Patient Outcomes Associated with Implementation of a Multiplex Assay for the Identification of *Staphylococcus aureus* Bloodstream Infections

1071

Jihye Kim, PharmD, BCPS[1], Poonam Mathur, DO[2], Michael Sasso, MD[4], Michael Davies, PhD[3], Trevor Caldwell, MD[3], David Craft, PhD[3]

[1]Department of Pharmacy, [2]Department of Medicine, [3]Department of Pathology, Penn State Milton S. Hershey Medical Center, Hershey, PA, [4]Department of Medicine, Lancaster General Hospital, Lancaster, PA

Corresponding contact information
Jihye Kim, Pharm.D.
jkim6@hmc.psu.edu

BACKGROUND

- *Staphylococcus aureus* blood stream infections are associated with significant morbidity and mortality. Timely initiation of appropriate antibiotics is associated with improved patient outcomes and decreased health care costs.
- Antimicrobial stewardship programs (ASPs) provide prospective audits and feedback to promote appropriate antimicrobial use. Recent studies have shown that rapid detection of bacteria in blood cultures improves patient outcomes in institutions with active ASPs.
- However, limited data is available evaluating the impact of rapid diagnostic tests on morbidity and mortality without additional ASP efforts.
- The purpose of this study was to assess the impact of rapid identification of *S. aureus* in patients with bloodstream infections without changing the current ASP activities at our medical center.

OBJECTIVES

- Primary: evaluate time to de-escalation of antimicrobial therapy in context of rapid multiplex assay results for *S. aureus*
- Secondary: determine time to microbiological cure, length of hospital stay, Intensive Care Unit (ICU) stay, and mortality

METHODS

- Single-center, pre-post, quasi-experimental study
- Inclusion criteria: patients > 18 years old with a *S. aureus* blood stream infection
- Study design:
  - Preintervention: September 2012 – June 2013
  - BioFire Diagnostics (Salt Lake City, UT) FilmArray and Blood Culture Identification (BCID) Panel implemented in June 2014
  - Intervention: July 2014 – May 2015
- Definitions:
  - Time to de-escalation: time from initiation of broad- spectrum antibiotic to 1)initiation of optimal antibiotic or 2)discontinuation of unnecessary antibiotics
- Statistical analysis: descriptive statistics using GraphPad Prism version 6 (La Jolla, CA)

RESULTS

Table 1. PATIENT CHARACTERISTICS

	Preintervention (n = 40)	Intervention (n = 70)	p-value
Age, mean ± SD	57 ± 15	61 ± 18	0.2899
Male, n (%)	22 (55)	52 (74)	0.0566
Comorbidities, n (%)			
None	1 (1.5)	2 (1.3)	1.0000
Diabetes Mellitus	15 (22.4)	32 (20.5)	0.8580
CKD	4 (6)	15 (9.6)	0.4435
Chronic Liver Disease	7 (10.4)	5 (3.2)	0.0468
Immunocompromised	16 (23.9)	30 (19.2)	0.4718
CVD	7 (10.4)	34 (21.8)	0.0584
Other	17 (25.4)	38 (24.3)	0.8669
Concomitant Infections, n (%)			
None	14 (31.8)	28 (30.8)	1.0000
Lung	8 (18.2)	9 (9.9)	0.1796
Urine	5 (11.4)	15 (16.5)	0.6062
Blood	2 (4.5)	1 (1.1)	0.2477
SSTI	5 (11.4)	18 (19.8)	0.3287
Bone and Joint	6 (13.6)	12 (13.2)	1.0000
IAI	0 (0)	2 (2.2)	1.0000
C. difficile	2 (4.5)	3 (3.3)	0.6608
Other	2 (4.5)	3 (3.3)	0.6608
APACHE II Score, mean ± SD	25 ± 7	20 ± 9	0.1225
Previous *S. aureus* Bacteremia, n (%)	0 (0)	3 (4)	0.5524
S. aureus in blood culture, n (%)			
MRSA	19 (48)	33 (47)	1.0000
MSSA	21 (52)	37 (53)	1.0000
De-escalation of Antimicrobials, n (%)	31 (77.5)	44 (63)	0.1386
Primary Service, n (%)			
Internal Medicine	15 (37.5)	34 (48.6)	0.3202
MICU	5 (12.5)	5 (7.1)	0.4919
Surgical	6 (15)	10 (14.3)	1.0000
Family Practice	0 (0)	3 (4.3)	0.5524
Hem/Onc	10 (25)	11 (15.7)	0.3133
Urology	0 (0)	1 (1.4)	1.0000
Neurology	2 (5)	1 (1.4)	0.2988
Cardiology	1 (2.5)	3 (4.3)	1.0000
Trauma	1 (2.5)	2 (2.9)	1.0000
ID Consult, n (%)	25 (63)	51 (73)	0.2883

CKD: Chronic Kidney Disease; CVD: Cardiovascular Disease; d: Days; ED: Emergency Department; Hem/Onc: Hematology/oncology; IAI: Intra-abdominal Infection; MICU: Medical Intensive Care Unit; n; Number; NS: Not Significant; SD: Standard Deviation

FIGURE 1. TIME TO DE-ESCALATION

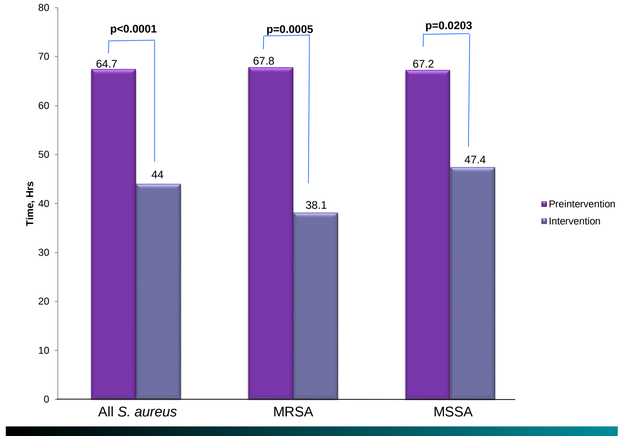
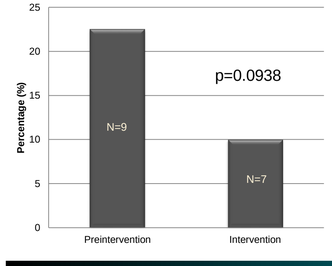


Table 2. SECONDARY OUTCOMES

	Preintervention	Intervention	p-value
Time to Blood Culture Clearance, d, median (IQR)	3 (1 – 6)	2 (1 – 4)	0.2108
ICU Stay, d, median (IQR)	7 (3 – 14)	3 (2 – 14)	0.1513
Hospital LOS, d, median (IQR)	9.5 (6 – 21)	9.0 (6 – 15)	0.3976

d: Days; Hrs: Hours; ICU: Intensive Care Unit; LOS: Length of Stay; IQR: Interquartile Range

Figure 2. ALL CAUSE MORTALITY



- Preintervention group had a higher mortality rate compared to the intervention group (23 vs 10%).
- Of those 16 patients, 9 patients had MRSA bacteremia and 7 patients had MSSA bacteremia.

ACKNOWLEDGEMENT

JK funded by BioFire to present this data.

SUMMARY

- A total of 110 patients with culture confirmed Methicillin Sensitive- and Methicillin Resistant-*S. aureus* bacteremia were included in the final analysis: 40 patients in the pre-intervention group and 70 patients in the intervention group.
- Chart review of pre- and post-intervention patient data revealed decreased time to de-escalation of empiric antimicrobial therapy (67 vs 44 hours, P < 0.0001) for patients with *S. aureus* bacteremia in the intervention group.
- Mortality (23 vs 10%), ICU stay (7 vs 3 days), length of hospital stay (10 vs 9 days), and time to microbiological cure (3 vs 2 days) were lower in the intervention group.

CONCLUSIONS

- Outcome data for patients with *S. aureus* bacteremia in our medical center indicates that implementation of a multiplex assay for rapid identification of positive blood culture bottles decreases time to de-escalation of empiric antimicrobial therapy without any additional effort of the ASP.
- Additional benefits are recognized in mortality, length of ICU stay, length of hospital stay, and time to microbiological cure.
- In addition to an appropriate in vitro analysis of methods, clinical microbiologists may want to consider using patient outcome data in their laboratory evaluations of multiplex test platforms to potentially justify the expense and return on investment for this type of syndromic testing.

REFERENCES

1. Albur et al. Factors influencing the clinical outcome of methicillin-resistant Staphylococcus aureus bacteraemia. Eur J Clin Microbiol Infect Dis 2012; 31:295-301.
2. Goff et al. Using rapid diagnostic tests to optimize antimicrobial selection in antimicrobial stewardship programs. Pharmacotherapy 2012: 32: 677-687.
3. Huang et al. Impact of rapid organism identification via matrix assisted laser desorption/ionization time of flight combined with antimicrobial stewardship team intervention in adult patients with bacteremia and candidemia. Clin Infect Dis 2013; 57:1237-1245.
4. Holtzman et al. Assessment of impact of peptic nucleic acid fluorescence *in situ* hybridization for rapid identification of coagulase-negative staphylococci in the absence of antimicrobial stewardship intervention. J Clin Micro 2011; 49: 1581-1582.
5. Kim et al. Outcome of vancomycin treatment in patients with methicillin-susceptible Staphylococcus aureus bacteremia. Antimicro Agents and Chemother 2008; 52:192-197.
6. Nagel et al. Impact of antimicrobial stewardship intervention on coagulase-negative *Staphylococcus* blood cultures in conjunction with rapid diagnostic testing. J Clin Micro 2014; 52: 2849-2854.
7. Perez et al. Integrating rapid pathogen identification and antimicrobial stewardship significantly decreases hospital costs. Arch Pathol Lab Med 2013; 137:1247-1254.
8. Wisplinghoff et al. Nosocomial bloodstream infections in US hospitals: analysis of 24179 cases from a prospective nationwide surveillance study. Clin Infect Dis 2004; 39:309-317.