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Original Article

Sustained virological response to pegylated interferon and ribavirin in patients with genotype 3 HCV cirrhosis

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ABSTRACT

Background: Chronic hepatitis C (CHC) virus infection in patients with cirrhosis is difficult to treat. There is limited data on the outcome of treatment for genotype 3 HCV infection with cirrhosis.

Aims: To determine sustained virological response (SVR) and its predictive factors in patients with cirrhosis due to genotype 3 HCV infection treated with pegylated interferon and ribavirin (RBV).

Methods: Consecutive patients with compensated cirrhosis due to HCV genotype 3 with positive HCV RNA treated with peg-IFN and RBV in our Gastroenterology Clinics during November 2005 to December 2006 were included in this study. Cirrhosis was diagnosed on the basis of liver biopsy and/or biochemical testing and ultrasound of abdomen. Primary end point of treatment was SVR.

Results: Of 66 patients, 32 (48.5%) were male. The mean age was 46.2±10.1 years; there were 61 (92.4%) patients with Child's A cirrhosis followed by 5 (7.6%) with Child's B type. 33 (50%) patients received pegylated interferon alfa-2a (180 µg/wk) with ribavirin and 33 (50%) received pegylated interferon alfa 2b (1 µg /kg/week) with ribavirin. EVR was achieved in 44 (66.7%), and ETR in 46 (69.7%); overall SVR was achieved in 38 (57.6%) patients. Factors predictive of SVR were age (p value = 0.03), treatment naïve status (p value = 0.04) and EVR (p value<0.001). Five patients were unable to complete the treatment due to side effects or cytopenias.

Conclusions: Treatment of patients with HCV genotype 3, compensated cirrhosis, with pegylated interferon and ribavirin is effective and well tolerated.

KEYWORDS: hepatitis C, pegylated interferon, compensated cirrhosis; genotype 3; HCV cirrhosis

Introduction

Hepatitis C (HCV) is the second most common chronic viral infection affecting 170 million people worldwide.[1-3] HCV is responsible for 25-30% of global cases of cirrhosis associated with an annual risk of hepatic decompensation and hepatocellular carcinoma (HCC) in up to 5% and 1-4% cases, respectively.[1,4,5] Treatment with pegylated interferon (Peg-IFN) and ribavirin (RBV) is considered the first line treatment for hepatitis C. There is sustained virological response (SVR) in 40-50% and approximately 80% in HCV genotype 1 and 2/3, respectively.[3,4] However, the response to the antiviral treatment depends upon many host- and virus-related factors including age, gender, HCV genotype and viral load and stage of liver fibrosis.[6] Liver fibrosis is an important negative prognostic factor in patients with HCV infection that makes the prognosis dismal.[7] Antiviral therapy in HCV-related cirrhosis is now recommended in order to stop viral replication and prevent HCC and ultimately hepatic decompensation.[3,4,8] Moreover, the achievement of an SVR is associated with a significant halt in the process of hepatic fibrosis,[9] reduction of liver-related mortality, and risk of complications.[7,10,11] Nevertheless, the response rates to anti-viral therapy differ with the stage of hepatic fibrosis.[12] Patients with cirrhosis have a lower chance of clearing serum HCV-RNA and are more prone to interferon and ribavirin related adverse effects than patients without cirrhosis.[13] Upto 38% of SVR has been reported in subjects with advanced fibrosis after standard interferon and RBV therapy. On the other hand, SVR by pegylated interferon monotherapy is reported to be 30% in patients with HCV cirrhosis.[14]

In Pakistan HCV infection reportedly affects approximately 10 million people and is the most common cause of chronic liver disease.[2] The HCV genotype type 3 is the most prevalent

genotype affecting 67-87% cases.[15-17] Due to lack of medical coverage by the government and poor economical state, most of our patients with genotype 3 HCV infection are treated with standard interferon and RBV therapy.[18] HCV genotype 3 is considered easy to treat, however such data has been extrapolated from subgroup analysis in larger trials, mostly conducted on a Caucasian population with genotype other than 3.[6,19] In addition, available data concerning rates of SVR with peg-IFN and ribavirin therapy in patients with genotype 3 HCV-related cirrhosis are limited. Lower rates of SVR for genotype 3 have been reported as compared to genotype 2 in few recent clinical trials after peg-IFN and RBV therapy.[20] However, many patients with advanced liver disease are usually excluded from pivotal randomised controlled studies. Hence, data regarding efficiency and tolerability of peg-IFN and RBV combination therapy for genotype 3 HCV-related cirrhosis is limited. There is no data available from Pakistan on treatment of patients with genotype 3 HCV-related cirrhosis with peg-IFN and RBV.

Therefore, we conducted an analysis of HCV genotype 3 cirrhotic patients treated with peg-IFN alfa 2a or 2b and RBV at the Aga Khan University Hospital, Karachi, Pakistan. The aim of the study was to determine the sustained virological response (SVR) and factors predicting SVR in patients with compensated cirrhosis due to HCV genotype 3 infections treated with peg-INF alfa 2a or 2b and ribavirin.

Patients and Methods

Study population

This was a prospective study. Consecutive patients with compensated cirrhosis with Child Turcotte Pugh (CTP) Class A and B due to genotype 3 HCV infection visiting Gastroenterology Clinics of The Aga Khan University Hospital, Karachi, Pakistan from November 2005 to December 2006 were included in the study. Cirrhosis was defined either as liver biopsy-proven cirrhosis (METAVIR stage 4)[21] or, in the absence of liver biopsy, as an AST–platelet ratio index (APRI) score greater than two on at least two occasions in the 6 months preceding treatment.[22] Features of cirrhosis on ultrasound such as irregular margins of liver, reduced size of liver, splenomegaly and/or dilated portal vein were also used as indicators for liver cirrhosis on ultrasound abdomen. All patients had detectable anti-HCV antibody (by ELISA-3) and HCV RNA PCR (COBAS Amplicor HCV qualitative assay) in serum with normal or elevated ALT. Those who were non-responders or had relapsed to prior treatment with standard interferon alfa 2a or 2b with or without RBV i.e. non-naïve patients were also included. HCV genotyping was performed by HCV-PCR reverse hybridisation (INNOLIPA) technique. All laboratory tests were performed at the central laboratory of The Aga Khan University Hospital, Karachi.

Patients were excluded from the study who had 1) HCV-related decompensated cirrhosis; defined as ascites, portosystemic encephalopathy, hepatorenal syndrome, hepatocellular carcinoma (HCC) and recurrent variceal bleed, 2) concomitant HBV, HDV or HIV infection, 3) major psychiatric illness, 4) hemoglobin < 8 g/dL, neutrophil count <1500 cells/mL , platelet count < 85,000/dL (4), 5) serum creatinine >1.5 mg/dL, 6) concomitant metabolic or autoimmune liver disease, 7) post liver transplant patients, 8) pregnancy, 9) uncontrolled seizures, 10) severe heart disease or other absolute contraindications for the treatment.

All patients had received either peg-IFN alfa 2a (Pegasys; Hoffmann-La Roche, Basel, Switzerland) 180 µg/week subcutaneously along with RBV or peg-IFN alfa 2b (Peg-Intron; Schering-plough, Kneilworth, NJ) 1.0 µg/kg/week along with RBV. RBV was given as 10-12 mg/kg in 2 to 3 divided doses. The decision to administer peg-IFN alfa 2a or 2b was based on the primary physician's discretion.

Assessment of response to antiviral therapy

The therapeutic responses were assessed as follows: (i) early virological response (EVR) defined as undetectable HCV RNA (<50 IU/mL) in serum after 12 weeks therapy, (ii) end of treatment response (ETR) defined as undetectable HCV RNA in serum at the completion of treatment which was assessed at 36 and 48 weeks depending on the duration of treatment, (iii) sustained virological response (SVR), defined as undetectable HCV PCR 24 weeks after completion of antiviral therapy (iv) non-responders (NR) defined as lack of clearance of HCV RNA at any point during the therapy and (v) relapser (RR), defined as re-appearance of HCV RNA within 24 weeks after completion of therapy.

Monitoring and follow-up of patients

Patients were assessed in out-patient clinics, initially 2 weekly for 1 month then 4 weekly until the end of treatment. Following treatment follow-up visits were conducted at weeks 12 and 24 post-treatment. Physical signs for hepatic decompensation, adverse effects of the antiviral therapy, complete blood count and ALT were recorded on each visit. ALT and HCV PCR were tested at weeks 12, 24, end of treatment and 24 weeks after completing the treatment. Treatment was terminated in case of clinical hepatic decompensation or hemoglobin < 7.0 g/dL, platelets <50,000/mm^3. However, peg-IFN or RBV dose was modified and erythropoietin and/or granulocyte-colony stimulating factor (G-CSF) were given in situations where hemoglobin was <7 g/dL and absolute neutrophil count (ANC) <750/mm^3. Patients with cirrhosis are usually prescribed a treatment of more than 6 months regardless of the HCV genotype.[21,23] We offered treatment for 36 weeks to patients who had achieved clearance of virus at 12 weeks, i.e. achieved EVR; the treatment was extended to 48 weeks if the EVR was not achieved but HCV PCR became undetectable at 24 week.

Clinical decompensation was defined as the development of ascites, hepatic hydrothorax, and porto-systemic encephalopathy or variceal bleed during treatment. The primary end point was SVR. Secondary end points were drug tolerability (i.e. number of patients who completed the treatment protocol, clinical or biochemical worsening and death). Data were also analysed to determine the predictors of SVR outcome.

The study was approved by the Ethical Review Committee of The Aga Khan University Hospital, Karachi.

Statistical Analysis

Data were analysed using SPSS for windows version 16.0 (SPSS Inc, Chicago, Illinois, USA). Results were presented as mean ± standard deviation for quantitative variables and frequencies (percentages) for qualitative variables. Age, gender, BMI, previous treatment status, Child's class, baseline hemoglobin, total leukocyte count (TLC), platelet count,

prothrombin time (PT), total bilirubin, albumin, alanine amino-transaminase (ALT), type of pegylated interferon used, and EVR were considered potential predicting factors for SVR. To assess the association between SVR and categorical variables, the Chi-square or Fisher exact test was used, where appropriate. Further, to assess the difference in proportions of the SVR and non-SVR groups and quantitative variables, the independent sample t-test was used.

To evaluate potential predicting factors for SVR, univariate and multivariate logistic regression analyses were performed. Factors that were significant in the univariate analysis were used in the multiple logistic regression models. A p value < 0.05 was taken to be significant.

Results

From November 2005 to December 2006, 350 patients received anti-viral therapy for HCV. Out of 350, 66 (18.86%) patients fulfilled the eligibility criteria and were treated with peg-IFN and RBV. Over all, there were 32 (48.5%) male and 34 female patients; the mean age of the patients was 46.23 ± 10.1 years. The mean body mass index (BMI) was 22.36 ± 3.1 kg/m^2. Other characteristics and baseline laboratory parameters of patients are described in **Table 1**.

Out of 66 patients, 33 (50%) received injection peg-IFN alfa 2a, 180 µg/week subcutaneously along with RBV and the other 33 (50%) patients received weight-based peg-IFN alfa 2b, 1 µg/kg/week along with RBV. Among those who received peg-IFN alfa 2b, 2, 8, 18 and 5 patients received 50 µg, 80 µg, 100 µg and 120 µg/week of doses, respectively, based on their body weight. All patients received RBV 10-12 mg/kg in 2–3 divided doses. Amongst the non-naïve patients the duration between previous standard interferon and RBV therapy and current peg-IFN and RBV therapy ranged from 7-72 months. There were 46 (67.7%) patients who received 36 weeks treatment and 15 (22.7%) patients received 48 weeks treatment, as they were unable to achieve EVR at 12 weeks.

Out of 66 patients the treatment was completed by 61 (92.42%) patients. Overall EVR was achieved in 44/66 (66.7%) cases while end of treatment response (ETR) was achieved by 46/66(69.7%) cases. However, among all patients SVR was achieved in 38/66 (57.6%) patients. Moreover, SVR was achieved in 38/61 (62.3%) patients who were able to complete anti-viral therapy.

When the demographic features and baseline characteristics were compared between patients who had and who had not achieved SVR there was no statistically significant difference except in the BMI (p value = 0.04) and baseline platelet counts (p value = 0.02) (**Table 2**). Baseline platelet counts were significantly higher amongst those who achieved SVR (p value = 0.02). Although the mean BMI was within normal range in both groups, it was significantly higher (23.01±3.48 vs. 21.48±2.26, p value = 0.04) in those who were unable to achieve SVR.

Out of 34 non-naïve patients 15 (44.1%) were non-responders and 19 (55.9%) had relapsed to conventional interferon with or without RBV. However, after treatment with pegylated interferon and ribavirin, 6/15 (40%) non-responders and 10/19 (52.6%) relapsers achieved SVR (p value = 0.46). Hence, similar response was observed with pegylated interferon and ribavirin among non-responders and relapsers following initial treatment.

EVR was achieved in 34/38 (89.5%) patients who were able to achieve SVR later on as compared to 10/28 (35.71%) patients, who did not achieve SVR (p value <0.001, OR 0.065, 95% CI 0.018-0.238). Furthermore, a higher proportion of patients who achieved ETR had achieved SVR as compared to those who failed to achieve SVR [38 (100%) vs. 8 (28.57 %)], p value<0.001, OR 0.174, 95% CI 0.093-0.326). There was no difference in achieving SVR for those who received peg-IFN alfa 2-a along with RBV or peg-IFN alfa 2-b and RBV (28% vs. 28.8%, p-value 0.59).

On univariate analysis younger age (p value = 0.09), lower BMI (p value = 0.054), Child's class A (p value = 0.11), naïve to treatment (p value = 0.07), baseline platelet count (p value = 0.03), baseline alkaline phosphatase (p value = 0.18) and achievement of EVR (p value<0.001) were found to be significant predicting factors for SVR (**Table 3**).

However, on multivariate logistic regression analyses age (p-value 0.03), naïve status for treatment (p-value 0.041) and EVR (p-value < 0.001) were found to be significant predicting factors for SVR (**Table 4**).

Table 1: Baseline characteristics of patients treated with antiviral therapy

Characteristics	n=66 n(%) or Mean ± SD
Gender	
• Male	32 (48.5)
• Female	34 (51.5)
Treatment status	
• Naïve	32 (48.5)
• Non-Naïve	34 (51.5)
Child class	
• A	61 (92.4)
• B	5 (7.6)
Hemoglobin (mg/dL)	12.94 ± 1.67
TLC count x10^9/L	6.36 ± 1.98
Platelets x10^9/L	178.36 ± 66.56
PT (control of 12 sec)	13.71 ± 4.28
Total bilirubin (mg/dL)	0.97 ± 0.33
Baseline ALT (IU/mL)	86.95 ± 43.19
Alkaline phosphatase (IU/mL)	83.76±29.95
Albumin (mg/dL)	3.48 ± 0.48

Table 2: Comparison of demographic features and baseline characteristics between patients who reached SVR and those who did not

Variables	SVR achieved (n=38)	SVR not achieved (n=28)	p value
Age (years)	44.39 ±11.15	48.71±8.0	0.07
Gender			
• Male	18 (56.25%)	14 (43.75%)	0.51
• Female	20 (58.82%)	14 (41.18%)	
BMI (kg/m^2)	21.48±2.26	23.01±3.48	0.04
Treatment status			
• Naive	22 (68.75%)	10 (31.25%)	0.06
• Non-naïve	16 (47.05%)	18 (52.94%)	
Child class			
• A	37 (60.65%)	24 (39.34%)	0.09
• B	1 (20%)	4 (80%)	
Hb (mg/dL)	12.76 ±1.62	13.19 ± 1.72	0.30
TLC x10^9/L	6.14 ± 1.86	6.66 ± 2.12	0.29
Platelets x10^9/L	213.63 ± 75.3	177.64 ± 46.05	0.02
PT (control of 12 sec)	13.38 ± 1.33	14.16 ± 6.43	0.53
Total bilirubin (mg/dL)	0.979 ± 0.34	0.97 ± 0.31	0.90
ALT (IU/mL)	84.74 ± 50.11	89.96 ± 32.16	0.60
AP (IU/mL)	88.05 ± 33.25	77.93 ± 24.15	0.15
Albumin (mg/dL)	3.49 ± 0.47	3.48 ± 0.51	0.90

Table 3: Univariate analysis of potential factors associated with SVR

Variables	SVR (n=38) n(%)	No SVR (n=28) n(%)	OR (95% CI)	p value
Age (years)	44.39±11.15	48.71±8.0	0.51(0.40-0.66)	0.09
Gender				
• Male	18(56.25%)	14(43.75%)	0.90 (0.33-2.39)	0.83
• Female (Ref.)	20(58.82%)	14(41.18%)		
BMI	21.48±2.26	23.01±3.48	1.19 (0.99-1.42)	0.054
Treatment status				
• Naive	22(68.75%)	10 (31.25%)	2.47 (0.90-6.76)	0.07
• Non-naive	16(47.05%)	18(52.94%)		
Child Class				
• A	37(60.65%)	1(20%)	0.16 (0.01-1.54)	0.11
• B	24(39.34%)	4(80%)		
Baseline Hb (mg/dL)	12.76±1.62	13.19±1.72	0.85 (0.63-1.14)	0.29
Baseline TLCx10^9/L	6.13±1.86	6.66±2.12	0.87 (0.67-1.12)	0.28
Baseline plateletsx10^9/L	213.63±75.3	177.64±46.05	1.009 (1.001-1.01)	0.03
Baseline PT (control of 12 sec)	13.38±1.33	14.16±6.43	0.95 (0.83-1.08)	0.49
Total bilirubin (mg/dL)	0.97±0.34	0.97±0.31	1.003 (0.22-4.41)	0.99
Baseline ALT (IU/mL)	84.74±50.11	89.96±32.16	0.99 (0.98-1.009)	0.62
Alkaline phosphate (IU/mL)	88.05±33.25	77.93±24.15	1.01 (0.99-1.03)	0.18
Albumin (mg/dL)	3.49±0.47	3.48±0.50	1.05 (0.38-2.92)	0.91
Type of peg-IFN				
• Pegasys	19(57.57%)	14(42.42%)	1.0 (0.37-2.65)	0.99
• Peg-Intron	19(57.57%)	14(42.42%)		
EVR	34(89.5)	10(43.5)	0.06 (0.01-0.23)	<0.001

Table 4: Multiple logistic regression analysis of potential factors associated with SVR

Variables	SVR (n=38) n (%)	No SVR (n=28) n (%)	OR (95% CI)	p value
Age (years)*	44.39 ±11.15	48.71±8.0	0.90(0.82-0.99)	0.03
Treatment status				
• Naive	22(68.75%)	10 (31.25%)	0.21 (0.04-0.93)	0.04
• Non-naive	16(47.05%)	18(52.94%)		
EVR	34(89.5)	10(43.5)	0.03 (0.006-0.22)	<0.001

**Age ±SD*

Due to the development of anaemia and neutropenia on anti-viral therapy, 10 (15.15%) patients required supportive erythropoietin or granulocyte colony stimulating factor (G-CSF) during treatment. Dose reduction of peg-IFN and RBV was required in 5 (8.2%) patients due to cytopenias, marked lethargy and myalgias.

Five (7.6%) patients were unable to complete the treatment due to either poor tolerance or various side effects not responding to supportive treatment. Two patients developed worsening thrombocytopenia and absolute neutropenia not responding to G-CSF therapy. Refractory anaemia that did not respond to erythropoietin treatment developed in two cases; one each developed ascites and hepatic encephalopathy. There were no death during the treatment period in these cirrhotic patients.

Discussion

We conducted an analysis of 66 patients who had compensated cirrhosis caused by hepatitis C genotype 3. Overall EVR and ETR were achieved in 44 (66.7%) and 46 (69.7%) cases, respectively. Out of 66 patients SVR was achieved in 38 (57.6%) patients including those who have not completed the full treatment. Moreover, SVR was achieved 38/61 (62.3%) patients who were able to complete anti-viral therapy.

In an analysis of 28 patients with HCV-related cirrhosis from India,[24] ETR and SVR were reported in 24 (85%) and 15 (53%) cases, respectively. However, they found a high relapse rate of 38% within 6 months following completion of antiviral therapy. Furthermore, dose modification was required in 2 (7.14%) cases and the treatment had to be stopped in 3 (11%) cases. One death was reported due to worsening liver failure in this study. In comparison to this study, lower ETR was reported in our patients but our patients were able to achieve higher SVR and there was no relapse six month after the completion of therapy. This difference in results by Sood *et al* might be explained due to inclusion of HCV genotypes other than type 3 in their study.[24] In a recently published study from Italy in patients with histologically proven HCV cirrhosis, peg-IFN and RBV therapy was compared with standard interferon and RBV; SVR rates were significantly higher in genotype 2/3 patients than in genotype 1 patients (69% versus 25%; p<0.0001). These results are in line with ours.[25] Similarly, a randomised control study from Switzerland has reported improved SVR in HCV-related cirrhosis with genotypes 2 and 3; the results were much better in treatment naïve patients.[14]

In another recent study conducted by Horoldt *et al*,[6] out of 61 patients 43 (70%) patients had achieved ETR, however only 39% achieved SVR; 35% genotype 1 and 39% of genotype 3 were able to achieve SVR. Failure to achieve SVR was found to be associated with lower platelet and neutrophil counts, and albumin level. Higher ETR and SVR reported in our study may be due to younger age and female gender of patients. Moreover, in the study by Horoldt *et al* the overall sample size and subgroups of different genotypes were small; therefore perhaps not enough to detect a difference with different genotypes. However, SVR of 57.6% in cirrhotic patients treated with peg-IFN and RBV therapy in our study is comparable to reports from Italy and Switzerland in HCV genotype 3 patients.[14,25]

The efficacy of pegylated interferon alfa-2a or 2b along with RBV in cirrhosis has been studied in various reports. Fried *et al*, have found SVR in 43% cases among patients with bridging fibrosis or compensated cirrhosis treated with peg-IFN alfa 2a and RBV for 48 weeks.[26] Moreover, the efficacy of 48-week therapy with peg-IFN alfa 2b 1.5 µg/kg/week plus RBV was compared against conventional IFN alfa-2b plus RBV in a randomised controlled trial. SVR was achieved in 48% cases who received peg-IFN alfa-2a and RBV. Consistent with the results of these studies no difference was found in SVR among those who were treated with peg-IFN alfa-2a or alfa-2b along with RBV (28% vs. 28.8%, p value = 0.598).

Besides genotypes other than 2 and 3, advanced age, male gender, obesity, high pretreatment viral load, degree of fibrosis and previous treatment with IFN and RBV therapy are the factors associated with worse outcome after anti-viral therapy for HCV.[27] In our study younger age, lower BMI, child's class A, naïve to treatment, higher base line platelets, alkaline phosphatase and EVR were found to be significant predicting factors for SVR on univariate analysis. However, amongst these, only younger age, naïve to treatment and EVR were the significant predictors on multivariate logistic regression analyses. Yu *et al* studied the predictive value (PPV) of rapid virological response (RVR) and EVR on SVR.[28] The positive

predictive value of RVR and EVR were 86.7% (39/45) and 71.9% (64/89), respectively. Nonetheless, there was no statistically significant difference between PPV of RVR and EVR.[28] Consistent with the evidence EVR and ETR were found as significant predicting factors for SVR in our study.

There is evidence that SVR after peg-IFN and RBV for 24 to 48 weeks associated with resolution of chronic hepatitis in approximately half of patients.[29] There has been recommendations to stop anti-viral therapy in the absence of EVR.[4] However, the value of more prolonged therapy (36–48 weeks) is now a major concern of clinicians and researchers.[23,29,30] Henceforth, our 46 (67.7%) patients received peg-IFN and RBV for 36 weeks and 15 (22.7%) patients received 48 weeks treatment, as they were unable to achieve EVR at 12 weeks.

Safety and tolerability of IFN and RBV are major points of concern in patients with cirrhosis. Bone marrow suppression is associated with IFN therapy while RBV can lead to significant hemolysis.[31] However, our patients tolerated the antiviral therapy well. Supportive treatment with erythropoietin and G-CSF does not affect SVR but helps continue peg-IFN and RBV; hence their use during antiviral therapy for HCV has been supported.[21] In addition to anti-viral therapy, 10 (15.15%) of our patients required erythropoietin or G-CSF during treatment. Dose reduction of peg-IFN and RBV was required in 5 (8.2%) patients due to cytopenias, marked lethargy and myalgias that was much lower than that was reported by Abergel et al (12.7-35.64%) with different doses of peg-IFN alfa-2b plus RBV[19] and 68-78% dose reduction rate with peg-IFN alfa-2a plus standard or reduced dose of RBV.[14] However, 2 (3%) of our patients developed worsening thrombocytopenia and absolute neutropenia not responding to G-CSF therapy and 2(3%) developed refractory anemia. One (1.5%) patient developed ascites and hepatic encephalopathy. No mortality was reported during the treatment period. Five (7.6%) patients were unable to complete the treatment due to either poor tolerance or various side effects not responding to supportive treatment that was again lower then few other studies.[14,19] Henceforth, the discontinuation rates for antiviral therapy were lower along with better tolerability of peg-IFN and RBV in our study patients.

However, there are a few limitations of this study. First, the study sample size is limited, secondly, it was a single centre study and a majority of them had Child's A cirrhosis, thirdly, it was an observational study and assignment of peg-IFN alfa 2a or 2b was on the physician's discretion; hence the study population received both types of peg-IFN.

These limitations can be resolved by observing that the majority of studies in cirrhotic patients have lower numbers of patients particularly if a subgroup analysis is performed for genotype 3 patients[6,14,24,25] The efficacy of two types of pegylated interferon in hepatitis C is reported in a Cochrane protocol.[32] According to personal communication with the author the results are similar with the two types of pegylated interferons. Therefore type of pegylated interferon can be excluded as a confounder in the results. Fourthly, patients naïve or non-naïve to peg-IFN and RBV were both included in the study, however no difference was found in SVR when subgroup analysis was performed to determine the type of peg-IFN used and the treatment status. However, more prospective studies or randomised controlled trials are needed to evaluate the efficiency and tolerability of peg-IFN and RBV therapy in patients with compensated cirrhosis and to find out the optimal duration of therapy or additional therapy required in non-responders or relapsers.

Conclusion

Treating patients with compensated cirrhosis due to HCV genotype 3 infection, with pegylated interferon and ribavirin, is effective and tolerated though supportive treatment with erythropoietin and G-CSF may be required in some cases. Our 34 (51.5%) patients were non-responders or relapsers to prior standard INF with or without RBV therapy. However, amongst the non-naïve patients 40% of non-responders and 52.63% of relapsers attained SVR.

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