Predictors of Sustained Virological Response to Pegylated Interferon/Ribavirin Therapy in Chronic Hepatitis C Infected Egyptian Patients in the Northeast Provinence

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Abstract

In Egypt, the prevalence rate of HCV antibody positivity has been estimated to be between 10-13%. Although patients with genotype 4 infection have traditionally been deemed 'difficult-to-treat', data related to treatment response in this patient population are limited and sometimes conflicting. The global standard combination therapy regimen using pegylated interferon (PEG-IFN) with ribavirin (RBV) used for viral; eradication, with sustained virological response (SVR) rates ranging from 66 to 80%.

Aim of the Study: To determine predictors of SVR to combination antiviral therapy in order to improve treatment outcome and to diminish the adverse effects of treatment in CHC infected patients.

Patients and Methods: A retrospective cohort study was conducted to include all patients (529 patients) with chronic naïve HCV infection treated with combination therapy (PEG-IFN/RBV) for 48 weeks and 24 weeks of follow-up (72 weeks). The predictors of response of pre-enrollment investigations and adverse events were documented at five main phases; at +0wks (baseline), +12 wks (EVR), +24 wks, +48 wks (ETR), and at +72 wks (SVR) in Ismailia Viral Hepatitis Center in the Northeastern provinence.

Results: The frequency of responders among male gender (75.7%) was significantly higher compared to responders among females (24.3%) ($p<0.0001$). The responder patients showed lighter body weights than that of non-responders ($80.19\pm11.70$ vs. $83.9\pm14.37$kg, respectively ($p$-value=0.002). The main predictors among responders compared to non-responders at baseline prior to initiation of therapy showed higher mean of albumin ($4.4\pm0.3$ vs. $4.3\pm0.6$mg/dl) and hemoglobin levels ($15.28\pm1.8$ vs. $14.1\pm1.7$) ($p=0.029$ and $p=0.001$, respectively). However, multiple univariate predictor factors showed significantly higher levels of; Total bilirubin, PT%, alkaline phosphatase, TSH, AFP, and Shistosomal Abs among non-responders compared to responders at baseline assessment ($p=0.0001$, <0.0001, 0.037, <0.0001, 0.0045, <0.0001 and <0.0001, respectively). The frequency of responders with low viral load ($\leq400x10^3$ IU/ml) (50.9%) was significantly higher than the frequency of non-responders (40.5%). The frequency of low pathological stage was significantly among responders (72.5%) than in non-responders (60.5%) ($p<0.01$). The frequency of responders treated with interferon $\alpha$-2a (66.8%) was significantly higher than the frequency of responders treated with interferon $\alpha$-2b (33.2%) ($p=0.01$) among all treated CHC patients (n=529) receiving combination therapy (PEG-IFN/RBV).

Conclusions: Predictors of SVR to antiviral therapy in the Egyptian CHC patients include male gender, lighter body weight, higher mean albumin, hemoglobin and lower mean alkaline phosphatase, total bilirubin, total leucocytes count, PT%, TSH, AFP, shistosomal Abs, interferon $\alpha$-2a, low viral load and low pathological stage.


Introduction

GLOBALLY chronic liver disease (CLD) is increasing with high rate of about 300,000 cases discovered per/year. HCV leads to progressive and life-threatening sequelae such as end-stage cirrhosis and liver cancer. According to the World Health Organization (WHO), about 3% of the world's population is infected with HCV [1]. In Egypt, the prevalence rate of HCV antibody positivity has been estimated to be between 10-13% [2]. Approximately 15-25% of HCV infections are estimated to progress to severe liver disease, which may take more than 30 years to develop [3]. HCV genotype 1 had a poor response to combination therapy and long duration of therapy and increasing the incidence of HCC. However, HCV genotype 2 & 3 show a better response to combination therapy and shorter course of therapy (24 weeks...
Hematological adverse effects in the form of anemia, neutropenia and thrombocytopenia are the primary laboratory abnormalities experienced during IFN plus RBV combination therapy and may necessitate dose modification and thus potentially impact outcome. This anemia is attributed to both RBV dose-dependent hemolysis and direct suppressive effect of IFN on erythropoiesis. Hematopoietic growth factors may be useful in the management of these side effects [17].

Another selective approach to optimizing treatment management has been to develop early predictors of virological response. One of these predictors is the early viral kinetic responses to IFN-based therapy and the other predictors of viral response included host immune system, host inherited resistance, viral load, viral genotype, body mass index (BMI), steatosis, hyperinsulinemia, compliance and adherence to treatment, side effects of combination therapy, co-morbid disease, thyroid disease, Biphasic thyroid destruction and psychosis.

The aim of this work is to determine the predictors of SVR to antiviral therapy in order to improve treatment outcome and to diminish the adverse events of treatment in chronic hepatitis C infected patients.

Patients and Methods

Type and site of the study:

This study was conducted as a retrospective study. The analysis was performed on the data collected from records of all patients with chronic HCV infection receiving combination therapy (pegylated interferon/ribavirin) at four phases; at baseline +0 wks, at +12 weeks (EVR), at +24 weeks, at +48 weeks and 24 weeks follow-up +72 weeks in the Ismailia Viral Hepatitis Center.

Data from patients records who ended +0, +12, +24, +48 & +72 weeks of pegylated interferon/ribavirin therapy was collected as follow:

Pre-enrollment data which include (at baseline +0 week); Glucose, Creatinine, Albumin, AST, ALT, Total Bilirubin, Complete blood count (CBC), Prothrombin time, Pregnancy test (if female), Hepatitis B-surface antigen (HBsAg), Anti-HCV Ab, Anti-nuclear antibodies (ANA) titer, Schistosomal Ab, Thyroid stimulating hormone (TSH), HCV RNA by PCR, AFP, Abdominal Ultrasoundography, Electrocardiogram (ECG) (men over 40, women over 50), Bilateral Fundus Examination, Liver histopathology.

Follow-up data which include:

- Lab. Data; Serum creatinine, ALT-AST, Total Bilirubin, CBC at +1, +2, +4 weeks then monthly till end of therapy (48 weeks), TSH and AFP at +24, +48 weeks of therapy and HCV RNA by PCR at +12, +24, +48 & +72 weeks of therapy.
- Clinical follow-up data include; Fever, Fatigue, Chills, Myalgia, Arthalgia, Musculo Skeletal pain, Headache, Nausea-Vomiting-Anorexia-Dyspepsia, Itching, Cough-Shortness of breath, Skin rash, Injection site reaction, Patient Weight, Insomnia, Depression and Decreased Concentration.
Type and Dose of Combination therapy (pegylated interferon/ribavirin):

**Type of pegylated interferon:**
- Peginterferon alfa 2a (peg-feron 180 µg as a fixed dosage) (manufactured by ROCHE CO./U.S.A.)
- Peginterferon alfa 2b (peg-intron 100,120 and 150 µg) based on a weight adjustment dosage (1.5 µg/kg) (manufactured by Schering CO./U.S.A.).

Dose of ribavirin (600-1400mg) as a weight adjusted dosage (12mg/kg) given orally each day in two divided doses with food (SIGMA PHARM industries-EGYPT-S.A.E.) (MEMPHIS CO.-Cairo-EYGPT) (Alkan Pharma S.A.E-EYGPT) (Schering-USA).

**Data management and statistical analysis:**

Gathered data was processed using Statistical Package of Social Sciences version 10 (SPSS version 16 Inc., Chicago, IL, USA). Quantitative data was expressed as median or means ± standard deviation (SD) as appropriate. Qualitative data will be expressed as frequency (numbers) and percent-

ages. The results for all categorical variables were given in the form of rates (%).

Student t-test was used to test significance of difference for quantitative variables that follow normal distribution. Chi Squares and Fishers Exact tests were used to test significance of difference for qualitative variables. A probability value (p-value) <0.05 was considered statistically significant.

The results of our cohort retrospective study conducted to all patients (529 patients) with chronic naïve HCV infection receiving combination therapy (PEG-IFN/RBV) for 48 weeks and those patients were followed-up for 72 weeks. The response of the patients were reported at five main phases; at +0wks (baseline), +12 wks (EVR), +24 wks, +48 wks (ETR) and at 24 weeks follow-up after ETR (+72wks, SVR) in the Ismailia Hepatitis Center.

**Study algorithm:** Flow chart represents the response of combination therapy (Peg-IFN/RBV) among all studied CHC patients divided into responders and non-responders (ETR+48 wks) during follow-up periods.

- Complets early virological response (cEVR) HCV RNA negative at 12 weeks.
- Partial early virological response (pEVR) >2 log decline in HCV RNA at week 12.
- End of treatment response (ETR) = HCV RNA negative at 48 weeks.
- Sustained virological response (SVR) undetectability of HCV RNA 6 months after and of treatment.
Results

Table (1) shows the patients characteristics of the responder and non-responder patients to combination therapy (PEG-IFN/RBV) in CHC naïve patients at end of treatment (ETR+48 wks). The frequency of responders in male patients (75.7%) was significantly higher compared to responders in female patients (24.3%) \((p<0.0001)\). However, the mean age of the patients was similar in both groups without statistically significant differences (44.69 vs. 45.01) years, in responders and non-responders groups, respectively. Mean weight of the responder patients were lighter in body weight than non-responder patients (80.19 ± 11.70 vs. 83.9 ± 14.37kg, respectively \((p-value=0.002)\)). Interferon \(\alpha\)-2a has a fixed dose of 180 \(\mu g\) administrated to all patients regardless to the body weight. Interferon \(\alpha\)-2b is administrated in a dose ranged from 100-150 \(\mu g\) according to body weight. The mean doses of Interferon \(\alpha\)-2b were similar in both groups without statistically significant differences (125.5 vs. 125.3 \(\mu g\), in responders and non-responders groups, respectively).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Responders (n=334)</th>
<th>Non-responders (n=195)</th>
<th>Used test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender: Male</td>
<td>253 75.7</td>
<td>115 59.0</td>
<td>(X^2=16.4)</td>
<td>&lt;0.0001**</td>
</tr>
<tr>
<td>Female</td>
<td>81 24.3</td>
<td>80 41.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years): (\leq40) years</td>
<td>83 24.9</td>
<td>51 26.2</td>
<td>(X^2=0.11)</td>
<td>0.74</td>
</tr>
<tr>
<td>(&gt;40) years</td>
<td>251 75.1</td>
<td>144 73.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>44.69 7.99</td>
<td>45.01 8.81</td>
<td>(t=0.40)</td>
<td>0.97</td>
</tr>
<tr>
<td>Weight (kilogram): (\leq75) kg</td>
<td>113 33.8</td>
<td>61 31.3</td>
<td>(X^2=0.36)</td>
<td>0.55</td>
</tr>
<tr>
<td>(&gt;75) kg</td>
<td>221 66.2</td>
<td>134 68.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>80.19 11.70</td>
<td>83.90 14.37</td>
<td>(t=3.2)</td>
<td>0.002**</td>
</tr>
</tbody>
</table>

** Highly significant \(p<0.01\). The frequency of responder patients among all CHC patients (n=529) receiving combination therapy (PEG-IFN/RBV) with either Interferon \(\alpha\)-2a (66.8%) was significantly higher than the frequency of responded patients with Interferon \(\alpha\)-2b (33.2%) \((p<0.01)\). The mean doses of Ribavirin were significantly lower in responders than in non-responders (1027.54 ± 172.48 vs. 1062.11 ± 140.05, respectively) \((p<0.01)\).

The responders showed higher mean of albumin (4.4±0.3 vs. 4.3±0.6mg/dl) and hemoglobin levels (15.28±1.8 vs. 14.1±1.7gm/dl, respectively) than non-responders group at baseline assessment, \((p=0.029\) and \(p<0.0001\), respectively).

However, the main findings of predictors of response to receiving combination therapy (PEG-IFN/RBV) prior to medication (at baseline) the non-responders showed significantly higher multi-predictor factors: Total bilirubin, PT%, alkaline phosphatase, TSH, AFP, and Shistosomal Abs than in responders \((p-value<0.0001, <0.0001, 0.037, <0.0001, 0.0045, <0.0001\) and \(<0.0001\), respectively).

The frequency of responder patients with negative shistosomal Abs (53.6%) was significantly higher than the frequency of non-responder patients with negative shistosomal Abs (29.7%) \((p<0.01)\). The frequency of responded patients with low viral load \((\leq400x10^3\) IU/ml) (50.9%) was significantly higher than the frequency of non-responded patients (40.5%). Interestingly, the frequency of non-responded patients with high viral load \((>800x10^3\) IU/ml) (42.1%) was significantly higher than the frequency of responded patients (38.3%) \((p=0.02)\). Other parameters including; blood glucose, serum creatinine, AST, ALT, platelets and PT show insignificant differences between responder and non-responder groups \((p>0.05)\).

Table (2) shows the results of baseline liver biopsy of the responder and non-responder patients prior to combination therapy (PEG-IFN/RBV). The Fibrosis stage of the patients was higher but insignificant in non-responders than in responders (2.98 vs. 2.82, respectively). The frequency of the patients with low pathological stage was higher significantly in responder patients (72.5%) than in non-responders (60.5%) \((p<0.01)\).
Table (2): Liver biopsy using METVIR score system among all CHC studied patients (n=529) prior to receiving combination therapy (PEG-IFN/RBV) in responders and non-responders.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Responders (n=334)</th>
<th>Non-responders (n=195)</th>
<th>Used test</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrosis index (0-6) Mean (SD)</td>
<td>2.82</td>
<td>2.98</td>
<td>t=1.4</td>
<td>0.22</td>
</tr>
<tr>
<td>Low pathological stage (0-3) (%)</td>
<td>242</td>
<td>118</td>
<td>X²=8.1</td>
<td>0.004**</td>
</tr>
<tr>
<td>High pathological stage (4-6) (%)</td>
<td>92</td>
<td>77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Necroinflammation index (0-18)</td>
<td>7</td>
<td>6.7</td>
<td>t=1.1</td>
<td>0.26</td>
</tr>
</tbody>
</table>

** Highly significant.

Discussion

Globally, the evident recommended treatment for CHC patients is combination therapy with PEG-IFN/RBV. The goal of this treatment is a SVR, defined as the absence of detectable viral RNA at 6 months after the end of treatment. Despite improvements that have increased SVR rates, treating CHC remains a challenge in certain populations such as those patients infected with HCV genotype part curly (genotypes 1 and 4), high viral load, obesity, cirrhosis and insulin resistance [9,3,18].

Testing is mandatory performed early prior to (+0 wk) and during treatment (particularly at the decision-making point of +12 wks, +24 wks, at the ETR and 6 months later (SVR). EVR defined by complete recovery of peripheral blood viraemia complete EVR (cEVR) and/or at least a 2-log reduction in viral titer partial EVR (pEVR) [19].

Predictors of response to therapy serve as decision tools for physicians to help identify patients who are likely or unlikely to achieve an SVR. Thus, considering pretreatment counseling in those patients will increase the likelihood of successful therapy.

Therefore, knowledge of predictors to these therapies is extremely valuable. Traditional predictors of response identified in international studies regardless of genotype can be divided into three groups: (1) epidemiological factors including patient age, sex, and race, (2) viral factors, most importantly the pretreatment viral load, RVR, and the genotype, and (3) histological factors including the amount of fibrosis and steatosis [20].

In our study, we achieved complete virological response at the end of treatment (ETR+48 weeks) in 334 patients (63.1% responders) and 195 patients failed to achieve this target at ETR+48 weeks (36.9% non-responders). SVR was achieved in only 40.3% of responder patients with 6.4% relapses rate and 16.4% dropout. The likely explanation for this lower SVR rate is the fact that the study group included a heterogeneous cohort of patients, HCV co-infection, and non-responders to previous therapies, all factors known to be associated with a lower rate of response. This is unfortunate since the data concerning PEG-IFN alfa-2a in genotype 4 patients is sparse and thereby the quest for this information remains partly unfulfilled [21].

This came in agreement with other study by Castillo et al. [22] reported that sustained responses are low with genotype 4 patients given 48 weeks of treatment (SVR ranged from 40 to 65%). Also, a similar finding was reported by Hadziyannis et al. [9] of whom patients achieved SVR rate of 52% after 48 weeks of treatment with combination therapy (PEG-IFN alfa-2a plus RBV). Moreover, in an older study by the same authors [23] demonstrated an SVR rates of 40-60% are obtained after 48 weeks of treatment and a full dosage of RBV. In this issue of the Annals, Al-Ashgar and colleagues [21] report the results of their retrospective analysis of 148 HCV genotype 4 patients who underwent therapy with PEG-IFN-alfa2a plus RBV for 48 weeks. Performing a subgroup analysis of their previously published data in treating 335 patients with various HCV genotypes, the investigators report an SVR of 44.6% in the entire cohort and 50.8% in those who completed therapy of genotype 4 patients [24]. Furthermore, the SVR observed in the study of Al-Ashgar et al. [24] (44.6% by ITT analysis) is the nearest SVR to ours (40.3%) but certainly lower than that reported previously in genotype 4 patients using PEG-IFN alfa-2b and weight-based, standard-dose RBV.

However, a much higher SVR response was achieved in other studies approximately 70% e.g., 69% by Kamal et al. [25], 68% by Hasan et al. [26], 55% by Al-Zayadi et al. [27] and 61% by El-Makhzangy et al. [28].

Subsequent other investigators reported SVR rates of 50%-79% in patients receiving PEG-IFN-a 2b plus RBV (800-1200mg/day) for 48 weeks and suggested that HCV-genotype 4a is easier to treat than previously believed [25-29].
Clearly in our study, the mean age of our patients was similar in both groups without statistically significant differences (44.69 vs. 45.01 years, in responders and non-responders groups; respectively). Confirmed by other investigators [28], no major effect of age as a predictor for SVR, which agreed with us in that the mean age of responders didn’t differ significantly from the mean age of non-responder.

Our data revealed that the frequency of responders in male patients (75.7%) was significantly higher compared to responders in female patients (24.3%) & was statistically significant (p<0.0001). In contrast to this, Kamal et al. [25] mentioned that sex did not predict response to PEG-IFN-α-2b/ribavirin therapy.

Also, the mean weight of our studied subjects particularly the responder patients was significantly lower than the mean weight of the non-responder patients (80.19±11.70 vs. 83.9±14.37kg, respectively) (p-value=0.002). Fried et al. [8] agreed with us as they found that the baseline factors that have been shown to predict good SVR to PEG-IFN alfa-2a plus RBV include HCV genotype (other than type 1 and 4) and body weight. However, in contrast to us, Kamal et al. [25] reported that weight and histological scores did not predict response to PEG-IFN-α-2b/ribavirin therapy.

Ultimately, the frequency of our responded patients with low viral load (≤400x10^3 IU/ml) (50.9%) was significantly higher than the frequency of non-responded patients (40.5%), while the frequency of non-responded patients with high viral load (>800x10^3 IU/ml) (42.1%) was significantly higher than the frequency of responded patients (38.3%) (p=0.02). At 12 weeks (EVR+12 weeks), the responder group shows significantly lower viral load than non-responder group (p<0.0001). This came in agreement with Rodriguez-Torres et al. [30] who identified similar factors that predict the response to PEG-IFN alfa-2a plus RBV treatment which include; EVR and baseline factors such as low viral load, absence of cirrhosis/bridging fibrosis and HCV genotype.

Our study reported that the fibrosis stage of the patients was higher but insignificant in non-responders than in responders (2.98 vs. 2.82, respectively). The frequency of the patients with low pathological stage was higher significantly in responder patients (72.5%) than in non-responders (60.5%) (p<0.01). Also, the mean inflammation grade of the responder patients was similar to non-responder patients (7.0 vs. 6.7, respectively) (p>0.05). Other investigators El-Makhzangy et al. [28] reported similar findings, patients with Metavir fibrosis score F1 or F2 had a significantly more frequent SVR compared with those with more advanced fibrosis F3/F4 (43/62 (69%) vs. 15/33 (45%), p=0.02).

Moreover, Gad et al. [4] a study conducted to assess the predictors of response to combination therapy (SVR) with CHC genotype 4, found that the lesser the fibrosis index; no severe fibrosis (p=0.0001), along with low serum AFP (p=0.0001), platelet count (p=0.03), treatment with PEG-IFN (p=0.04). Similarly, Hadziyannis et al. [23] reported that SVR rates of 40-60% are obtained after 48 weeks of treatment and a full dosage of RBV. The best higher range of response rates are achieved in patients with lower viral load and absence of cirrhosis. Also, Kamal et al. [18] found that low baseline histological grade and stage, low baseline HCV RNA (p<0.001) and low baseline body mass index (p=0.013) were associated with SVR in patients with chronic HCV-genotype 4 treated with PEG-IFN-α 2b and RBV. Also, in an earlier study by Sugimoto et al. (2003) confirmed that the predictors of response to antiviral therapy with PEG-IFN/RBV are fibrotic severity (10% poorer response with cirrhosis if genotype 1). Additionally confirming our finding multiple previous studies on HCV genotype 4, predictive factors were confirmed, including pretreatment viral load and stage of fibrosis [25,26,31,32].

Also in our study, we further looked in depth into other factors concerning the response and the impact on the haematological indices. Reporting a significantly higher mean of hemoglobin levels in responders than in non-responders group at baseline assessment (15.28 ± 1.8 vs. 14.1 ± 1.7, respectively) (p<0.0001).

Strikingly, patients with a null response to PEG-IFN alfa-2a plus RBV demonstrated lower hemoglobin levels than patients who achieved full virological response, suggesting a systemic resistance to treatment [33]. Suggesting that changes in hemoglobin values may be associated with virological response to therapy.

Also in our study, we reported that there were significantly higher mean of albumin levels among responders than in non-responders group at baseline assessment (4.4 ± 0.3 vs. 4.3 ± 0.6gm/dl, respectively) (p=0.029). These finding were in agreement with El-Zayadi et al. [27] who had found that patients with SVR were significantly had higher
levels of serum albumin and had less pretreatment necro-inflammatory grade.

However, Gad et al. [4] conducted a study to assess the predictors of SVR in patients with CHC genotype 4 and found that Baseline factors not associated with SVR include: serum albumin, hemoglobin, Metavir activity score and viral load. All parameters disagreed with our finding.

Furthermore, in our study, we reported a significantly higher in multiple biochemical parameters; mean of total bilirubin, total leucocytes count, PT%, alkaline phosphatase, TSH, AFP, and schistosomal Abs in non-responder group than in responder group at baseline assessment (p<0.0001, <0.0001, <0.0001, 0.037, 0.0045, <0.0001 and <0.0001, respectively). Interestingly, the frequency of responded patients with negative schistosomal Abs (53.6%) was significantly higher than the frequency of non-responded patients with negative schistosomal Abs (29.7%) (p<0.01). In agreement with our study, confirmed by an earlier study [4] demonstrated that the presence of AFP level was found to predict SVR. The multiple studies refer that higher AFP levels correlated with a negative treatment outcome [4,10].

In genotype 4 patients, treatment with both alfa-2a and alfa-2b forms of PEG-IFN has shown lower AFP levels to be predictive of good SVR [4]. Higher serum AFP levels are serving as surrogate markers of more advanced fibrosis and hence, it act as a negative predictor of SVR. In addition, the utility of AFP as a predictor of response and possibly as an indicator of liver fibrosis and/or inflammation is worth further evaluation [20].

In disagreement with our finding El-Makhzangy et al. [28] found no impact of pre-treatment ALT, serum bilirubin, alkaline phosphatase, TSH, Metavir activity score and viral load (≥600,000, >600,000 IU/ml) on SVR.

Further we reported a low rate of response (SVR) in combined infection (schistosomiasis and HCV) than in HCV alone, the presence of associated schistosomiasis has determined the response (SVR) of Egyptians with chronic hepatitis C to combination therapy (PEG-IFN/RBV). The SVR being 44% in those not previously receiving parental anti-schistosomal therapy (PAT) and only 30% in those who had been given (PAT) (Esmat et al.) [34]. In a previous study, Hassan et al. [35] had evaluated the relationship between to schistosomiasis and liver cirrhosis in HCV among Egyptian patients.

El-Shazly et al. [36] conducted a study to compare the response to recombinant human alpha-2 interferon therapy in 2 groups of Egyptian patients having CHC: group 1 with schistosomiasis (36 patients) or group 1 without schistosomiasis (24 patients). The overall response rate at 6 months were significantly lower (p<0.001) in group 1 (14% and 33% respectively) than in group 2 (63% and 71% respectively). The liver histology also improved significantly in group 2 (46%) compared with group 1 (14%) after completion of therapy (p<0.05). On the other hand the overall relapse rate in responders, by 6 months after cessation of therapy, was significantly higher (p<0.05) in group 1 (92%) than in group 2 (59%). These results show that the presence of associated schistosomiasis has to be considered as an important factor in determining the response of Egyptian patients with CHC to therapy with interferon.

In contrast to this finding, Derbala et al. [10] had studied the impact of bilharziasis and fibrosis stage on the treatment of hepatitis C virus genotype 4 with peginterferon alfa-2a. They found that PegIFN-α2a combined with ribavirin results in improvement in sustained response in HCV genotype 4, irrespective of history of bilharzial infestation.

Our study revealed that the mean doses of Interferon α-2b were similar in both groups without statistically significant differences (125.5 vs. 125.3 µg, in responders and non-responders groups, respectively). The frequency of responded patients among all CHC patients (n=529) receiving combination therapy (PEG-IFN-RBV) with Interferon α-2a (66.8%) was significantly higher than the frequency of responded patients with Interferon α-2b (33.2%) (p<0.01).

Confirmed with us by two previous studies (including 100 and 38 patients, respectively) using the alfa-2a form of PEG-IFN in genotype 4 patients suggests that the response rates may be higher [10].

PEG-IFN-α-2a plus RBV may increase SVR among patients with chronic hepatitis c as compared to PEG-IFN-α-2b plus RBV according to a systematic review of randomized controlled trials. The relative benefit increase was 14.6%. For patients at similar risk to those in this study (41.0% had SVR when not treated with PEG-IFN-α-2a plus RBV), this leads to an absolute benefit increase of 6%. 16.7 patients must be treated for one to benefit (number needed to treat = 16.7).
Predictors of Sustained Virological Response to Pegylated Interferon/Ribavirin Therapy

References


9- HADZIYANNIS S.J., PAPATHEODORIDIS G.V.: Recent


