Medication Adherence in Hepatitis C

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Hepatitis C Virus (HCV)

- Blood-borne virus (Single stranded RNA virus - Flaviviridae family)
- Virus officially identified in 1989
- Six major genotypes identified
- Est. 170 million people worldwide infected
- 0.5%-0.8% gen pop in England ~ 230,000 (HPA 2011)
- Majority of those infected are undiagnosed – asymptomatic
Natural History of HCV Infection

Exposure (Acute phase)

- Resolved: 15% (15)

Chronic

- Stable: 80% (68)
- Chronic: 20% (17)

Cirrhosis

- Slowly Progressive: 75% (13)
- Cirrhosis: 25% (4)

HIV and Alcohol

- HCC Transplant: 20%
- Death: 25%

References:

Alter MJ Semin Liver Dis 1995; 15:
Management of Hepatitis C NIH Consensus Statement 1997; March 24-26:15(3).
Hepatitis C is curable
Evolution of HCV Treatment

IFN: interferon; RBV: ribavirin
Peg-IFN: peginterferon
DAA: direct-acting antiviral
SVR: sustained virologic response

### Antiviral Treatments for HCV

<table>
<thead>
<tr>
<th>Pegylated Interferon</th>
<th>Ribavirin</th>
<th>Boceprevir</th>
<th>Telaprevir</th>
</tr>
</thead>
<tbody>
<tr>
<td>SC Injection (Pen or PFS)</td>
<td>Oral</td>
<td>Oral</td>
<td>Oral</td>
</tr>
<tr>
<td>Once weekly</td>
<td>Up to 7 tabs per day (in two divided doses)</td>
<td>12 caps per day (in three divided doses every 7-9 hrs)</td>
<td>6 tabs per day (in three divided doses every 8 hrs)</td>
</tr>
<tr>
<td></td>
<td>With food</td>
<td>With light meal or snack</td>
<td>With high fat meal (approx. 20 grams/fat)</td>
</tr>
</tbody>
</table>
## Side-Effects of Antiviral Treatments

### Peg Interferon and Ribavirin
- Fatigue, headache, nausea, pyrexia and myalgia
- Haematological – anaemia, neutropenia, thrombocytopenia
- Depression, anxiety
- Concentration, memory and visual disturbances, insomnia

### Boceprevir
- Anaemia
- Neutropenia
- Thrombocytopenia
- Dysgeusia, diarrhoea
- Fatigue, nausea, headache

### Telaprevir
- Anaemia
- Neutropenia, thrombocytopenia
- Pruritis, Rash
- Diarrhoea, nausea, anorectal symptoms
Summary

• HCV is curable and treatment is finite over a defined time course
• Duration and regimen depends on genotype, extent of Liver disease and viral response on treatment
• Treatment regimens can be complex
• During treatment patients must attend for frequent review and blood tests
What are the potential risks of non-adherence in HCV?

- Patient will not achieve an SVR
  - Consequences to individual
  - Consequences to others
- Development of resistance to antivirals
Adherence in HCV – What do we know

• Data with Peg/Rbv:
  - decreased drug exposure (due to dose reduction = decreased SVR)

• HOWEVER little data on decreased drug exposure from missed doses

• Little data published on rates of missed dose adherence and relationship to virological response

• No formal guidelines on assessment adherence in HCV
SVR rates by degree of adherence to Telaprevir in treatment-naïve patients (ADVANCE/ILLUMINATE)

>95% adherence to telaprevir

≤95% adherence to telaprevir

95% adherence corresponds to 4.2 days missed doses

SVR rates by degree of adherence to Boceprevir in treatment-naïve patients (SPRINT 2, BOC arms pooled)

Data is shown for combined boceprevir arms of SPRINT-2 (n=704); Only patients who took at least one boceprevir dose are included. Patients who discontinued during the lead-in were excluded.

Currently Unanswered Questions

• How should we assess adherence in HCV?

• What is the impact of patients perceptions and beliefs about their illness on antiviral adherence?

• What level of adherence do we need for virological response?

• How does antiviral adherence change over time?

• Is there any difference between drugs and regimens?

• How can adherence be optimised in this group?
How do we encourage adherence?
How we currently prepare patients for treatment

1. Assess patient eligibility for treatment
   - Is the patient suitable to start treatment?
   - Screen for co-morbidities
   - Check laboratory parameters
   - Check for drug-drug interactions

2. Explain what to expect
   - Discuss potential side-effects
   - Review treatment duration and stopping rules
   - Motivate: review possible treatment outcomes
   - Highlight the importance of adherence

3. Educate the patient to enable successful treatment
   - Give pregnancy counselling
   - Give dose and administration information and food advice
   - Discuss importance of attending clinic visits
   - Discuss management of adverse effects
What do we currently do to help patients?

- MDT links are key
- Link medication taking to daily routine
- Encourage use of reminder and available support systems
- Initial observation of injection technique etc
- Aim to assess adherence at each visit (self report, clinical indicies etc)
- Manage side-effects
- Expect non-adherence and try to problem solve!
Assessment of Medication Adherence in the DAA complex Hepatitis C clinic

Preliminary Analysis
Frequency of non-adherence
• *During the last week, how many times have you missed taking a dose of your medicines?* (None, one dose, 2 dose, 3 or more doses)

Modified Morisky Scale (Aliotta, 2004)
• 6 item scale
• Patients indicate if they perform any of the behaviours (yes/no)
• 2 subscales: Motivation, Knowledge

Additional 9 items related to medicines use
• *Do you have a routine to help you take your medicines regularly?*
• *Do you think the medicines you have been prescribed are the best ones for you?*
• Items assess behaviours and beliefs
• Generated from literature search and expert opinion as the Modified Morisky was deemed to be lacking in possible key domains
Demographics

- $N = 37$
- 21 males (57%)
- Average age: $53.62 \pm 9.76$ years
- Minimum age 26 years and maximum age 74 years
Results

Approximately one-fifth of patients (n = 8; 21%) missed one or more doses of their medication over the last week.

<table>
<thead>
<tr>
<th></th>
<th>Frequency (%)</th>
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<tbody>
<tr>
<td>I did not miss any doses</td>
<td>29 (78)</td>
</tr>
<tr>
<td>I missed one dose</td>
<td>3 (8)</td>
</tr>
<tr>
<td>I missed two doses</td>
<td>2 (5)</td>
</tr>
<tr>
<td>I missed three or more doses</td>
<td>3 (8)</td>
</tr>
</tbody>
</table>
Patients who were non-adherent over the last week were more likely to:

• Only take their medicine when they felt they needed to ($X^2 = 11.63, p = 0.005$)

• Forget to take their medicine ($X^2 = 10.01, p = 0.004$)

• Be careless about taking their medicine ($X^2 = 8.57, p = 0.013$)

• Not have a regular medicine-taking plan ($X^2 = 6.51, p = 0.021$)

• Not be confident when there was disruption to their routine ($X^2 = 6.43, p = 0.027$)
The majority of patients (n=26; 70%) had concerns about their medicines

<table>
<thead>
<tr>
<th>Concern</th>
<th>Frequency (%)</th>
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<tbody>
<tr>
<td>Possible side effects</td>
<td>23 (62)</td>
</tr>
<tr>
<td>How the medicines may damage my body in the long term</td>
<td>9 (24)</td>
</tr>
<tr>
<td>Taking too many medicines</td>
<td>9 (24)</td>
</tr>
<tr>
<td>Whether the medicines will be of any help</td>
<td>4 (11)</td>
</tr>
<tr>
<td>Whether their effectiveness will wear off over time</td>
<td>4 (11)</td>
</tr>
</tbody>
</table>
Conclusions

• Small sample – we only have data from 37 patients
• Preliminary results suggest that although most patients have concerns about side effects of treatment, they are adherent
• Non-adherence appears to be associated with:
  • Low motivation (as conceptualised by the Modified Morisky i.e. forgetfulness and carelessness
  • The absence of symptoms or other health threats (only taking their medicine when they felt they needed to)
  • Poor planning of medicine-taking behaviour (not having a routine and not being confident when there are disruptions to one’s routine)