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RESEARCH ARTICLE

The ETR (End Treatment Response) of Chinese Brand Human recombinant interferon alpha 2a plus Ribavirin in chronic hepatitis C patients selected from Combined Military Hospitals in Pakistan

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ABSTRACT

This Study was carried out to determine the End of Treatment Response (ETR) of a Chinese Source Human Recombinant Interferon Alpha 2a and Ribavirin in chronic hepatitis C affected patients, selected from different combined military hospitals in Pakistan. In this study hepatitis affected non-cirrhotic patients from different combined military hospitals in Pakistan were selected from September 2010 to April 2011. Sixty seven patients were selected based on the inclusion exclusion criteria. Fifty seven patients completed the 24 weeks therapy for Hepatitis C. The Patients (n=57) had persistently raised serum aminotransferase (ALT), positive HCV antibodies by 3rd generation ELISA, positive HCV RNA by polymerase chain reaction. Study group patients underwent 24 weeks therapy with a Chinese source Interferon and Ribavirin and subsequently followed up for the End of Treatment Response by the assay of HCV RNA by polymerase chain reaction at 24 weeks. Patients of chronic hepatitis C (44 males and 13 females) had age range 20-56 years. After 24 weeks of therapy with a Chinese source Interferon and Ribavirin, 73.7% patients showed a favourable ETR manifested by Negative HCV RNA polymerase chain reaction.Treatment with a Chinese source Interferon and Ribavirin combination therapy for 24 weeks produces a favourable End of Treatment Response in patients of chronic hepatitis C from different military hospitals in Pakistan.

Keywords: Chronic Hepatitis C, Interferon and Ribavirin.

1. INTRODUCTION

Hepatitis C virus is one of the most common blood-borne viruses and is associated with significant morbidity and mortality. It affects 170 million people worldwide and 2.4%-6.5% people in Pakistan. Hepatitis due to hepatitis C virus (HCV) is an important public health problem worldwide[1]. HCV causes hepatitis, cirrhosis and hepatocellular carcinoma (HCC), and globally reported HCV prevalence ranges between 1% and 3%[2] .Pakistan is endemic proportion of viral hepatitis with prevalence of Hepatitis C about 6% in general population. The annual liver related admissions and mortalities in established GI and liver centres ranges from 25 – 35% in various parts of the country. All these places are enormous economic burden on health cost in national budget[3]. In chronic HCV infection, a sustained response to treatment can be achieved with interferon alpha in 10% to 20% of patients, in spite of high relapse rates[4]. The addition of Ribavirin to this treatment results in a more than two-fold increase in sustained response rates[5-6].Currently, the aim of treatment in hepatitis C infection is the eradication of HCV, which helps to delay the progression to terminal liver disease and to prevent the development of HCC[7].Genotype 2-3, low viral burden, low body weight, female gender, young age, and the absence of bridging fibrosis or cirrhosis in biopsy are associated with a sustained viral response in the treatment of chronic HCV infection[8-9]. In this study, we evaluated End Treatment Response (ETR) rates with INTEFEN (interferon alpha 2a) plus Ribavirin in patients selected from Combined Military Hospitals in Pakistan. According to the World Health

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Organization (WHO) estimates, South-East Asia is considered a high risk region for HCV with a prevalence of 2.15%[10]. HCV is one of the most common chronic infections in Pakistan. This review is based on evidence gathered from published data related to the magnitude, genotype, disease characteristics and therapeutic response to antiviral therapy for HCV in Pakistan. The aim of this study was to determine the End of treatment Response after 24 weeks of therapy with a Chinese Source Interferon and Ribavirin in Chronic Hepatitis C patients.

2. PATIENTS AND METHODS:

In this study data was collected from combined military hospitals of various areas of Pakistan from September 2010 to April 2011. The patients were given Injection INTEFEN(Human recombinant interferon alpha 2a) 3 MIU administered subcutaneously 3 injections per week on alternate days and Ribavirin 800 to 1200mg daily in 2 to 3 divided doses.

65 patients were selected amongst which 57 completed the treatment. Patients had persistently raised serum amino transferase (ALT), positive HCV antibodies by 3rd generation ELISA and positive HCV RNA by polymerase chain reaction. Exclusion criteria was, those treated previously with IFNand Ribavirin, history of neoplastic, autoimmune, severe cardiac or pulmonary disease, those currently using immunosuppressant and or steroids and pregnant patients. All patients were assessed in out-patients setting for safety, tolerance and efficacy at the end of week 1, 2 than every 4 weeks for 24 weeks. Biochemical and haematological profiles were checked initially fortnightly and then monthly for 24 weeks. Serum HCV RNA was done after 24 weeks of treatment. Patients having HCV RNA negative by PCR after 24 weeks of treatment were considered to achieve ETR.

METHODS ADOPTED:

It was a case series of cohort pattern, which was based on computerized database of patients with chronic hepatitis C treated at The Combined Military Hospitals of Pakistan. Patients with genotypes 2 and 3, who received interferon therapy, were included.Patients with genotype other than 2 and 3; those features of decompensated liver disease like ascites, variceal bleeding or portosystemic encephalopathy; and those with co-morbid conditions like positive hepatitis B surface antigen, positive HIV (Human Immunodeficiency virus), other chronic liver diseases i.e. alcoholic liver disease, hepatotoxic drugs, autoimmune chronic hepatitis, haemochromatosis and cirrhosis with child class C were also excluded[83].Variables of patients at the outset including age, gender, weight, Baseline alanine aminotransferase (ALT), Aspartate Aminotransferase (AST), haemoglobin, platelet count and Total Leucocyte count were recorded. All patients were counseled regarding both options of interferon therapies available, i.e. standard interferon and ribavirin or pegylated interferon and ribavirin, with complete information regarding duration and Results. As the Treatment was available to the entitled patients on Free of cost Basis so economic status of the patient was not considered in this study. Study patients were followed fortnightly for first month and monthly thereafter. On each visit, detailed history and examination regarding possible side effects of therapy were done. Complete blood count and liver function tests were carried out on each follow-up. Duration of treatment, side effects experienced during therapy and number of injections used was recorded.Patients who received 90% of standard duration and dose of therapy were declared to have completed treatment. Standard therapy was defined as minimum of 72, thrice weekly injections of standard interferon with Ribavirin > 800 mg/day. Patients who lost to follow-up and those in whom treatment has to be discontinued due to side effects were considered as non-responders for intention to treat analysis.

3. RESULTS AND DISCUSSION:

Out of 65 selected patients, **57** patients successfully completed this treatment with standard Interferon 3 MIU (INTEFEN) plus Ribavirin >800 mg per day in two or three divided doses for 24 weeks. Treatment was discontinued due to intractable side effects in 4, while 1 patient lost to follow up. Extreme weakness with inability to tolerate therapy was responsible for discontinuation in 2 patients, severe depression in 1, thyroid dysfunction and recurrent leucopenia resulted in stopping injection therapy in one patient. After 24 weeks of therapy following were the recorded Patients Variables.

RESPONSE AFTER 24 WEEKS OF THERAPY (n=57)

VARIABLES	MALE	FEMALES
HCV RNA POSITIVE	12(27.2%)	3(23.0%)
HCV RNA NEGATIVE	32(72.7%)	10(76.9%)
ALT NORMAL	36(81.8%)	9(69.0%)
AST NORMAL	36(81.8%)	10(76.9%)

The patients were evaluated for their End of Treatment Response (ETR) after 24 weeks of Interferon and Ribavirin therapy. Before the start of the treatment all 57 patients were positive for HCV RNA by Qualitative PCR. After the

successful completion of the treatment, among 44 male patients, 12 patients (27.2%) were Positive for HCV RNA by real time Qualitative PCR. 32 male patients were Negative for HCV RNA by Real time qualitative PCR. Whereas ALT and AST levels were normal for 36 male patients.In case of Female patients, 3 females (23%) were positive for HCV RNA by real time qualitative PCR, whereas 10 female patients (76.9%) were Negative for HCV RNA by real time qualitative PCR. ALT and AST levels were normal for 9 and 10 female patients respectively.

Hepatitis C is a major healthcare problem in Pakistan. Measures should be taken at the national level to identify its actual burden and to control factors responsible for its spread. Genotype 3 was the predominant type of virus in the studied patients. End of treatment response achieved with Interferon and Ribavirin therapy was 73.7% with better outcome in patients with high baseline ALT, age < 40 years.The treatment cost using a Chinese source Interferon is almost half as compared to the brand leader. While the results from this study show that the response rate towards Chinese source Interferon is comparable if not superior to the Brand Leader. I.e. Roferon A, Intron A.

4. CONCLUSION:

Since genotype 3 is the predominant in Pakistan and this genotype shows excellent response to the Standard Interferon and Ribavirin, so by treating the patients using Chinese source Interferon a lot of money can be saved, in most of the cases the Interferon therapy is provided from the Government institutes, so keeping in view the results of this study a lot of public money can be used by purchasing the less expensive brands having comparable efficacy to the brand leader.

The use of Pegylated interferon should only be considered keeping in view the affordability and economical status of the patient and providing the combination therapy to the patients at large.

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Conflict of Interest: None Declared

