Introduction

• Time to appropriate antimicrobial therapy is essential to reduce mortality and morbidity in sepsis-related bloodstream infections (BSI) [1]. Standard practice for identification (ID) and antimicrobial susceptibility testing (AST) of a positive blood culture can take up to 48 hours [2].

• GenMark® ePlex® Blood Culture Identification (BCID) panels are automated, qualitative nucleic acid multiplex in vitro diagnostic test, combining electrowetting and GenMark’s eSensor® technology, for the simultaneous detection and ID of multiple Gram positive (GP) and Gram negative (GN) bacteria and fungi from positive blood cultures following Gram staining.
  o Electrowetting uses electrical fields to directly manipulate droplets on the surface of a hydrophobically coated printed circuit board.
  o eSensor® technology uses a solid-phase electrochemical method for determining the presence of one or more of a defined panel of bacterial or fungal target sequences.

• Molecular assays, such as the ePlex® BCID panels, enable clinicians to rapidly identify clinically relevant BSI and their resistance genes when blood culture are initially positive. This allows for early antimicrobial interventions, while quickly ruling out blood culture contamination, resulting in cost savings.

Methods

• At the time of initial positivity, blood cultures were Gram stained and tested in parallel as per Figure 1.

• Data was collected from Electronic Patient Record (EPR) and Telepath laboratory system in 2 Microsoft Excel databases.

• The data collected included:
  o Time to ID.
  o Time to resistance determinants/AST.
  o Concordance of results.
  o Clinical data:
    ▪ Blood culture contamination.
    ▪ Possible AMS interventions.

Results

• 21 blood cultures were tested.
• 2 blood cultures were mixed:
  o Enterococcus faecium and Citrobacter (required a GN and a GP card for ID).
  o Staphylococcus epidermidis and Enterococcus faecalis (required 3 GP card for ID).

Table 1 – Average Time to Identification and Resistance Profiles for GN/GP Bacteria

<table>
<thead>
<tr>
<th>ePlex® System</th>
<th>Standard Methodology</th>
<th>Average Time to Identification</th>
<th>Average Time to Resistance Determinants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Time</td>
<td>297 min *(4 hr 47 min)</td>
<td>1874 min *(31 hr 14 min)</td>
<td>1577 min *(26 hr 17 min)</td>
</tr>
<tr>
<td>Identification</td>
<td>(n=21 panels)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Time</td>
<td>293 min *(4 hr 53 min)</td>
<td>3755 min *(62 hr 35 min)</td>
<td>3462 min *(57 hr 42 min)</td>
</tr>
<tr>
<td>Resistance</td>
<td>(n=15 panels)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* ePlex® processing time = 40 min. ePlex® BCID panels were only used during working hours so there was a delay in some cases between blood culture flagging positive and being loaded onto the ePlex® machine (i.e., if flagged/positive overnight).

• The fungal ePlex® ID was Malassezia furfur.
  o This failed to grow in our laboratory.
  o ID and AST was performed at the UK Mycology Reference Laboratory – the final report was received 38 days after the blood culture initially flagged positive.
  o Early ID allowed for an early change to an appropriate antifungal agent.

• Taking into account the selection of organisms and resistance determinants on the ePlex® panel, concordance with final culture ID and AST results was 100%.

• Three isolates had no targets determined on the ePlex® BCID panels and were not detected – Prevotella denticollo, Pseudomonas fluorescens/Pseudomonas picketti and Raoultella spp.

• Although the sample set was small, the results of ePlex® BCID panels could have resulted in potentially 50% earlier AMS interventions for positive blood cultures with GN/GP bacteria. This may increase with the sample size.

• Early ID of Serratia marcescens, Enterobacter cloacae complex and Citrobacter would have allowed for early change from empiric treatment to more appropriate treatment based on clinical picture, allowing for more targeted therapy and improved sepsis management.

• Early ID of Staphylococcus aureus without detection of mecA or mecC resistant determinants would allow for early de-escalation from empiric vancomycin to targeted flucloxacillin.

• Early ID of Enterococcus faecalis without detection of vanA or vanB resistant determinants would allow for early de-escalation from empiric linezolid to targeted amoxicillin.

• Early ID of blood culture contaminants in the four cases could have resulted in potential savings of over €30,000 (based on local financial costs).

• While no Multi-Drug Resistant Organisms (MDROs) were included, the ePlex® would have potentially allowed for the early exclusion of VRE BSI in 2 cases and the potential early exclusion of ESBL/CPE BSI in 7 cases.

Conclusion

The potential benefits of the ePlex® BCID system include: 
• Reduced laboratory time to result.
• Earlier ID of MDROs (e.g. VRE, MRSA, ESBL and CPE) resulting in earlier infection prevention and control interventions.
• Earlier appropriate treatment on the basis of ID and resistance profile, thereby improving sepsis management.
• AMS interventions - earlier more targeted treatment, escalation or de-escalation of treatment as appropriate, and early ID of blood culture contaminants.
• Cost saving related to early blood culture contaminant recognition.

References:
2. Table et al. Blood Culture Turnaround Time in UK Acute Care Hospitals and Implications for Laboratory Process Optimisation. JCM Aug 2018 22 (Quick ahead of print)