (Amin *et al.,* 2004) Jasmshoro (9%) and Mardan (9%) (Almani *et al.,* 2002; Khan *et al.,* 2004).

Pakistan is a underdeveloped country and the literacy rate is also low, due to which lack of information regarding the pathogenecity, routes of transmission and the proper procedures of diagnosis proper screening facilities or expertise in screening blood and blood products for possible HCV infection in public sector hospitals is partly contributing towards the spreading of the disease and treatment are rarely followed. Therefore HCV infection has become an economic burden on the people of Pakistan and especially in District Mardan KPK.

In the present study we determined the End of Treatment Response (ETR), which may be defined as the absence of HCV RNA at the end of 6 months Interferon therapy, in CHC patients. The average calculated ETR was 78.13% and resistance calculated was 21.86%. Different Tehsil of District Mardan KPK province had different ETR rates; like ETR was very high in Tehsil Tkhatbhai followed by Tehsil Kattlang and then Tehsil Mardan [Figure 1].

The average response rate of interferon combination therapy with Ribavirin in chronic HCV patients of District Mardan population was 78.13% [Table 1]. Although District Mardan has different population groups which may vary regarding response to interferon based therapy. Instead, the response rate

was similar to other studies conducted internationally (Mann *et al.,* 2006; Strader *et al.,* 2004) as well as locally (Wazir *et al.,* 2002), when combination therapy treatment with Ribavirin and interferon.
In District Mardan prevalence of HCV infection has been recorded as 9% (Khan *et al.,* 2004). The high ETR rate in district Mardan might be due to the high prevalence of HCV genotypes 2 and 3 and might be due to high literacy rate, as by adopting proper procedures for diagnosis and treatment, the efficacy rate might be increased as compared to those who have no or little knowledge.

Conclusion

The above discussion shows that antiviral therapy against HCV infection in chronic HCV patients of District Mardan KPK province is 78.13%. The high response rate may be due to the prevalence of genotypes 2 and 3.

Acknowledgement

We are grateful to the Department of Microbiology Hazara University, Mansehra and DHQ hospital, Mardan for approving and facilitating this study. We are thankful to Mr. Aurangzeb Tubassum Dealing assistant HP&C, DHQ Hospital, Mardan for providing lab facilities. We also appreciate Dr. Kashif Haleem and Dr. Isfahan Dr. Azam Hayyat, Miss Nadia Jabeen, Mr. M. Junaid and Muhammad Iqbal Ahmad Alvi Department of Microbiology Hazara University Mansehra, Pakistan for helpful discussions and advice during development of the manuscript.

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