Defining the Impact of Transfusion Transmission of Hepatitis E Virus

Hepatitis E Study Group

Transfusion Microbiology, NHSBT, Colindale
Blood Borne Virus Unit, PHE, Colindale
Changing HEV epidemiology

Background

- HEV is four genotypes, 1-4, geographically, pathogenicity and host defined
- Humans are dead end hosts and do not usually pass on infection
- No licensed vaccine
- Understanding of HEV infection in England and Wales has changed
  - HEV is now most common cause of enteric acute hepatitis
  - Estimated 60 000 infections/year in England
  - High seroprevalence rates of ~13% adults
  - Very high rate of asymptomatic infections
Hepatitis E as an Emerging Zoonosis
England 2002-2013
Emerging zoonotic clade of HEV
HEV and blood safety?
Rationale for the study

- Evidence of acute HEV infection in our blood donors, with detectable viraemia
- Transfusion-associated HEV is recognised and has been reported from several countries including the UK
- Significant proportion (35-40%) of blood components given as haematological support to immunosuppressed individuals
- Current evidence suggests up to 60% of HEV infections in the immunocompromised SOT recipient may lead to chronic infection
- Lack of comprehensive data on the prevalence of donors presenting with asymptomatic viraemia at time of donation, transmission rates and clinical impact in exposed patients
- Growing momentum in Europe to address HEV and blood safety
Joint NHSBT-PHE study: HEV and Blood Safety

Study Aims

By donor screening for HEV RNA

- The incidence of HEV infection in blood donors
- The prevalence and duration of viraemia

By recipient look back

- The rate of HEV transmission
- The outcome of HEV infection from blood components
Incidence of HEV infection in blood donors

- 9382 minipools tested (x24) = 225,168 individual donations

- 79 donors whose index sample contained HEV RNA
  - = 0.03% of donations HEV RNA positive
  - = 1:2850 donations HEV RNA positive
HEV infected and viraemic donors

• None of the donors reported an illness at time of donation
• All viraemic donors were previously seronegative (testing of archived samples), supporting diagnosis of primary HEV infection
• 71% infected donors were anti-HEV seronegative at donation i.e. very early infection
• Development of symptoms (infrequent) was associated with appearance of antibody response
• All infected, initially seronegative donors seroconverted and cleared virus during follow up
Fate of viraemic donations

- 79 RNA positive donations (genotype 3)
- 129 blood components
- 67 Discarded or recalled
- 62 Transfused

60 recipients
- 43 recipients followed up
  - 25 no evidence of infection at week 16 (58%)
  - 18 evidence of infection (42%)
- 17 not possible to follow up
# The 129 components generated from 79 viraemic donations

<table>
<thead>
<tr>
<th>Component</th>
<th>Number produced</th>
<th>Number Recalled/Discarded (%)</th>
<th>Number Transfused (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red Blood Cells</td>
<td>71</td>
<td>48 (68%)</td>
<td>23 (32%)</td>
</tr>
<tr>
<td>Pooled Platelets</td>
<td>15</td>
<td>3 (20%)</td>
<td>12 (80%)</td>
</tr>
<tr>
<td>Apheresis Platelets</td>
<td>24</td>
<td>1 (4%)</td>
<td>23 (96%)</td>
</tr>
<tr>
<td>FFP</td>
<td>12</td>
<td>9 (75%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>6</td>
<td>6 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pooled Granulocytes</td>
<td>1</td>
<td>0 (0%)</td>
<td>1 (100%)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>129</strong></td>
<td><strong>67 (52%)</strong></td>
<td><strong>62 (48%)</strong></td>
</tr>
</tbody>
</table>
Relationship between component type and transmission

<table>
<thead>
<tr>
<th>Component</th>
<th>Number of * recipients</th>
<th>Infected Recipients (%)</th>
<th>Uninfected Recipients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red Blood Cells</td>
<td>16</td>
<td>4 (25%)</td>
<td>12 (75%)</td>
</tr>
<tr>
<td>Pooled Platelets</td>
<td>10</td>
<td>4 (40%)</td>
<td>6 (60%)</td>
</tr>
<tr>
<td>Apheresis platelets</td>
<td>14</td>
<td>7 (50%)</td>
<td>7 (50%)</td>
</tr>
<tr>
<td>FFP</td>
<td>2</td>
<td>2 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pooled Granulocytes</td>
<td>1</td>
<td>1 (100%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>43</strong></td>
<td><strong>18 (42%)</strong></td>
<td><strong>25 (58%)</strong></td>
</tr>
</tbody>
</table>

* Only 43 out of 60 exposed recipients were available for follow up
Transmission rates

• Recipients tested for HEV RNA, anti-HEV IgM and IgG at regular intervals whenever possible

• Follow up period of 16 weeks post transfusion in order to exclude transmission

• Where there was evidence of infection, follow up until seroconversion and HEV RNA clearance

• 42% transmission rate: Confirmation of donor-derived transmission by alignment of viral sequences from donor–recipient pairs

• All genotype 3, predominantly clade 2
Outcome in HEV infected recipients
Outcome in 18 HEV infected recipients (1)

Immunocompetent recipients
• 8 cleared infection rapidly, with seroconversion

Immunocompromised recipients
• 4 viraemic at time of death (week 10-15)
• 2 exhibited prolonged viraemia (week 4-42) before development of anti-HEV and RNA clearance
• 1 remains viraemic at week 43
• 3 responded to intervention
## Outcome in 18 HEV infected recipients (2)

<table>
<thead>
<tr>
<th>Inferred immunosuppression</th>
<th>Number of recipients</th>
<th>Median number of weeks from transfusion *</th>
<th>Proportion (%) who developed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>to RNA detection</td>
<td>to seroconvert</td>
</tr>
<tr>
<td>None or mild</td>
<td>8</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Moderate</td>
<td>6</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Severe</td>
<td>4</td>
<td>9</td>
<td>37.5</td>
</tr>
</tbody>
</table>

* Only numerate values included

** excludes those who died whilst infected
Clinical outcome HEV-infection

- Evidence of prolonged viraemia, one patient still viraemic
- One case of symptomatic post transfusion hepatitis
- Evidence of the eventual development of the antibody response leading to viral clearance
- Appearance of antibody coincides with subclinical hepatitis with raised LFTs
- Understanding what influences outcomes is very complex
  - Level and pattern of immunosuppression
  - Underlying medical conditions
  - Measure of morbidity
  - Length of follow up
What is a proportionate response? Have we got all the answers we need?

- Deal with the source of infection…animal husbandry
- NAT screen donors…all or bespoke donor panel?
  - Best NAT strategy?
  - Understand local epidemiology
- Select panel of immune donors
- Modify components, pathogen reduction…..HEV escapes
- Screening and surveillance of immunocompromised patients for HEV, to facilitate intervention, as for CMV
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