The Role of Cholesterol on Sustained Virological Response (SVR) in the Treatment of Genotype 1-Infected Hepatitis C (CHC) Patients with Peginterferon alfa-2a (PEG) and Ribavirin (RBV)

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INTRODUCTION

HCV life cycle is associated with cholesterol metabolism in host cells. So, cholesterol lowering drugs as statins are under discussion to inhibit HCV RNA replication. Otherwise, clinical researchers recently found that higher cholesterol levels are significant positive predictive factors on Sustained virological response (SVR). The “Association of German Independent Gastroenterologists” (Bundesverband der Niederlassungsfreien Gastroenterologen Deutschlands e.V.) in cooperation with Roche, Germany, is conducting a nationwide observational study including screening and treatment phases to determine the quality of treatment for chronic hepatitis C (CHC) in routine clinical practice.

OBJECTIVE

- Aim of this analysis is to evaluate the role of cholesterol in the treatment of HCV-patients with genotype 1 under real life conditions.

METHODS

- This evaluation is part of a large ongoing German multicentre, open-label observational study including anti-HCV-positive adults with detectable HCV RNA. The nature of this study allowed doing and duration of both peginterferon alfa-2a (40KD) and ribavirin to be at the discretion of the physician.
- The screening data include age, sex, weight, height, duration and source of infection, prior antiviral treatment, clinical symptoms, histology, genotype, viral load, concomitant diseases and social status.
- The study data includes patients who completed treatment with peginterferon alfa-2a (40KD) plus ribavirin. The data collection was performed online via the internet.
- The documented data should reflect the clinical routine as intended by the doctors in charge. Therefore, the statistical analysis remains descriptive.
- Due to the cross-sectional character of the study, the status of data was frozen on May 15th, 2007, including queries solved.

RESULTS

Patients

- Until May 2007 the online data documentation has been completed for a total of 13590 HCV patients including: 9323 patients with screening data and 4058 patients with completed treatment with peginterferon alfa-2a (40KD) in almost all cases plus ribavirin.
- Cholesterol was specified in 2432 of the 4058 patients: - Cholesterol was normal in 1783 patients and - Cholesterol was elevated (≥200 mg/dl; >5.2 mmol/l) in 649 patients.
- In 1429 of the 2432 patients genotype (GT) 1 was specified.
- The proportion of GT1-patients was lower in patients with normal cholesterol (999 of 1783 patients, 56.0%) than in patients with elevated cholesterol (430 of 649 patients; 66.3%).
- Two populations were defined:
  - Group N: normal cholesterol was normal in 999 GT1-patients (69.9%) and
  - Group E: elevated cholesterol was elevated (≥200 mg/dl; ≥5.2 mmol/l) in 430 GT1-patients (30.1%, see Figure 1).

Baseline data

- Baseline data were: mean age 44.4 (N) vs. 45.3 (E) years, rate of advanced fibrosis and a better tolerance of interferon based therapy in patients with elevated cholesterol. Other reasons for withdrawal were comparable between both groups.
- Differences between patients with normal vs. elevated cholesterol were seen in the cumulative doses for 48 weeks: - Peginterferon alfa-2a: 58.1% of group N vs. 69.4% of group E received 80% of the recommended dose (see Figure 5).

Table 1: Baseline data of genotype 1-patients with completed treatment

<table>
<thead>
<tr>
<th>Group</th>
<th>N (Cholesterol normal)</th>
<th>Group E (Cholesterol ≥200 mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male / female)</td>
<td>41.5% / 58.5%</td>
<td>38.6% / 61.4%</td>
</tr>
<tr>
<td>Age (mean ± SD in years)</td>
<td>44.4 ± 12.5</td>
<td>45.3 ± 11.8</td>
</tr>
<tr>
<td>Weight (mean ± SD in kg)</td>
<td>75.6 ± 14.6</td>
<td>74.7 ± 12.9</td>
</tr>
<tr>
<td>BMI (mean ± SD in kg/m²)</td>
<td>25.3 ± 4.4</td>
<td>25.3 ± 3.8</td>
</tr>
<tr>
<td>Duration of infection (years)</td>
<td>12.5 ± 9.5</td>
<td>12.9 ± 9.0</td>
</tr>
</tbody>
</table>

Figure 1. Study patients

Figure 2. Baseline data

Figure 3. RVR, EVR and EOT

Figure 4. SVR

Figure 5. Cumulative doses

Figure 6. Discontinuation rates

CONCLUSIONS

- About one third of the patients had elevated cholesterol (≥200 mg/dl; >5.2 mmol/l).
- In patients with available liver biopsy, patients with elevated cholesterol had a lower proportion of patients with advanced fibrosis (33% vs. patients with normal cholesterol (50%) (p<0.001). Despite the same viral load at baseline, better virological responses in patients with elevated cholesterol were observed. Apart from a direct biological effect in patients with higher cholesterol, additional causes may be a lower rate of advanced fibrosis and a better tolerance of interferon based therapy in patients with elevated cholesterol.

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