Original Article

**Efficacy of Conventional Interferon alpha–2 b plus Ribavirin combination in the treatment of chronic Hepatitis C naive patients**

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**ABSTRACT**

**Objective:** To assess the efficacy of combination therapy of Conventional interferon alpha-2b plus ribavirin in patients of chronic hepatitis C.

**Methods:** Records of 65 patients (43 males and 22 females) of chronic hepatitis C treated with combination therapy of interferon alpha-2b plus ribavirin from January 2003 to December 2003 were analyzed for base-line parameters, response rates and any adverse effects.

**Results:** End-treatment response was found in 86.04% male patients and 86.36% female patients. Sustained response was found in 81.39% male patients and 86.36% female patients.

**Conclusions:** The study shows that conventional interferon plus ribavirin combination therapy remains an effective therapy in the treatment of chronic hepatitis C naive patients in our set-up. (Rawal Med J 2005;30:9-11).

**Key Words:** Hepatitis C naïve patients, interferon, ribavirin

**INTRODUCTION**

One hundred and seventy million of world’s population is infected with hepatitis C,\(^1\) 80% having chronic hepatitis and 20% cirrhosis and its sequale.\(^2\) Hepatitis C virus (HCV) infection has become the most common cause of chronic liver disease in America, Europe, Australia,\(^1\) as well as in Pakistan.\(^3\) Combination of interferon and ribavirin has increased sustained virological response two-fold as compared to interferon
monotherapy, thus reducing relapse rate.\(^5\) The mechanism by which this enhancement of activity occurs with combination therapy is not clearly known.\(^6\) Aim of the present study was to assess efficacy and safety of combination therapy of interferon alpha-2b plus oral ribavirin in naive patients with chronic HCV infection.

**METHODS**
Records of 65 naïve chronic hepatitis C patients treated with combination of interferon alpha plus oral ribavirin, in Medical A unit, PGMI, Lady Reading Hospital, Peshawar from January 2003 to December 2003, were analyzed. All studied patients were HCV-RNA positive by PCR with raised serum ALT levels. Quantitative PCR, genotyping, and histological status were not known in any of the studied patients. None of the patients were cirrhotic as determined clinically and by ultrasound. None of the patients was co-infected with HBV. All studied patients received interferon alpha at a dose of 3 million units, subcutaneously, three times a week in combination with ribavirin 400mg, three times daily for 6 months.

All patients were assessed in an outpatient setting for safety, tolerance and efficiency during treatment period. Hemoglobin, white blood cell count and platelet count were performed weekly during first month, fortnightly during 2nd and 3rd month, and monthly during the remaining period. For consistency with other reports and current clinical practice, we adopted conventional definitions of NIH on hepatitis C.\(^7\) These include End of Treatment Response, defined as normal serum ALT levels and undetectable serum HCV-RNA levels at the end of therapy and Sustained response, defined as a response that persists for at least six months after the stoppage of successful therapy.

**Statistical Analysis**
Statistical analysis was carried out by using student’s t-test for the comparison of means and chi-square test for the comparison of proportions. P value of less than 0.05 was considered to be significant.

**RESULTS**
Out of sixty-five naive patients studied, 43 were males and 22 females. Both gender groups were comparable regarding different baseline characteristics (table-1). Serum ALT levels became normal in 39 out of 43 male patients (90.69%), as compared to 20 out of 22 female patients (90.90%), (P > 0.05). Serum HCV-RNA became negative in 37 out of 43 male patients (86.04%), as compared to 19 out of 22 female patients (86.36%), (P > 0.05). Thus, ETR was found to be 86.04% in male patients and 86.36% in female patients.
Table 1. Baseline characteristics of patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/Female</td>
<td>43</td>
<td>22</td>
</tr>
<tr>
<td>Mean Age (yrs) ± SD</td>
<td>401±2</td>
<td>37±5</td>
</tr>
<tr>
<td>Mean serum ALT(IU) ± SD</td>
<td>113±15</td>
<td>98±18</td>
</tr>
<tr>
<td>Mean Hb (gm%) ± SD</td>
<td>12.7±0.3</td>
<td>11.2±0.4</td>
</tr>
<tr>
<td>Mean TLC/cm³ ± SD</td>
<td>8140±540</td>
<td>9230±330</td>
</tr>
<tr>
<td>Mean platelet count ± SD</td>
<td>204340±7000</td>
<td>164700±5000</td>
</tr>
<tr>
<td>Presence of cirrhosis</td>
<td>Nil</td>
<td>Nil</td>
</tr>
</tbody>
</table>

SD= Standard Deviation, ALT= Alanine Aminotransferase

Serum ALT levels remained normal and HCV-RNA PCR remained undetectable at the end of 6 months follow-up period in 35 out of 43 male patients (86.04%), as compared to 19 out of 22 female patients (86.36%), (P > 0.05), as shown in Table 2.

Table 2. Response in the patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Males (n=43)</th>
<th>Females (n=22)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normalization of ALT</td>
<td>39/43 (90.69%)</td>
<td>20/22 (90.90%)</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Loss of HCV-RNA</td>
<td>37/43 (86.36%)</td>
<td>19/22 (86.36%)</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>End Treatment Response</td>
<td>37/43 (86.04)</td>
<td>19/22 (86.36%)</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Sustained Response</td>
<td>35/43 (81.39)</td>
<td>19/22 (86.36%)</td>
<td>P &gt; 0.05</td>
</tr>
</tbody>
</table>

The type and frequency of adverse events were similar in both gender groups and reflected the known safety profile of interferon; febrile feeling, nausea, insomnia, anorexia and rash were more common. None of these were treatment limiting. No patient died. Hemoglobin concentration fall was less in male patients as compared to female patients, but statistically not significant (P > 0.05). Leukocyte and platelet count decreased in both the gender groups during therapy, but remained within normal range except in four patients: 3 male and 1 female. The respective treatment was temporarily discontinued for 3 to 12 days in these patients, where it was restarted after restoration of leucocytes and / or platelets count.
DISCUSSION

Discrepancies between serum HCV-RNA responses and the serum ALT responses to interferon treatment have been reported. In the present study, serum HCV-RNA levels remained detectable after treatment despite persistently normal serum ALT levels in 2 out of 43 male patients (04.65%), as compared to 1 out of 22 female patients (04.54%), (P > 0.05). In contrast, in all patients in whom serum HCV-RNA levels became undetectable, had normal serum ALT levels as well; this is in contrast to others.

The efficacy in terms of normalization of serum ALT levels and HCV-RNA clearance at the end of treatment (end-treatment response) and at the end of 6 months follow-up period (sustained response) is greater as compared to other studies, the reason may be that HCV genotype 3 is the most prevalent type in our set-up. Histological status on liver biopsy was not available in any of the studied patients, in contrast to other studies. Greater improvement in the knodell inflammatory score has been reported with combination regimen as compared to interferon monotherapy. HCV genotype, pretreatment serum HCV-RNA levels, and the presence of fibrosis or cirrhosis at baseline (on histology) influence the initial response to treatment with interferon herapy. A SVR is more common in patients with serum HCV-RNA level of less than 2.5 million copies/ml and HCV genotypes other than type-1, therefore, determination of the viral genotype and the pretreatment serum HCV-RNA level is of great significance but may not be necessary in every patient.

It has been reported that female patients respond better to combination therapy as compared to male patients; we also noted the same, but statistically the difference in results was not significant. The only important risk associated with combination therapy was hemolytic anemia. The fall in the hemoglobin concentration occurred during the first month, emphasizing the need for careful monitoring of patients during treatment with ribavirin. We conclude from our experience, that the combination of interferon and ribavirin is safe and effective for the treatment of naïve patients with chronic hepatitis C.

REFERENCES