Audit of voriconazole therapeutic drug monitoring (TDM) at a tertiary teaching hospital in England following the introduction of e-prescribing (Epic®)

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Conflicts of interest

- Astellas
- Gilead
- Pfizer
- MSD
Voriconazole

- Voriconazole is a triazole antifungal that is commonly used in the treatment of invasive aspergillosis
- Therapeutic drug monitoring (TDM) is key to the effective use of voriconazole:
  - non-linear pharmacokinetics
  - serum concentrations are influenced by several factors including:
    - Age
    - Weight
    - Genetic polymorphisms
    - Altered drug absorption
    - Drug interactions
  - Voriconazole trough levels greater than 6mg/L are associated with an increased likelihood of hepatotoxicity
- Evidence to support the use of TDM during voriconazole treatment is growing
- National guidelines support its use (Ashbee et al 2015)
Audit standards

• All in-patients commencing voriconazole should be reviewed by a microbiologist

• Voriconazole pre-dose levels should be taken within 5-7 days of:
  • Commencing therapy
  • A change in dose
  • Side effects thought to be related to voriconazole
  • On request by AFS team

• All levels should be therapeutic (i.e. between 1 – 6mg/L)
  • If out of range then evidence of review and change in management instituted

• Turnaround time should be ≤3 days
Cambridge (Addenbrooke’s hospital)

• Teaching hospital (1,100 beds)
  • 70,000 inpatient admissions
  • 170,000 total admissions per annum

• Specialities include:
  • Transplantation (bone marrow, liver, kidney, pancreas, bowel)
  • Neurosciences
  • Infectious diseases
  • Plastic surgery

• Big user of antifungal drugs; the “biggest in the region”
Methods

• **Inclusion criteria:** all inpatients on voriconazole

• Retrospectively analysed over the three month period (January – March 2016)

• Patients were identified using the Epic system and in-house dispensing reports
  • Report from EPIC
  • Costing report from inpatient pharmacy (Cheqs system)
  • Laboratory sendaway tests

• **Exclusion criteria:** outpatients

• Voriconazole pre-dose serum levels were analysed by the Mycology Reference Laboratory, Bristol, England

• Part of antifungal stewardship (AFS) programme (Micallef et al 2015)
Results

- 39 patients were identified as receiving voriconazole in the study period.
- 22 (56%) male
- Age range 2 – 82 years (median 54; IQR 42 – 67 years)
Results

• 37/39 (95%) of patients had evidence of review by microbiology in the medical notes

• Six patients died prior to a level being taken and one patient was discharged prior to day 5 of therapy (with levels taken elsewhere)

• A total of 28 voriconazole levels were reported for the remaining 32 patients
Reason for the level to be taken

- Starting therapy: 9
- No previous result: 9
- Dose change: 4
- Efficacy concern: 3
- Side effects: 2
- Concern re: absorption: 1
### Reason for the level to be taken

<table>
<thead>
<tr>
<th>Reason for taking level</th>
<th>Total number</th>
<th>Appropriate</th>
<th>Inappropriate</th>
<th>Reason</th>
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<td>5</td>
<td>4</td>
<td>Late</td>
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<tr>
<td>No previous result</td>
<td>9</td>
<td>0</td>
<td>9</td>
<td>Late</td>
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<td>Dose change</td>
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<td>Efficacy concern</td>
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<tr>
<td>Side effects</td>
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<td></td>
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<tr>
<td>Concern re: absorption</td>
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<td>1</td>
<td></td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>28</strong></td>
<td><strong>15</strong></td>
<td><strong>13</strong></td>
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</tbody>
</table>
17/28 (61%) had a level >1mg/L
11/28 (39%) had a level >2mg/L
11/28 (39%) had a level <1mg/L
Results

- Actions performed for those with levels <1mg/L

- Increase dose 2
- Switch drug / formulation 4
- Stop 2

- Nothing 3
Turnaround time

Range 3 – 25 days (median 8 days)
2 (7%) had a TAT of ≤3 days
11 (39%) had a TAT of ≤7 days
Summary of results

• Microbiology approval obtained 37/39 (95%) of the time
• 28 levels taken from 32 eligible patients
• 15/28 (54%) levels appropriate
  • Room for improvement re: appropriateness of taking levels (especially timing after starting therapy)
• 9/12 (75%) low levels actioned
  • Room for improvement re: action after receiving low levels
• 2/28 (7%) had acceptable turnaround time
  • Dramatic room for improvement re: turnaround times
Limitations

• Look into reasons why:
  • levels weren’t taken
  • low levels weren’t actioned
  • The turnaround times are so long
Plan

- Education of clinical teams (especially haematology and respiratory medicine) and pharmacy

- Recomence AFS programme
  - This needs to be adequately resourced

- Look into laboratory working patterns
  - In-house testing has been refused…
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