Open Forum Infectious Diseases
CORRESPONDENCE

Challenges in Antimicrobial Stewardship: Rapid Diagnostics and Optimization of Therapy Among Immunocompromised Patients

Dear Editor—We commend Buss et al. [1] on their study showing that among immunocompromised patients with bloodstream infections (BSI), the use of a multiplex polymerase chain reaction (mPCR) reduced the time to organism identification and appropriate antimicrobial therapy (AAT), but the addition of antimicrobial stewardship (AS) interventions did not significantly impact the time to AAT. The authors point to the need for additional studies assessing the use of mPCR for BSIs in this patient population. We report our institutions' experience using mPCR to guide treatment of BSI among patients with hematological malignancy or hematopoietic stem cell transplantation.

We conducted a retrospective pre/post intervention study evaluating the impact of use of the Verigene System (Nanosphere, Northbrook, IL) for blood culture identification in the management of BSI among patients admitted to a cancer center. This platform has a different microbiological panel than that used by Buss et al. Three periods were assessed: pre-intervention (11/1/2014 to 3/31/2015), intervention with mPCR and AS (4/1/2015 to 12/31/2015), and postintervention with mPCR alone (1/1/16 to 10/1/2016). During the intervention period, providers were notified of mPCR results by a member of the AS team in real time via email. Modifications to therapeutic strategies were recommended as appropriate. The mPCR reports did not include templated comments. During the nonintervention periods, blood cultures were reported per standard practices. Onset time for therapies was date and time of blood culture collection. Descriptive statistics were used to compare the 3 periods, with use of chi-square for comparison of categorical associations and use of Kruskal-Wallis and Wilcoxon rank-sum for comparison of medians. Ninety-five unique patients were reviewed, and 112 unique BSI episodes were identified. Demographic and microbiological characteristics are shown in Table 1 and Supplementary Table 1.

During the pre-intervention period, 3/22 (14%) patients underwent escalation of therapy, compared with 10/50 (20%) in the intervention period and 9/40 (23%) in the postintervention period ($P = .70$). Two patients during each period following introduction of mPCR required escalation due to detection of $bla_{\text{CTX-M}}$; the other patients had escalation due to clinical deterioration. All 3 patients who had escalation during the pre-intervention period were escalated due to their clinical status and not due to infection with a multidrug-resistant organism. De-escalation of therapy from the initial regimen was seen in 3/22 (14%) patients during the pre-intervention period and 6/50 (12%) and 7/40 (18%) patients during the intervention and postintervention periods, respectively. The median (interquartile range [IQR]) time to escalation was 102 (69–108), 115 (49–160), and 136 (22–192) hours in the pre-intervention, intervention, and postintervention periods, respectively ($P = .96$). The median (IQR) time to de-escalation was 130 (120–298), 156 (99–217), and 85 (64–335) hours in the pre-intervention, intervention, and postintervention periods, respectively ($P = .73$). The median (IQR) duration of therapy per BSI episode was 14.5 (9–19) days in the pre-intervention period, 12.5 (8–18) days in the intervention period, and 13.5 (7–19) days in the postintervention period ($P = .85$). Duration of therapy was similar across periods for patients with BSI due to gram-positive and gram-negative organisms. The median number of hours to identification of organism (IQR) was longer in the pre-intervention period (74.1 [55.4–88.3] hours) compared with the periods after introduction of mPCR (36.1 [23.6–60.8] hours; $P < .001$). Results by type of organism are displayed in Supplementary Table 2.

Our results showed that introduction of mPCR in positive blood cultures resulted in a decrease in the number of hours to pathogen identification but did not impact the spectrum of antimicrobial coverage or duration of therapy. Similar to Buss et al. [1], we observed no apparent benefit of AS in time to de-escalation of antibiotic therapy among cancer patients. This contrasts with the results of Banerjee et al. [2], who showed that use of mPCR in conjunction with AS decreased time to antibiotic de-escalation by an average of 20 hours; however, their cohort included <40% immunocompromised hosts. Alternatively, centers with higher rates of extended-spectrum beta-lactamases (ESBLs) or carbapenemase-producing Enterobacteriaceae (CPE) could potentially see a benefit in time to escalation of therapy.

Current guidelines recommend that among neutropenic patients with clinical or microbiologically documented infection, antibiotics be continued for at least the duration of neutropenia [3]. Recent studies exploring outcomes among high-risk neutropenic patients undergoing de-escalation before resolution of neutropenia showed shorter duration of antibiotics without an increase in mortality [4, 5]. However, neither of these studies was powered to primarily assess differences in mortality.

The limitations of our study include its retrospective design, use of a single center, and use of an mPCR platform that provides rapid identification but not rapid susceptibility testing.

Antibiotic stewardship programs should develop pathways implementing mPCR

Table 1. Patient Demographic, Clinical, and Microbiological Characteristics

	Pre-intervention	Intervention[c]	Postintervention[d]	
	n = 20	n = 43	n = 32	*P* Value
Demographic characteristics[a]				
Age , y	60 (35–66)	58 (45–67)	59 (49–66)	.92
Male gender	12 (60)	28 (65.1)	20 (62.5)	.92
ATG	0	10 (23.3)	5 (15.6)	.06
Steroids[e]	5 (25)	18 (41.9)	10 (31.2)	.37
Neutropenia	11 (55)	29 (67.4)	24 (75)	.33
Hematologic malignancy				
Leukemia	13 (65)	25 (58.1)	21 (65.6)	.64
Lymphoma	5 (25)	9 (20.9)	3 (9.4)	
Multiple myeloma	1 (5)	5 (11.6)	3 (9.4)	
Type of stem cell transplant				.40
None	11 (55)	17 (39.5)	10 (31.2)	
Autologous	4 (20)	6 (14)	6 (18.8)	
Allogeneic	5 (25)	20 (46.5)	16 (50)	
GVHD				.50
Skin	0	1 (2.3)	3 (9.4)	
Gastrointestinal	1 (5)	3 (7)	4 (12.5)	
Multiple sites	1 (5)	1 (2.3)	1 (3.1)	
Oral only	0	2 (4.7)	0	
Any site	2 (10)	7 (16.3)	(25)	
Clinical and microbiological characteristics of BSI episodes[b]				
Neutropenic fever	11 (50)	20 (40)	22 (55)	.35
Source of infection				.17
Genitourinary	2 (9.1)	2 (4)	1 (2.5)	
Intra-abdominal	2 (9.1)	3 (6)	8 (20)	
Vascular catheter	6 (27.3)	28 (56)	20 (50)	
Indwelling device	1 (4.5)	0	0	
Respiratory	1 (4.5)	3 (6)	2 (5)	
Skin and soft tissue	1 (4.5)	3 (6)	3 (7.5)	
Unknown	9 (40.9)	11 (22)	6 (15)	
Type of organism				
Gram-positive	14 (63.6)	24 (48)	24 (60)	.36
Gram-negative	8 (36.4)	26 (52)	16 (40)	.36
Polymicrobial	4 (18.2)	4 (8)	5 (12.5)	.45

Abbreviations: AS, antimicrobial stewardship; ATG, antithymoglobulin; BSI, bloodstream infection; GVHD, graft-vs-host disease; mPCR, multiplex polymerase chain reaction.

[a]Cohort including unique patients, n = 95.

[b]Cohort including all bloodstream infections, n = 112.

[c]Intervention: use of multiplex PCR and antimicrobial stewardship.

[d]Postintervention: use of multiplex PCR alone.

[e]Use of prednisone >1 mg/kg or equivalent in the 2 weeks before positive blood culture.

while ensuring safe de-escalation of antibiotics among immunocompromised patients.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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