Introduction

Early appropriate empirical antibiotic treatment is associated with reduced all-cause mortality in septic patients.1,2 Delays in antibiotic administration have also been associated with increases in in-hospital, risk-adjusted sepsis mortality in patients admitted to the emergency department.3 However misuse and overuse of antibiotics contributes to increased drug related toxicity, the selection of pathogenic organisms (such as Clostridium difficile) and the emergence of resistance.4 Therefore a balance between prevention of infection related mortality and judicious antibiotic use should exist.

The Infectious Diseases Society of America/Society for Healthcare Epidemiology of America Stewardship Guidelines suggest various strategies to promote judicious use of antimicrobials in order to improve patient outcomes, control resistance and decrease healthcare expenses.5 One strategy the guidelines suggest is antibiotic stewardship based on diagnostic results. Blood cultures, the gold standard in bacteremia diagnostics, however detect bacteremia in only about 50% of patients who are clinically suspected of having sepsis and that value may decrease after antibiotic administration.6,7 In addition, blood culture and subsequent antimicrobial susceptibility testing, can take 2-5 days.8 During this time no clinical data is available to support patient treatment, therefore patients are typically treated empirically. However, in a meta-analysis of 70 studies, empiric antibiotic therapy was not appropriate in 46.9% of patients, indicating that nearly half of infected patients are not treated optimally in the absence of diagnostic information. In addition, these patients showed over two times higher odds of death.7

Rapid diagnostic assays have been associated with improvements in time to appropriate antibiotic therapy by enhancing early identification of causative organisms.6,9,10 Data supports bundling rapid diagnostic technology and antimicrobial stewardship programs to reduce antibiotic utilization and improve emergency time and de-escalation.

Research Question

• The T2Bacteria Panel is an FDA and CE Mark cleared and blood culture-independent assay for detection of bacteremia due to the most common ESKAPE pathogens: Escherichia coli; Enterococcus faecium; Staphylococcus aureus; Klebsiella pneumoniae; and Pseudomonas aeruginosa, and provides species identification within 3 to 5 hours after blood culture.

• In this study, we hypothesize that the T2Bacteria Panel, a direct from whole blood diagnostic assay, has the potential to provide accurate and timely diagnosis of bacteremia, which might support the direct therapeutic management of ED patients in the emergency department.

Methods

As part of the prospective, non-interventional T2Bacteria Panel clinical study, a subset of ED patients were enrolled from Ochsner Medical Center (New Orleans, LA) and Tampa General Hospital (Tampa, FL). The study was approved by the review boards of both institutions.

Inclusion Criteria

Patients ≥ 18 years old with blood cultures obtained per standard of care

Exclusion Criteria

• Patients who could not provide consent

• Any subject that was previously enrolled in the study (i.e. subjects were unique and had exactly one result)

• Patients that did not have sufficient blood collected for T2 testing (at least one tube ≥ 5 mL)

Blood Collection

Two blood cultures were obtained from each patient. Each blood culture was sent to the lab for processing and testing. The samples were processed within 30 min of draw. To ensure optimal performance and testing, T2 Biosystems recommends processing the blood within 30 minutes of sampling. One blood culture was sent for identification and antimicrobial susceptibility testing. The other blood culture was processed for the T2Bacteria assay as soon as possible in order to maintain the quality of the specimen.

Data Analysis

• Samples were analyzed for bacterial growth using both methods and both positive percent agreement (PPA) and negative percent agreement (NPA) were calculated for each species.

• T2Bacteria results were compared against: (i) the "matched" blood culture drawn concurrently with T2Bacteria, (ii) other blood cultures within ±14 days of the T2 draw, (iii) other cultures in non-blood matrices within ±14 days of the T2 draw and (iv) against a Sanger sequencing method.

• Time required to species identification was also compared.

• This was a non-interventional study and thus we reviewed patient history to assess potential impact of the T2Bacteria result.

• Data were retrospectively analyzed for opportunities for antimicrobial escalation or de-escalation. Opportunities for antimicrobial stewardship intervention were defined as: Escalation of therapy including initiation of effective antimicrobial therapy (based on antibiogram and spectrum of activity of active antibiotic at time of T2 result)

• De-escalation of therapy

• Discontinue MRSA coverage when S. aureus negative

• Discontinue narrow anti-Ps coverage when Ps negative

• Discontinue gram negative coverage when S. aureus positive

Results

Figure 2: Positive percent agreement (PPA) and negative percent agreement (NPA) of the T2Bacteria Panel against matched blood culture

Table 1: Comparison of T2Bacteria Panel and blood culture time to result

<table>
<thead>
<tr>
<th>Time to species identification (h)</th>
<th>Mean ± SD</th>
<th>T2Bacteria</th>
<th>Blood culture</th>
<th>Difference (mean ± SD)</th>
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Potential impact of T2Bacteria results on patient care

• A total of 29 potential opportunities for antimicrobial stewardship intervention were identified for the 23 patients with a positive T2 result

• 43% (10/23) of patients with positive T2 results had opportunity for earlier escalation of antibiotics/inflation of effective therapy based on institutional antibiograms

• 19 opportunities for S. aureus and P. aeruginosa de-escalation were identified

Table 2: Patient examples of the potential for impact of positive and negative T2Bacteria results

Conclusions

• T2Bacteria provides rapid and sensitive detection of bloodstream infections caused by the majority of concerning pathogens most commonly identified in ED patients

• The T2Bacteria assay can be a useful antimicrobial stewardship tool that has the potential to impact the care of patients, including reduction in time to effective therapy and antimicrobial stewardship.

Disclosures

OS, SE, JC and DB are employees of T2 Biosystems, Inc, the manufacturer of the T2Bacteria Panel.

References


Figure 1: T2BX Instrument

Figure 3: T2Bacteria panel coverage of blood culture positive species

Time to species ID, blood culture vs. T2Bacteria

• Difference in mean time to ID between blood culture and T2Bacteria was 66.1 hrs. (Table 1)

• When considering only species on the T2Bacteria Panel, the mean time difference was 56.6 hrs. This difference was significant with either all BC species or only species on the T2Bacteria Panel (p<0.001).

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