Infection with hepatitis C virus genotype 3 – Experience of a tertiary health care centre in south India

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Abstract

To analyse the response rate and the predictive values of virological, biochemical and histological factors on HCV antiviral therapy in HCV genotype 3 infected patients, we retrospectively studied 21 HCV genotype 3 infected patients, who underwent HCV antiviral therapy. Low (57%) sustained viral response (SVR) rate and significant association of SVR with normalization of alanine transaminase (ALT) levels were observed in our study. Absence of early viral response (EVR) showed high (80%) predictive value on SVR. Absence of EVR and normalisation of the ALT levels can predict the outcome of HCV antiviral therapy.

Key words: Early viral response, pegylated interferon, ribavirin, standard interferon, sustained viral response

Introduction

Management of HCV infection is one of the current health concerns because of the high risk of chronic infection and lack of a suitable vaccine. Ideal response to therapy otherwise known as sustained viral response (SVR) is the absence of viraemia measured by an HCV RNA assay with the lower detection limit of ≤50 IU/mL at 6 months after completion of therapy.[1]

Earlier studies point out many pre-treatment biochemical, virological, host and histological factors that might influence the treatment outcome of HCV infection.[2,3] Recent studies report that viral kinetics measured during earlier weeks of treatment can predict the treatment outcome.[4,5] We have studied the response rate and the predictive value of various factors on HCV antiviral response in an Indian population infected with HCV genotype 3, since genotype 3 is the most prevalent in India.

Materials and Methods

On the account of earlier studies reporting lower rates of response to antiviral therapy in HCV genotype 3 patients, we retrospectively studied HCV genotype 3 infected patients who were managed with antiviral therapy in our outpatient liver clinic during the period 2004–2007. All patients were treated for 24 weeks with dosage of pegylated interferon alpha-2b (50 µg) or pegylated interferon alpha-2a (180 µg) or standard interferon alpha-2b (3 million units) and ribavirin (800–1000 mg). We selected 21 patients on the availability of the documented laboratory data at 6 months post-therapy to analyse the parameters influencing the primary outcome variable which was SVR. The Ishak’s scoring system[6] was used for histological analysis. Fourteen of the 21 patients had a combination therapy of pegylated interferon alpha-2b or pegylated interferon alpha-2a with ribavirin, which is the standard of care for Hepatitis C infection.[7] Seven of 21 had standard interferon alpha-2b with ribavirin. All these patients were negative for HIV antibody and hepatitis B surface antigen. None of them had history or documented evidence of autoimmune liver disease, iron storage disorders, renal disease and alcohol intake because of the retrospective nature of this study; hence these parameters were not available for analysis; likewise sample collection time and its influence on the asparate transaminase/alanine transaminase (AST/ALT) levels were also not available for the analysis.

Plasma viral RNA was extracted using QIAmp RNA Mini Kit (Qiagen, Hamburg, Germany) and quantitated by a real-time PCR using artus HCV RG RT PCR kit (Qiagen, Hamburg, Germany). Genotyping was done by reverse transcriptase PCR using type-specific primers (Invitrogen, USA) for the core region[8] and/or sequencing of the NS5B region.[9] Univariate analysis was carried out instead of multivariate analysis due to the lean sample number for all parameters measured, using SPSS for Windows, version 16 (SPSS Inc., Chicago, IL, USA). Continuity correction was done for analysis. A P-value of <0.05 was taken as significant.

Results

Median age of our study patients was 50 years, which included 15 men and 6 women. Median ALT, AST and viral loads were 77, 70 and 5.5 ×10^5 IU/mL, respectively. Twelve
(57.1%) of 21 patients who underwent combination therapy experienced SVR. Of the 12 patients who experienced SVR, 10 (83%) of them had standard of care. Out of 9 patients who did not experience SVR, 5 (55%) of them had standard of care; this difference was not statistically significant [Figure 1]. Other pre-treatment parameters such as viral load (<8×10^5 IU/mL), age (<40 years), gender, alanine transaminase (ALT [3× upper limit of normal]) levels, AST/ALT ratio and liver histology reported to have relevance to HCV treatment outcome were analysed and the results are shown in Table 1. Of 21 patients studied, only 16 patients had data for liver histology. Nine of 12 (75%) patients with SVR had normalisation of ALT levels, while of the remaining 9 patients who did not experience SVR, only 1 (11%) had normalisation of ALT levels; this difference was statistically significant (P-value 0.003, not shown in Table 1). Of all the parameters compared between patients with and without SVR, normalisation of ALT levels in patients with SVR was statistically significant (not shown in Table 1). Positive predictive value (PPV) of EVR on SVR in this study is 50%, and negative predictive value (NPV) of EVR on SVR is 80%.

Discussion

In this study, we found the proportion of HCV genotype 3 infected patients who experienced SVR was lower (57.1%) than earlier published studies.[10,11] Plausible reasons for the observed lower SVR rate in our study could be due to the ethnic differences between our study population and those in earlier studies,[12] non-compliance to therapy due to the side effects like decrease in hemoglobin levels associated with HCV antiviral regimen and the fact that all our patients did not undergo the standard of care. Our result of poor response rates is in agreement to studies carried out earlier in Indian population.[13,14] These reports contrast with earlier reports that describe HCV genotype 2/3 as having response rates as high as 76–82%.[10]

We found factors like age, gender, viral load, ALT levels, cirrhosis and ALT/AST ratio not to be significantly associated with SVR, which could be due to the small sample size of our study. Being tertiary care hospital, timely follow-up of the patient on treatment was challenging. We, however, present this preliminary report due to paucity of published studies on treatment response in HCV-infected individuals in the Indian sub-continent.

To conclude our study shows an overall low treatment response (57.1%) in patients infected with HCV genotype 3. SVR at 6 months post-therapy was found to be associated with normalisation of the ALT levels. This finding suggests that in a low-cost setting like ours, measurement of ALT levels may be considered as an alternative to expensive viral RNA quantitation. However, careful documentation of confounding factors such as influence of alcohol intake and time of sample collection must be done. A larger study is warranted to establish these findings.

Acknowledgements

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References


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Figure 1: Summary of patients with measurement of sustained viral response (SVR).

Table 1: Univariate analysis of all parameters with primary outcome measured

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cut-off value</th>
<th>No. of patients</th>
<th>SVR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment viral load</td>
<td>&lt;4×10^5 IU/mL</td>
<td>9</td>
<td>4</td>
<td>0.682</td>
</tr>
<tr>
<td></td>
<td>&gt;4×10^5 IU/mL</td>
<td>11</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>&lt;40 years</td>
<td>6</td>
<td>5</td>
<td>0.296</td>
</tr>
<tr>
<td></td>
<td>&gt;40 years</td>
<td>15</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Men</td>
<td>15</td>
<td>9</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>ALT (3×ULN)</td>
<td>&lt;105 U/L</td>
<td>15</td>
<td>9</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>&gt;105 U/L</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Cirrhosis b</td>
<td>Yes</td>
<td>9</td>
<td>5</td>
<td>1.000</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>7</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>AST/ALT ratio</td>
<td>&lt;1.0</td>
<td>13</td>
<td>8</td>
<td>0.948</td>
</tr>
<tr>
<td></td>
<td>&gt;1.0</td>
<td>8</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

This table shows the parameters measured, cut-off value used for analysis, number of patients who were above or below the cut-off value and number of patients with SVR. Final column shows the level of statistical significance of each parameter (P-value ≤ 0.05 is significant). *Analysis was done for only 20 patients with pre-treatment viral load. †Biopsy data were available for only 16 patients.


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