ORIGINAL ARTICLE

Frequency of Iron Overload in Patients of Chronic Hepatitis C Undergoing Therapy and Treatment Response in Patients with Iron Overload

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ABSTRACT

Aims: To determine the frequency of iron overload in patients with chronic hepatitis C undergoing interferon plus ribavirin therapy and to evaluate the treatment response in patients with iron overload.

Methods: This descriptive case series study was conducted in Hepatitis Clinic and Gastroenterology Outpatient Department, Services Hospital Lahore over a period of six months, from June 2013 to December 2013. Two hundred and eleven patients were included in the study. Interferon was started in a dose of 3 million units subcutaneously thrice a week and weight based ribavirin was given. Basal serum iron levels were measured in every patient at the start of treatment. Presence or absence of iron overload was documented. HCV RNA was assessed by polymerase chain reaction (PCR) for a successful end of treatment response (ETR).

Results: One hundred and seven (50.7%) patients were male and one hundred and four (49.3%) patients were female. Ages of the patients ranged between 16-60 years with mean age 37.6±9.9. One hundred and four (49.3%) patients were of 16-35 years of age with mean age 29.7±5.095 years. One hundred and seven (50.71%) patients had their ages between 36-60 years with mean age 45.20±6.94 years. Forty four (20.9%) patients of chronic hepatitis C were found to be in iron overload; among these 26(59.1%) patients were males and 18(40.9%) patients were females. Thirty-two (72.7%) patients of chronic hepatitis C with iron overload did not achieve successful ETR and twelve (27.3%) patients with iron overload achieved successful ETR.

Conclusion: It was concluded from the study that higher levels of serum iron levels were identified in the patients of chronic hepatitis C. Presence of iron over load is associated with poor response to INF therapy. Therefore, routine biochemical assessment of the serum iron status should be done in these patients prior to initiation of therapy to improve the ETR of costly INF therapy.

Keywords: Interferon, iron overload, chronic hepatitis C, end of treatment response.

INTRODUCTION

Hepatitis C virus (HCV) infection is a growing public health problem. A worldwide prevalence of hepatitis C is 3%, affecting approximately 170 million people globally. It is the most common blood born infection. Eighty percent of infected patients with hepatitis C virus develop chronic hepatitis, and 25-30% of them will progress to cirrhosis[1,4]. 25% of these progress to hepatocellular carcinoma with an annual risk of 1- 4% per year.[4] World Health Organization (WHO) defines chronic hepatitis C as a high burden of disease for Pakistan. It has estimated that about 10 million persons infected with hepatitis C virus in Pakistan, with reported prevalence varies from 2.4-6.5%[4,5]. Hepatitis C has six major genotypes 1-6. Genotypes 1 and 4 are more refractory to interferon therapy compared with genotypes 2 and 3[1,2,3]. In Pakistan commonest genotype type is 2 and 3 and type 1 is less common[4,6].

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The treatment of hepatitis C has evolved over the years. In third world countries like Pakistan combination therapy including of ribavirin and conventional IFN or ribavirin with addition of poly ethylene glycol linked interferon (PEG-IFN)[7] is still practiced. Treatment of chronic hepatitis C with interferon and ribavirin combination has proved to be effective in terms of virological response[4,8]. The most important predictive factors, which affects the response of treatment are age, race, body mass index, hepatitis C virus genotype, pretreatment virological load, alcohol abuse, liver fibrosis stage, insulin resistance and iron over load[3]. Iron overload is frequently observed in 40 to 74% cases of chronic hepatitis C[3,7]. Liver is an important organ for the storage of iron, where a third of body's total iron is stored in the form of ferritin or hemosiderin. Physiological capacity of liver for iron storage is limited. In the presence of iron overload, this capacity exceeded and lead to liver injury[3].

Iron act as an important co-morbid factor in disease progression of hepatitis C to advanced liver

fibrosis[3,7]. Iron induces oxidative stress in the hepatocytes, which leads to cell membrane damage, DNA instability and mutagenesis. Due to these effects, iron is considered a proinflammatory, profibrogenic factor and a carcinogenic[3,9,10]. It has been noticed that effectiveness of interferon depends on the regulation of hepatitis C virus (HCV) translation factors, the expression of which up regulated by iron. Therefore, iron is a negative prognostic factor in the treatment course of chronic hepatitis C and it is linked to resistance to the response of interferon-ribavirin treatment[3,9,11]. There was very limited local data available regarding the frequency of iron overload in chronic hepatitis C and effects of iron overload on treatment response in chronic hepatitis C. There was also a big difference between the available data of iron overload frequency and effects of iron overload on treatment response in the local and international studies. In a study of Devrajani et al[9] it was reported that serum iron overload was found in 74% patients of chronic hepatitis C and in a study of Sikorska et al[3] it was reported that serum iron overload was found in 10% to 40% patients with chronic hepatitis C. In a study done by Olynyk et al[12] it was stated that iron overload was found in up to 88% non responder patients of chronic hepatitis C, treated by standard interferon. In another study by Franchini et al[13] it was concluded that iron overload did not correlate with treatment response. Therefore, this study was designed to determine the frequency of iron overload in chronic hepatitis C patients and to evaluate the treatment response in patients of chronic hepatitis C with iron overload. This study will signify the magnitude of iron over load in patients of chronic hepatitis C. If the results of this study are eventful, then it is suggested to incorporate the determination of iron overload prior to initiation of treatment of chronic hepatitis C.

PATIENTS AND METHODS

This was a descriptive case series comprised 211 patients and conducted in Hepatitis Clinic and Gastroenterology outpatient Department, Services Hospital Lahore. Inclusion criteria included patients of both genders between the ages of 16 years to 60 years; patients with compensated liver disease, naïve for interferon therapy, planning to receive interferon therapy; patients giving consent to participate in the study and patients with hepatitis C virus genotype 2 and 3.Exclusion criteria included patients who had history of repeated blood transfusions, patients who were receiving iron replacement therapy for anemia, known cases of chronic kidney disease, thalassemia and hereditary hemochromatosis as evidenced from history, examination and investigations. Serum iron

levels were measured in all the selected patients. The outcome variable of this study was iron overload. Basal serum iron levels were measured at the start of standard treatment with Interferon plus ribavirin in patients of chronic hepatitis C. Interferon was started in a dose of 3 million units subcutaneously thrice a week and weight based ribavirin was given. 1000 mg of ribavirin was used in patients less than 75 kg and 1200 mg was used in patients more than 75 kg. Hepatitis C virus RNA by polymerase chain reaction (PCR) was assessed for the end of treatment response (ETR).

RESULTS

107(50.7%) patients were male and 104(49.3%) patients were female. Ages of the patients ranged between 16-60 years with mean age 37.6±9.9. 104(49.3%) patients were of 16-35 years of age with the mean age 29.7±5.095 years. 107(50.71%) patients had their ages between 36-60 years with mean age 45.20±6.94 years. 44(20.9%) patients of chronic hepatitis C were found to be iron overloaded. 26(59.1%) patients were males and 18(40.9%) were females. 32(72.7%) patients of chronic hepatitis C with iron overload did not achieve successful ETR and 12(27.3%) patients with iron overload achieved successful ETR.

DISCUSSION

Chronic hepatitis C affects more than 170 million people in the world[1,2,3]. Its prevalence in Pakistan estimated by various studies is between 2.4-6.5%[4]. The treatment of chronic hepatitis C in third world countries is still well established with conventional interferon or pegylated interferon in combination with ribavirin[4,8]. Lower levels of serum and hepatic iron levels in chronic hepatitis C has been associated with an improved response to INF[14]. Iron overload is a negative prognostic factor in the treatment of chronic hepatitis C and is linked with development of resistance to INF[3,9,11]. Several mechanisms have been proposed for the explanation of the relation between HCV infection and iron overload. It has suggested that iron may promote HCV replication[15].

One hundred and seven (50.7%) patients were males and this difference of prevalence with respect to gender reflected in various studies conducted countrywide as well as worldwide, where male patients were in overwhelming majority[3,9]. Ages of the patients ranged between 16-60 years with mean age 37.6±9.9 which was similar in accordance with already published study[9].

In our study, 20.9% patients of chronic hepatitis C had iron overload, supporting the already

established fact by different worldwide conducted studies[3,16] where 28% had iron overload[16]. But our study is in contrary to the local study, where 74% a larger number had iron overload. The local study was on a small scale as far as number of patients was concerned as compared to our study[9]. Out of 44 patients with iron-overload, 32(72.7%) patients with iron overload were failed to achieve successful ETR, supporting the fact already published by international studies, where 88% had failed to achieve ETR[12,17].

CONCLUSION

It concluded from the study that the higher levels of serum iron levels identified in the patients of chronic hepatitis C and iron over load's presence is associated with poor response to INF therapy. Therefore, routine biochemical assessment of the serum iron status in these patients is an important step in the management protocol to improve the ETR of costly INF therapy.

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