ORIGINAL ARTICLE

Therapy Induced Anemia in Patients with Chronic Hepatitis C Receiving Combination Therapy of Pegylated Interferon Alpha and Ribavirin

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ABSTRACT

Aim: To determine the frequency of therapy induced anemia in patients with Chronic Hepatitis C receiving combination therapy of pegylated interferon alpha and ribavirin.
Study design: It was a descriptive cross sectional survey.
Duration: From Feb 2012 to Sep 2012.
Materials and methods: A total of 50 newly diagnosed patients of chronic hepatitis C considered candidates for receiving interferon-alpha and Ribavirin at standard doses for 24 weeks coming to District Headquarter Teaching Hospital, Sahiwal were enrolled.
Results: During the study period, majority of the patients were between 41-50 years i.e. 32%(n=16), mean and standard deviation was recorded as 38.33±4.60, 38%(n=19) male patients and 62%(n=31) were found female. Frequency of therapy induced anemia at 2nd week of therapy was 24%(n=12) were found anemic.
Conclusion: The frequency of therapy induced anemia in patients with Chronic Hepatitis C receiving combination therapy of pegylated interferon alpha and ribavirin at 2nd week of therapy reveals a significant anemia.
Keywords: Chronic Hepatitis C, combination therapy of pegylated interferon alpha and ribavirin, anemia.

INTRODUCTION

Viral hepatitis is a serious global health problem.[1] Chronic hepatitis C virus infection is present in 3-10% of Pakistani population and genotype 3 is the most prevalent subtype in our populations.[2] The recommended treatment for hepatitis c is pegylated alpha interferon and Ribavirin therapy for 24 or 48 weeks.[3] About 65% of the patients developed adverse effect during therapy in the form of flu like symptoms, sleep disturbance, lack of appetite, depression, persistent fever, anemia, thrombocytopenia, neutropenia and skin rash.[2] Ribavirin also causes doses-dependent reversible hemolytic anemia that, in combination with the myelosuppressive effects of interferon, results in a mean drop in hemoglobin (Hb) level of 3.7 g/dl within 4 weeks.[3] This anemia <10/dl occurred din 20.5% of patients at week 2 after the start of treatment. Patients whose Hb(hemoglobin) value was than 12 g/dl before the start of treatment, 14% had to discontinue, Ribavirin owing to severe anemia. Discontinuation was more common among patients aged 60 years or old.[4] In univariate analysis, reduction of the Ribavirin dose significantly influenced Ribavirin-induced hemolytic anemia[5]. In CHC (Chronic hepatitis C) patients treated with interferon alpha (IFN), IFN alphpa and Ribavirin (IFN+RIB) anemia was observed in 37.5% and 56.6% cases respectively.[6] On mulutivariate analysis, pretreatment hemoglobin of less than 14 g/dl level and age 55 years or older and patient with impaired renal function may be at increased risk of Ribavirin induced anemia.[5] On a regimen of standard interferon and high-dose Ribavirin (1000-1200 mg/d), 54% of patients had a greater than 3 g/dl decline in hemoglobin at some point during the 48 week of treatment.[7] The average Hemoglobin decline is 2-3g/dl over the first 4 week of therapy, for many patients this response is impaired by concomitant interferon-related bone marrow suppression. Approximately 8-9% of the patients receiving combinatin therapy experienced decrease in Hemoglobin concentrations to <10g/dL, 12-22% of the patients require Ribavirin and/or interferon alpha dose reduction and 6-26% of patients discontinued combination therapy because o adverse effects.[7] According to the study conducted natinall. There was mean hemoglobin (Hb) fall of 0.87d/dl at 3 months and 2g/dl at 6 months of antiviral therapy 10% of the patients developed anemia after 6 months and 2g/dl at 6 months of antiviral therapy, 10% of the patients developed anemia after 6 months of antiviral therapy[8].

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In Pakistan therapy induced anemia (Hb≤11g/dl) was found in 7% of cases at three months[8]. Pretreatment hemoglobin of less than 12g/dl and age 55 years or older and patients with impaired renal function may be at increased risk of therapy induced anemia[6].

According to the available evidence the therapy induced anemia is ore prominent and frequent during the treatment as well. In this study we planned to find out the frequency of anemia at 2 weeks. If this frequency presents to be higher then we may recommend that early management steps for its control must be taken.

MATERIAL AND METHODS

A total of fifty (50) patients related to the study were collected in specially designed proforma. Purpose and risk, benefits of the study was explained to the patients and the written informed consent was taken. When the patient received in Hepatology OPD, if fulfilling inclusion criteria. Therapy (pegylated interferon alpha 2b in dose of 1.5mcg/kg once a week plus Ribavirin 1200mg daily) was started and Hemoglobin levels were repeated at the end of first week, and finally at 2nd week to assess therapy induced anemia. If anemia was detected at any time during the course of treatment further actions were undertaken in a compassionate and befitting manner. Patients were managed according to standard protocol. These patients were observed very closely with frequent follow ups in the OPD. Hemoglobin was done at hospital laboratory. All these information was collected through proforma.

The data was analyzed through SPSS (statistical package for social sciences) version 14.0. Quantitative variable of study were age which was calculated by mean ± SD and qualitative variables were gender and therapy induced anemia were measured by frequency and percentage.

RESULTS

A total of 50 patients were recruited after fulfilling the inclusion/exclusion criteria to determine the frequency of therapy induced anemia in patients with Chronic Hepatitis C receiving combination therapy of pegylated interferon alpha and ribavirin.

Table 1 : Age Distribution of the Subjects (n=50)

Age (in years)	=n	%age
20-30	12	24
31-40	15	30
41-50	16	32
51-55	7	14
Total	50	100
Mean and S.D.	38.33±4.60	

Age distribution of the patients reveal that 24%(n=12) of the patients were found between 20-30 years of age, 30%(n=15) were found between 31-40 years, 32%(n=16) were found between 41-50 years while only 14%(n=7) were recorded between 51-55 years of age, mean and standard deviation was recorded as 38.33±4.60 (Table 1). Table 2 reveals 38%(n=19) male patients and 62%(n=31) were found female. Frequency of therapy induced anemia at 2nd week of therapy was calculated in Table 3, where 24%(n=12) were found anemic while 76%(n=38) were not anemic (Table 3).

Table 2: Gender of the subjects (n=50)

Gender	=n	%age
Male	19	38
Female	31	62
Total	50	100

Table 3: Frequency of therapy induced anemia at 2nd week of therapy (n=50)

Anemia	=n	%age
Yes	12	24
No	38	76
Total	50	100

DISCUSSION

Currently worldwide 130–170 million people are infected with hepatitis C virus (HCV).[9] Over 70% of HCV infections become chronic and if untreated may lead to cirrhosis and hepatocellular carcinoma, necessitating liver transplantation.

The ability to enhance treatment response rates renders ribavirin central to the treatment of HCV infection. Maximizing the benefit of ribavirin to patients requires striking the right balance between its antiviral activity and its treatment-limiting side-effect, hemolytic anemia.

In Pakistan, therapy induced anemia (Hb≤11 g/dl) was found 7% of cases at three months.[8] I was intended to determine the frequency of anemia at 2nd week of therapy. It was rationalized that if this frequency presents to be higher then we may recommend that early management steps for its control must be taken.

In our study we found 24% of the patients with anemia which is in contrast with a study conducted by Nomura H and colleagues who conducted the study to identify the factors contributing to ribavirin-induced anemia, they found a 2 g/dL decrease in hemoglobin concentrations in patients with anemia was observed at week 2 after the start of treatment. The hemoglobin concentration in patients with > or =2 g/dL decrease at week 2 was observed to be significantly lower even after week 2 than in patients with <2 g/dL decrease ($P < 0.01$).

Oze T, and workers conducted a study[10] in Japan to examine the factors correlated with the progression of ribavirin-induced hemolytic anemia in patients with chronic hepatitis C treated by interferon and ribavirin combination therapy and found that out of 482 patients whose Hb value was more than 12 g/dl before the treatment, 68 patients (14%) had to discontinue ribavirin owing to severe anemia. Patients in the "2 by 2"-positive group (Hb decline over 2 g/dl) and the group with lower CL/F (apparent clearance) were significantly more likely to discontinue ribavirin owing to severe anemia. Discontinuation was more common among patients aged 60 years or older than for those under 60 years old (21% vs. 9%, P <0.001). Among patients aged 60 years or older, only the "2 by 2" standard was significantly associated with the discontinuance of ribavirin owing to severe anemia in a multivariate analysis (odds ratio, 4.18; P < 0.001).

The results of this study regarding age are also in agreement with the above study as we range of our subjects were upto 55 years only, however, on the other hand a limitation of the study was also observed due to the reason that we did not stratified anemia according to age as we also have 30.4% of the patients in elderly age group of our study i.e. >40 years of age and in our country due to poor socioeconomic class patients may also not improve their Hb level during treatment.

However, following the results of this study and other studies reveal that anemia at 2 weeks may be the reason for discontinuation of therapy and the other notable parameter may be that therapy at elderly age can cause anemia in patients with Chronic Hepatitis C receiving combination therapy of pegylated interferon alpha and ribavirin. Moreover, therapy induced anemia diagnosed very early (after 2nd week) may help to take early management steps for its control.

CONCLUSION

The frequency of therapy induced anemia in patients with Chronic Hepatitis C receiving combination therapy of pegylated interferon alpha and ribavirin at 2nd week of therapy reveals a significant anemia.

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