Hepatitis C virus reinfection among HIV positive men who have sex with men

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HIV/HCV Coinfection

• Liver disease is the one of the leading non-AIDS causes of death in HIV infected individuals (13%) \(^1\)

• Hepatitis C virus (HCV) accounts for approximately two-thirds of liver disease in HIV infected individuals

• Coinfection with HIV leads to:
  • Reduced HCV spontaneous clearance rates
  • Increase in HCV related progression to cirrhosis by 2-3 fold\(^2\)
  • Reduction in HCV treatment success

HCV among HIV infected MSM

- Epidemic of sexually transmitted HCV occurring among the HIV infected men who have sex with men (MSM) population since early 2000s
- Primary incidence of HCV among HIV MSM estimated at 0.6/100py\(^1\) to 2/100py\(^2\)
- High rate of reinfection following treatment of acute HCV among HIV MSM (n=52) found in Amsterdam: 15.2 per 100py (95%CI, 8-26.5 per 100py)\(^3\)

1. Yaphe S et al. STI 2012;88:558-564
2. Van der Helm AIDS 2011;25:1083-1091
Aim

1. Calculate HCV reinfection incidence among HIV infected MSM in London
2. Compare reinfection incidence between individuals who were either previously treated or spontaneously cleared their primary infection
3. Describe spontaneous clearance rates and sustained viral response (SVR) rates of HCV reinfection

Study Design

- Retrospective analysis of all HIV/HCV coinfect ed individuals between 2004-2012 at Chelsea and Westminster Hospital, London

- Inclusion:
  - HIV infected MSM
  - No reported history of injecting drug use
  - Achieved HCV infection SVR through treatment or spontaneous clearance with at least one subsequent HCV PCR result

Definitions

Reinfection
- Any newly positive HCV RNA PCR 24 weeks or more following end of treatment or clearance of the virus; or
- Newly positive HCV RNA PCR within 24 weeks of end of treatment or clearance if reinfected with a different genotype
# Study characteristics

<table>
<thead>
<tr>
<th>Incident infection</th>
<th>All incident infections</th>
<th>Primary infection</th>
<th>Treated HCV Infection</th>
<th>Spontaneously cleared HCV infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>191</td>
<td>145</td>
<td>87</td>
<td>27</td>
</tr>
<tr>
<td>Median age (IQR)</td>
<td>41 (38-47)</td>
<td>41 (37-43)</td>
<td>39 (34-43)</td>
<td>36 (35-42)</td>
</tr>
<tr>
<td>Follow-up</td>
<td></td>
<td></td>
<td></td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Median testing interval, days (IQR)</td>
<td>112 (62-224)</td>
<td>106 (62-210)</td>
<td>99 (55-161)</td>
<td>189 (89-343)</td>
</tr>
<tr>
<td>cART use during follow-up (%)</td>
<td>129 (89)</td>
<td>82 (94)</td>
<td>22 (81)</td>
<td>21 (81)</td>
</tr>
<tr>
<td>Median peak ALT during follow up (IQR)</td>
<td></td>
<td></td>
<td></td>
<td>38 (26-55)</td>
</tr>
<tr>
<td>Median CD4 at last negative HCV RNA PCR/first positive HCV RNA (IQR)</td>
<td></td>
<td></td>
<td></td>
<td>547 (444-681)</td>
</tr>
</tbody>
</table>
HCV Reinfection Incidence

Overall reinfection rate

- Reinfection post-treatment
- Reinfection post-spontaneous clearance
- Second reinfection rate

HCV reinfection Incidence per 100py

Overall:
7.8 per 100 py
(95%CI 5.8-10.5 per 100py)

Martin TCS, et al. AIDS 2013 (in press)
HCV Reinfection Incidence

- Overall reinfection rate
- Reinfection post-treatment
- Reinfection post-spontaneous clearance

Post-treatment: 9.6 per 100py (95%CI 6.6-14.1/100py)
Post-spontaneous clearance: 4.2 per 100py (95%CI 1.7-10/100py)

Comparing reinfection post-treatment versus post-spontaneous clearance: p=0.15

Martin TCS, et al. AIDS 2013 (in press)
HCV Reinfection Incidence

Second reinfection: 23.2 per 100 py (95% CI 11.6-43.4 per 100py)

Martin TCS, et al. AIDS 2013 (in press)
HCV reinfection outcomes

• Total of 54 reinfections
• 20% spontaneous clearance rate
• Treatment outcome with pegIFN+RBV
  • Genotype 1/4: 73% SVR (N=22)
  • Genotype 2/3: 100% SVR (N=2)

Martin TCS, et al. AIDS 2013 (in press)
Conclusion

- High HCV reinfection rates among HIV MSM (7.8 per 100py, 95%CI 5.8-10.5)
  - Lower than found in Amsterdam (15.2 per 100py, 95%CI: 8-26.5), but overlapping confidence intervals
  - Longer testing interval in our study (3.6 months vs 3 months) may underestimate true reinfection incidence
  - Some apparent relapses in our study may have been reinfections
- Weak evidence for protective immunity following spontaneous clearance (p=0.15)
- Spontaneous clearance rate (20%), similar to rates in primary infection among HIV+ individuals
Limitations

• Retrospective study
• No phylogenetic analysis performed to confirm true reinfection not late relapse
• Variable testing intervals with potential to affect results
• Possible reinfection is emergence of non-dominant strain
  – Unlikely to substantially alter results as only 4 of 54 reinfections were genotype switches
  – For majority of individuals long duration (>6 months) from clearance of first virus to reinfection
  – 3 spontaneously cleared and the other was successfully treated
Implications

- Targeted sexual education for MSM who acquire HCV infection
- Enhanced surveillance of individuals who have previously been infected with HCV
  - New UK guidelines recommend 3-6 monthly HCV PCR post clearance of virus
- Spontaneous clearance rate (20%) supports initial monitoring before treatment of reinfection
Implications: cost-effectiveness

- Cost-effectiveness of HCV testing (6 month LFTs + yearly Ab test) and treatment in HIV/HCV MSM (neglecting prevention benefit)\(^1\):
  - $43,700/QALY (pegIFN+RBV), $53,800/QALY (Triple therapy)
  - Under UK willingness-to-pay, triple therapy not cost-effective (~£38,000)

- Modelling has shown HCV treatment for monoinfected injecting drug users could be an effective\(^2,3\) and cost-effective\(^3\) means of HCV prevention
  - In some settings, treatment for those with ongoing infection risk can be more cost-effective than for those without ongoing risk due to prevention benefit\(^3\)

- Further cost-effectiveness work needed on treatment strategies in HIV/HCV MSM including prevention benefit

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1. Linas BP et al. CID 2012;55:279-290
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