Impact of Diagnostic and Antimicrobial Stewardship on Time-to-Appropriate Therapy and Clinical Outcomes in Multi-Drug Resistant *Pseudomonas* Infections

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BACKGROUND

- Timely effective therapy in multi-drug resistant (MDR) *Pseudomonas* (PsA) species infections has a direct impact on patient survival.
- In recent years, new treatment options, such as the novel beta-lactam/beta-lactamase inhibitors (BL/BLIs) have become available to combat these infections including Ceftolozane-tazobactam (C/T) and Ceftazidime-avibactam (C/A)
- Studies have shown delays in time-to-appropriate therapy (TAP) in utilization of BL/BLIs for carbapenem-resistant Gram-negative infections is associated with poor clinical outcomes.
- In 1/2019, we implemented reflex testing algorithms for faster identification alongside active antimicrobial stewardship (AMS) team intervention in order to improve clinical outcomes by decreasing TAP.

OBJECTIVES

- To determine the impact of early diagnostics and AMS on TAP and clinical outcomes of patients with MDR PsA infections utilizing the novel BL/BLIs.
- **Primary Outcome**:
  - Time-to-appropriate therapy (TAP)
- **Secondary Outcomes**:
  - Time from index culture to final susceptibilities
  - 30-day inpatient mortality
  - Hospital length of stay (LOS)
- **Safety Outcome**
  - Incidence of acute kidney injury (AKI)

METHODS

- Single center, retrospective cohort chart review study of adult patients ≥ 18 years old
  - Pre-AMS: 1/2018 to 12/2018; Post-AMS: 1/2019 to 12/2019
- Included patients who received at least 72 hours of C/A or C/T
- AMS intervention encompassed:
  - Implementation of automatic reflex algorithms (Figure 1)
  - Real-time pharmacist-driven antimicrobial optimization
  - Infection control notification and isolation initiation
- Meropenem non-susceptibility defined using CLSI M100 breakpoints
- Descriptive statistics and chi-square analysis for comparison. *P* value of <0.05 was considered statistically significant.

METHODS

FIGURE 1: AMS Intervention

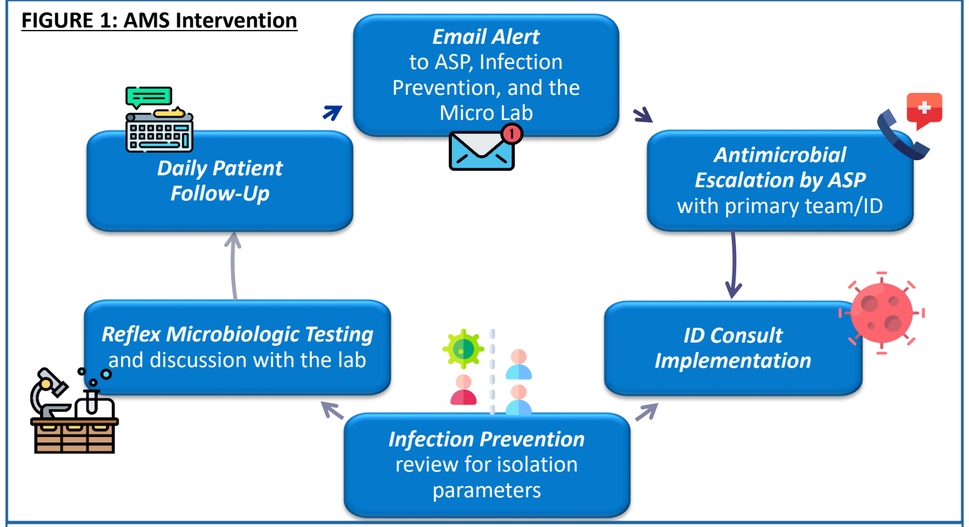
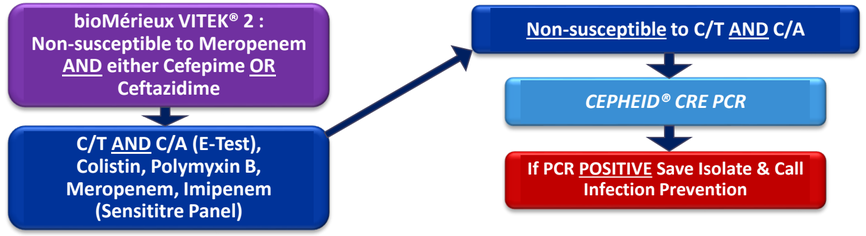


FIGURE 2: Reflex Testing Criteria for MDR PsA from Any Source



RESULTS

TABLE 1: Baseline Characteristics

Patient & Therapy Characteristics	Pre-AMS (n=36)	Post-AMS (n=40)	p-value
Age, median (IQR)	60 (38-67)	47 (37-70)	0.58
Male gender, n (%)	23 (64%)	31 (78%)	0.22
ICU at time of index culture, n (%)	20 (56%)	20 (50%)	0.65
APACHE II score, median (IQR)	14 (14-26)	20 (17-26)	0.60
Solid Organ Transplant, n (%)	14 (39%)	9 (23%)	0.14
Empiric use of BLBLI, n (%)	20 (56%)	25 (63%)	0.64
Concomitant antibiotic[a], n (%)	28 (78%)	21 (53%)	**0.03**

[a]Receipt of concomitant antibiotic with Gram-negative coverage

- Carbapenemases were identified among three isolates (VIM = 2; KPC = 1).
- Most common infections were pneumonia (56.6%) and bacteremia (18.4%).

RESULTS

TABLE 2: Isolate Susceptibilities

	Drug tested, # Susceptible of all isolates for both groups							
	AG	TIG	LEV	ATM	TZP	TMP/SMX	FEP/CAZ	PB/CST
Pseudomonas spp.	59	--	6	3	2	--	4	34

Abbreviations: AG, aminoglycoside; ATM, aztreonam; CAZ, ceftazidime; CST, colistin; FEP, cefepime; LEV, levofloxacin; PB, polymixin b; TIP, tigecycline; TMP/SMX, sulfamethoxazole-trimethoprim; TZP, piperacillin-tazobactam

TABLE 3: Clinical & Safety Outcomes

Clinical and Therapy Outcomes	Pre-AMS (n=36)	Post-AMS (n=40)	Odds Ratio (95% CI)	p-value
TAP (hours), median (IQR)	120 (83-165)	76 (51-101)	--	**0.003**
Time from index culture to final susceptibilities (hours), median (IQR)	122 (95-140)	90 (72-100)	--	**<0.001**
30-day mortality, n (%)	8 (22%)	8 (20%)	1.62 (0.45-5.79)	1.000
Hospital LOS (days), median (IQR)	26 (12-59)	19 (13-37)	--	0.330
Beta-lactam dose appropriate, n (%)	26 (72%)	35 (88%)	--	0.148
Safety Outcomes	**Pre-AMS (n=36)**	**Post-AMS (n=40)**	**Odds Ratio (95% CI)**	**p-value**
Acute kidney injury, n (%)	10 (28%)	10 (25%)	0.87 (0.31-2.41)	0.392

CONCLUSIONS

- Our study identified a **decrease in TAP** in MDR PsA infections and a trend toward decreased LOS by implementing diagnostic and AMS initiatives.
- As a result of this algorithm and AMS intervention, our institution has seen an increase in appropriate utilization of C/A and C/T.
  - Polymyxin B and aminoglycoside use **decreased** from 72% in the pre-AMS group to 42% in the post-AMS group without a difference in outcomes
- Our study also emphasizes the importance of **multi-disciplinary collaboration** among AMS pharmacists, microbiology, and ID physicians
- In an adequately powered study, our intervention could impact patient survival through timely initiation of effective therapy with novel BL/BLIs.
  - Limitations to the study included the sample size in order to predict statistical significance, as well as AMS coverage that was absent on weekends and overnight

REFERENCES

- Lodise TP Jr, Patel N, Kwa A, et al. Predictors of 30-day mortality among patients with Pseudomonas aeruginosa bloodstream infections: impact of delayed appropriate antibiotic selection. Antimicrob Agents Chemother 2007; 51:3510-5
- Gallagher JC, Satlin MJ, Elabor A, et al. Ceftolozane-Tazobactam for the Treatment of Multidrug-Resistant Pseudomonas aeruginosa Infections: A Multicenter Study. *Open Forum Infect Dis*. 2018;5(11). doi:10.1093/ofid/ofy