Incidence of *Clostridium difficile* infection is significantly higher in patients treated with prophylactic quinolone antibiotics alongside chemotherapy

Emily Renninson, Oliver Allon, Jessica Bailey  
Oncology Department, Cheltenham General Hospital, Gloucestershire Hospitals NHS Foundation Trust

### Background

- *Clostridium difficile* (C. diff) is a gram-positive, spore-forming anaerobic rod shaped bacterium.  
  - It causes a spectrum of disease ranging from mild diarrhoea to fulminant colitis and death.  
- Antibiotics are widely recognised as the leading cause of C. diff infection 1, 2, 3.  
- Clindamycin, cephalosporins, quinolones, co-amoxiclav and aminopenicillins are the most common risk factors.  
- Prophylactic antibiotics (typically quinolones), are prescribed alongside myelosuppressive chemotherapy regimes because trials including the ‘SIGNIFICANT’ trial 2005 have shown increased morbidity and mortality with this approach.  
  - Fluoroquinolone prophylaxis was associated with lower incidence of Fabre’s Neutropenia and mortality following the first cycle of myelosuppressive chemotherapy for solid tumours.  
- Therefore, quinolone antibiotics are given as part of many chemotherapy regimes.  
- However, use of quinolone antibiotics has been linked with increased incidence of C. diff infection.  
- It was suggested that C. diff rates in our Oncology Haematology centre were higher than expected…

### Methodology

- 2651 patients were treated with chemotherapy in our Oncology and Haematology centre in 2016.  
- There were 30 cases of *C. difficile* infection in our centre in 2016.  
- 24/28 (85.7%) patients had received chemotherapy in the preceding 30 days.  
- Therefore, quinolone antibiotics are given as part of many chemotherapy regimes.  
- 4/28 (14.3%) patients had received chemotherapy with quinolone prophylaxis.

### Results

#### Results for patients with *C. difficile* infection after chemotherapy

<table>
<thead>
<tr>
<th></th>
<th>C. diff positive</th>
<th>C. diff negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy with quinoline</td>
<td>24 (0.9%)</td>
<td>2480 (99.1%)</td>
<td>2504</td>
</tr>
<tr>
<td>Chemotherapy without quinoline</td>
<td>28 (1.1%)</td>
<td>2623 (98.9%)</td>
<td>2651</td>
</tr>
</tbody>
</table>

*The difference in frequency of C. diff infection between quinoline (n=4) and non-quinoline (n=24) groups wasn’t statistically significant, although suggestive of clinical correlation.*

- Fisher’s exact test p-value was 0.0659.

#### Subset analysis: C. diff infection within 30 days of chemotherapy

<table>
<thead>
<tr>
<th></th>
<th>C. diff positive</th>
<th>C. diff negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy with quinoline</td>
<td>4 (2.7%)</td>
<td>143 (97.3%)</td>
<td>147</td>
</tr>
<tr>
<td>Chemotherapy without quinoline</td>
<td>20 (0.8%)</td>
<td>2484 (99.2%)</td>
<td>2504</td>
</tr>
<tr>
<td>Total</td>
<td>24 (0.9%)</td>
<td>2627 (99.1%)</td>
<td>2651</td>
</tr>
</tbody>
</table>

*The difference in frequency of C. diff infection between quinoline (n=4) and non-quinoline (n=20) groups was statistically significant.*

- Fisher’s exact test p-value was 0.0045.

### Conclusions

- C. diff infection is an important clinical issue resulting in significant morbidity and a risk of mortality as well as causing chemotherapy delays.
- In 2016, our centre accounted for the majority of cases in the trust (n=30; target for the whole trust n=37).
- We found that C. diff infection within 30 days of chemotherapy was significantly higher in those patients receiving quinoline prophylaxis.
- At present, we continue to prescribe quinoline prophylaxis for myelosuppressive regimes as the morbidity and mortality of Fabre’s Neutropenia is felt to outweigh that from C. diff infection. We will continue to always justify antibiotic use in our trust.

### Discussion

- There are likely to be other factors contributing to the high rate of C. diff infection seen in our centre compared to the trust as a whole.
- Our Oncology and Haematology patients can be immunosuppressed even without chemotherapy.
- Our centre is relatively large for the size of the trust; we treat and admit patients from Gloucestershire, Herefordshire and Worcestershire (a county and surrounding of over a million), whereas the remainder of the trust only serves Gloucestershire.
- Perhaps our trust’s C. diff ‘allowance’ should be increased to reflect this?

### Definitions

- *“Positive” stool sample was defined as: patients with C. diff gene and/or toxin detected.  
  - C. diff infection was defined as: positive stool sample with associated symptoms requiring admission (diarrhoea, colitis etc.).

### References

5. Quality Improvement Commission data from 2016: Gloucestershire Hospitals NHS Foundation Trust