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Augmenting utility of rapid diagnostic testing in treatment of Gram-negative bacteremia with stewardship intervention

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Background

Traditional blood cultures are the most commonly used diagnostic tool to isolate causative organisms in bloodstream infections (BSI). Pathogens are generally identified within 5 days. The advent of rapid diagnostic tests (RDTs) have allowed prompt identification of pathogenic organisms and may decrease time from empiric to definitive therapy. Additionally, the absence of resistant markers (i.e. CTX-M) identified by RDTs and calculated negative predictive values (NPV) help predict susceptibility in target bug-drug scenarios. A high calculated NPV supports early de-escalation strategies and decreases time to targeted therapy.

Table 1: Predictive values by bug-drug combination at CMMC

Target Organism	n	Target Drug	Resistance marker	Resistant isolates (n)	Isolates identified by RDT (n)	NPV (%)
E. coli	107	Ceftriaxone	CTX-M	27	23	95%
K. pneumoniae	33	Ceftriaxone	CTX-M	9	9	100%

NPV: negative predictive value

Objective

To assess time to de-escalation of antimicrobial therapy with stewardship intervention in patients with Gram-negative bacteremia

Methods

An IRB-approved single-center pre-post cohort study was conducted to evaluate time to antimicrobial de-escalation in adult patients with *E. coli* or *K. pneumoniae* bacteremia as identified by our institution's RDT before and after stewardship intervention. The antimicrobial stewardship team monitored RDT results daily and intervened as appropriate. These target pathogens were selected based on NPV >95% to ceftriaxone calculated during a retrospective analysis at our institution (See *Table 1*). At the point of RDT result, patients meeting inclusion criteria with no detected resistance marker were recommended to be treated with ceftriaxone. Polymicrobial cultures, those resulting in performance assay discrepancies, patients with documented beta-lactam allergy, and those with no de-escalation during the study period were excluded. Treatment recommendations for those with detected resistance markers were based on local susceptibility data and patient-specific variables. Secondary outcomes included days of therapy (DOT) of target narrow-spectrum agents (first to third generation cephalosporins, aminopenicillins), carbapenems, and non-carbapenem anti-Pseudomonal (NCAP) beta-lactams (ceftazidime, cefepime, piperacillin-tazobactam, aztreonam), treatment failure, and length of hospital stay.

Results

These results are from an interim analysis assessing patients between January 1 and September 30, 2018 (pre) and January 1 to March 31, 2019 (post). A total of 12,893 cultures were evaluated during the retrospective study period and 41 met criteria for inclusion. In the prospective group, 2,238 cultures were assessed and 12 were included. Baseline characteristics were similar between study groups (See *Table 2*). *E. coli* comprised the majority in each group. Mean time to de-escalation was 74.6 hours and 50 hours in the pre- and post-intervention groups, respectively [p=0.139] (See *Figure 1*). An increase in DOT of target agents [p=0.48] and NCAP beta-lactams [p=0.25] and decrease in carbapenem DOT [p=0.41] was noted. Treatment failure [p=0.174] and length of hospital stay [p=0.4] were similar in both groups (See *Table 3*).

Table 2: Baseline characteristics

Characteristic	Retrospective (n=41)	Prospective (n=12)	P-value
Mean age (SD), years	65.9 (16.9)	74.5 [18.9]	0.07
Male; n (%)	16 (39)	4 (33)	0.72
E. coli; n (%)	35 (85.3)	9 (75)	0.4
K. pneumoniae; n (%)	6 (14.6)	3 (25)	0.4
Risk factors for resistant pathogen; n (%)			
Presence of indwelling catheter	8 (19.5)	1 (8.3)	0.67
Dialysis	4 (7.8)	0 (0)	N/A
Diabetes	15 (36.6)	5 (41.6)	0.75
IVDA	0 (0)	0 (0)	1
Immunocompromised	7 (17)	1 (8.3)	0.67
Mean time to identification – RDT; hours (SD)	23.7 (9)	28.9 (12.8)	0.06
Mean time to identification – C&S; hours (SD)	72.2 (14.9)	74.3 (13)	0.33
Mean time to initial antibiotic therapy; hours (SD)	19.6 (28.6)	14.1 (13.2)	0.26

Figure 1: Primary outcome – Average time to de-escalation

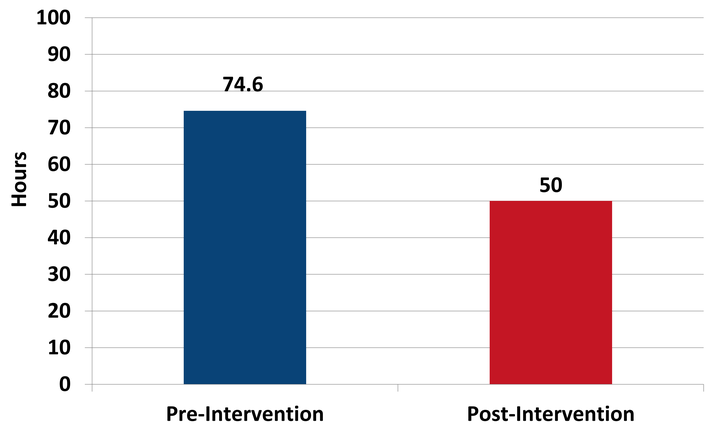

Table 3: Secondary outcomes

Outcome	Pre-intervention (n=41)	Post-intervention (n=12)	P-value
DOT per 1,000 patients days			
Target agents	5.19	5.25	0.48
NCAP β-lactam	1.73	2.33	0.25
Carbapenem	1.29	1.08	0.41
Length of stay; days	10.9	11.9	0.4
Treatment failure; n	2	2	0.17

Discussion

The results of the study support rapid de-escalation to target agents such as ceftriaxone in patients with *E. coli* or *K. pneumoniae* bacteremia with no identified resistance markers. Study limitations include protocol compliance (estimated at 60%) and Stewardship Team availability. Limitations affecting practice adoption included evaluation of select Gram-negative pathogens and local resistance patterns.

Conclusion

Appreciation of NPVs and utilization of pharmacist intervention allowed for early de-escalation of empiric therapy in patients with Gram-negative bacteremia. We plan to continue NPV assessment of other mono- and polymicrobial Gram-negative bacteremia and reinforce education to improve protocol compliance.

The authors of this study have no conflict of interest to disclose.

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