Direct-Acting Antivirals against HCV Infection in Elderly patients: Are they so well Tolerated and Safe as we thought?

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Background & Aims

• Progression of HCV-related hepatitis towards cirrhosis and HCC is more rapid in the elderly patients [1,2].
• They are more likely to suffer from extrahepatic manifestations of HCV infection, such as fatigue and neuropsychological disorders [3].
• Polytherapy and polypharmacy are frequent in elderly patients due to associated comorbidities.
• IFN-based regimens in patients aged ≥ 65 years had more side effects, higher discontinuation rates, and lower SVR rates, probably due to a reduced stimulatory effect of IFN on the aged immune system [4-6].

Background & Aims

• New direct-acting antivirals agents (DAAs) are highly safe and well tolerated.

• There are few data about elderly patients from clinical trials.
  – Simeprevir: Number of patients > 65 years is too small to draw meaningful conclusion and no data at all is available for patients over the age of 73 years [7]
  – Sofosbuvir: Lack of clinical experience treating patients older than 75 years of age [7]
  – Sofosbuvir + Ledipasvir: 4-8% of patients aged > 65 years [8,9]
  – Ombitasvir + Paritaprevir + Ritonavir + Dasabuvir: Proportion of patients aged 65 years (4-16%) but all trials excluded patients over 70 years of age [10-13]
  – Daclatasvir: experience in the elderly population is even poorer [14]

• However, data from IFN-free regimens suggest that SVR rates are not influenced by age.

• Therefore, patients aged > 65 years, in whom comorbidities exist, might especially benefit of these therapies.

Methods

• All HCV-infected elderly patients (≥ 65 years) in clinical follow-up at two hospitals of Spain (Universitary Hospital of A Coruña and Alvaro Cunqueiro Hospital) who initiated anti-HCV therapy were included (August 2012-October 2015) in the study.
• Epidemiological, clinical characteristics, HCV treatment and concomitant medications were recorded.
• A descriptive analysis was performed using SPSS 19.0
Baseline Characteristics of the Study Population

- **N = 121 HCV mono-infected patients**
- Women: 52.9%
- Age: **72.6 ± 7.4 years**
  - 10.7% > 80 years
- HCV Viral Load: **6.52 ± 6.93 IU/mL**

Figure 1. HCV Genotypes Distribution in Elderly Patients.

- G1: 95.9%
- G2: 0.8%
- G3: 0.8%
- G4: 2.5%
- G1a: 6.9%
- G1b: 6%
- ND: 87.1%
Liver Fibrosis & Previous HCV Treatment Exposure

Figure 2. Liver Fibrosis (Transient Elastography).

Figure 3. Previous HCV Treatment Exposure.

Stiffness: 16 (10 – 21.2) KPa
DAA Combinations used in Elderly HCV Patients

Figure 4. Direct-Acting Antivirals Combinations used to treat HCV Infection in Elderly patients.

- Ombitasvir + Paritaprevir/r + RBV: 1 patient
- Ombitasvir + Paritaprevir/r + Dasabuvir: 2 patients
- Ombitasvir + Paritaprevir/r + Dasabuvir + RBV: 23 patients
- Sofosbuvir + Daclatasvir + RBV: 31 patients
- Sofosbuvir + Ledipasvir: 20 patients
- Sofosbuvir + Ledipasvir + RBV: 13 patients
- Sofosbuvir + Simeprevir: 5 patients
- Sofosbuvir + Simeprevir + RBV: 11 patients
- Sofosbuvir + RBV: 3 patients
- PegIFN + RBV + Simeprevir: 3 patients
- PegIFN + RBV + Telaprevir: 7 patients
- PegIFN + RBV + Boceprevir: 2 patients

Number of HCV patients

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Ribavirin Dose Adjustment were required in almost half of patients

- Treatment Duration
  - 12 weeks: 82.6%
  - 24 weeks: 14.9%

- Ribavirin Use: 61.2%
  - 800 mg: 12.2%
  - 1000 mg: 50%
  - 1200 mg: 37.8%

Figure 5. Ribavirine reduction during HCV treatment

RBV reduction: w4 (60.6%), w8 (6.1%), w12 (33.3%)
More than 85% of Patients were with Concomitant Medication

Figure 6. Number of concomitant drugs in Elderly HCV Patients.

Table 1. Concomitant Medication according to drug-families.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Antihypertensives</td>
<td>63 (52.1)</td>
</tr>
<tr>
<td>Statins</td>
<td>10 (8.3)</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>23 (19)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>11 (9.1)</td>
</tr>
<tr>
<td>Levothyroxine</td>
<td>9 (7.4)</td>
</tr>
<tr>
<td>Proton-Pump Inhibitors</td>
<td>32 (26.4)</td>
</tr>
<tr>
<td>Antidiabetic Oral Agents &amp; Insuline</td>
<td>20 (16.5)</td>
</tr>
</tbody>
</table>

Concomitant Treatment Modification: 33.9%
Efficacy & Adverse Events

• **SVR12: 95.1%**
  – 66.1% are still on treatment

• **Adverse Events: 43.8%**

• **2 Hepatic Decompensation**
  – Encephalopathy
  – Hydropic decompensation

• **Treatment Discontinuation (2.4%)**

• No mortality

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**Table 2. Most frequent Adverse Events recognized during HCV Treatment.**

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>N (%)</th>
</tr>
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<tbody>
<tr>
<td>Anemia</td>
<td>42 (34.7)</td>
</tr>
<tr>
<td>Bilirubin increased</td>
<td>13 (10.7)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>45 (37.2)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>4 (3.3)</td>
</tr>
<tr>
<td>Irritability</td>
<td>3 (2.5)</td>
</tr>
<tr>
<td>Dry mucous</td>
<td>18 (14.9)</td>
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Conclusions

- High rates of SVR (95.1%) were observed among HCV-infected elderly patients under DAAs based regimens.
- The presence of adverse events was frequent (43.8%) but only 2.4% discontinued treatment for this cause.
- The majority (86.8%) had concomitant medication that need to be adjusted in third of them.
- Moreover, 42.9% of patients required a dose reduction of RBV.
- These findings highlight the high rates of response to DAAs-based therapy in elderly HCV population but with a special caution with RBV-doses adjustment.
Acknowledgements

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