Traditional vs. Alternative Agents in Patients with Lower Respiratory Tract Infections Caused by Carbapenem-Resistant *P. aeruginosa* Susceptible to Traditional Agents

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Background

- The rise of antimicrobial resistance across the world remains a threat to human health.
- In 2019, the Centers for Disease Control and Prevention (CDC) reported 32,600 cases of multidrug-resistant (MDR) *P. aeruginosa* in hospitalized patients resulted in 2,700 deaths in 2017.[1]
- According to IDSA, for infections caused by carbapenem-resistant *P. aeruginosa* (CRPA) susceptible to traditional β-lactams, the administration of a traditional agent as high-dose extended-infusion therapy is suggested, after antibiotic susceptibility testing results are confirmed.[2]
- However, comparative effectiveness studies to guide treatment decisions for infections caused by carbapenem-resistant *P. aeruginosa* (CRPA) susceptible to traditional agents (non-carbapenem β-lactams and fluoroquinolones) are unavailable.[2]
- This study aims to compare clinical outcomes between patients treated with traditional and alternative treatment regimens for lower respiratory tract infection (LRTI) caused by CRPA that remain susceptible to traditional agents.

Methods

- Multi-center, retrospective cohort from January 2016 to December 2019 conducted at two major teaching health-systems in Michigan that comprise most hospitals located within the Detroit-area.
- We included adults with CRPA (resistant to ≥ 1 carbapenem; meropenem or imipenem) that were susceptible to ≥1 traditional agent (piperacillin-tazobactam, cefepime, ceftazidime, ciprofloxacin, or aztreonam) by CLSI breakpoints isolated from an LRTI sample.
- LRTIs were defined per CDC/ NHSN definitions plus cultures positive for CRPA.[3]
- All other antibiotics used to treat the CRPA infection were considered alternative agents.
- We excluded patients who were pregnant, those with known colonization, cystic fibrosis, or who expired ≤24 hours after antibiotic receipt.
- Primary outcome was 30-day mortality and secondary outcomes included 30-day readmission and 30-day recurrence.

Results

Table 1. Baseline Demographics

Characteristics	Alternative Therapy (n=35)	Traditional Therapy (n=53)	P value
Demographics			
• Age in years, median (IQR)	62 (18.0)	61 (22)	.881
• Age over 60 years, n (%)	18 (51.4)	28 (52.8)	.897
• Male sex, n (%)	20 (57.1)	37 (69.8)	.223
• BMI, median (IQR)	24 (14.0)	24 (9.8)	.609
Race, n (%)			
• African American	17 (48.6)	35 (66.0)	.103
• Caucasian	15 (42.9)	13 (24.5)	.071
• Hispanic	0 (0.0)	1 (1.9)	.414
• Other/unknown	3 (8.6)	4 (7.5)	.862
Severity of illness factors			
• SOFA score, median (IQR)	6 (8.0)	6 (4.0)	.520
• APACHE II score, median (IQR)	24 (8.0)	25 (10.0)	.550
• CCI, median (IQR)	4.0 (5.0)	4.0 (4.5)	.874
Co-morbid conditions			
• COPD	16 (45.7)	17 (32.1)	.196
• Moderate to severe CKD	8 (22.9)	16 (30.2)	.450
• Chronic dialysis	4 (11.4)	6 (11.3)	.988
• MI	3 (8.6)	3 (5.7)	.679
• PVD	1 (2.9)	6 (11.3)	.151
• HF	11 (31.4)	14 (26.4)	.610
• HIV	1 (2.9)	0 (0.0)	.398
• CVD	7 (20.0)	14 (26.4)	.490
• Dementia	3 (8.6)	2 (3.8)	.341
• Asthma	2 (5.7)	6 (11.3)	.469
• Connective tissue disease	2 (5.7)	5 (9.4)	.698
• Mild liver disease	0 (0.0)	3 (5.7)	.273
• Diabetes (no end-organ damage)	7 (20.0)	6 (11.3)	.261
• Diabetes (with end-organ damage)	8 (22.9)	13 (24.5)	.857
• Hemiplegia	5 (14.3)	5 (9.4)	.483
• Tumor without metastasis	2 (5.7)	2 (3.8)	1.000
• Tumor with metastasis	3 (8.6)	4 (7.5)	1.000
• IV drug use	0 (0.0)	3 (5.7)	.273
Immunosuppression factors			
• Neutropenia	2 (5.7)	8 (15.1)	.304
• Chemotherapy within 90 days*	1 (2.9)	4 (7.5)	.644
• High dose corticosteroids	0 (0.0)	1 (1.9)	1.000
MDR risk factors			
• Antibiotics within 90 days*	22 (62.9)	32 (60.4)	.815
• Hospitalization within 90 days*	18 (51.4)	34 (64.2)	.235
• Admitted from LTC facility	13 (37.1)	16 (30.2)	.497
• Surgery within 30 days*	3 (8.6)	3 (5.7)	.596

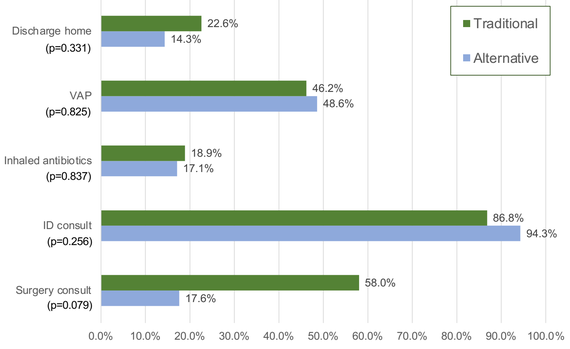
Abbreviations: COPD, chronic obstructive pulmonary disorder; CKD, chronic kidney disease; moderate to severe CKD, KDOQI CKD Stage III-V or GFR < 60 ml/min or on chronic dialysis; MI, myocardial infarction; PVD, peripheral vascular disease; HF, heart failure; CVD, cerebrovascular disease; HIV, human immunodeficiency virus; CCI, Charlson comorbidity index; BMI, body mass index; Mild liver disease, chronic hepatitis without cirrhosis.
**From time of index culture collection.*

Table 2. Susceptibility Characteristics

Characteristics	Traditional Therapy (n=53)*	Alternative Therapy (n=35)*	P value
Isolate Susceptibility, n (%)			
• Cefepime-S	24 (45.3)	17 (50.0)	.797
• Piperacillin-tazobactam-S	18 (35.3)	11 (33.3)	.897
• Ciprofloxacin-S	9 (22.5)	5 (20.0)	.848
• Aztreonam-S	7 (17.9)	5 (20.8)	.816
• Ceftazidime-S	24 (60.0)	17 (68.0)	.758

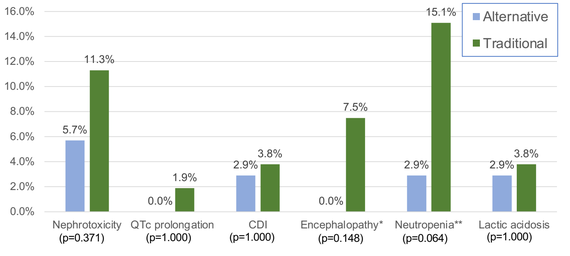
**Of those patients with susceptibility information available. Abbreviations: S, susceptible per CLSI guidelines.[4]*

Figure 1. Comparison of Clinical Characteristics



Abbreviations: VAP, ventilator-associated pneumonia; ID, infectious diseases.

Figure 2. Safety Profile Comparisons



*Abbreviations: CDI, Clostridioides difficile infection. *altered mental status, somnolence, or new onset seizures. **ANC decrease to < 1500 cells/mm3; or 50% decrease in ANC if baseline ANC < 1500 cells/mm3 from initiation of antibiotic.*

Results

- In total, 88 patients, 'traditional' treatment (n=53) and 'alternative' treatment (n=35), were included from 2 institutions in Detroit, MI, USA: median(IQR) age 62(19.5) years, 64.8% male, and 59.1% African American.
- Median(IQR) APACHE II and Charlson Comorbidity index scores were 24(10) and 4(5), respectively.
- Most patients received traditional therapy (n=53), most commonly with cefepime (62.3%) or piperacillin-tazobactam (41.5%). Of those, extended infusion was utilized in the majority of patients, 57.6% and 54.5%, respectively.
- While 35 (39.8%) were treated with alternative agents, most commonly ceftolozane-tazobactam (62.9%) or an aminoglycoside (28.6%) alone or in combination.
- Thirty-day mortality was not significantly different between traditional and alternative therapy groups (18.9% and 11.4%), respectively (p=.392).
- There was no significant difference between 30-day recurrence (17.0% and 20.0%) or 30-day readmission (22.6% and 17.1%) between groups.

Conclusion

- Clinical outcomes did not differ significantly between patients receiving traditional vs. alternative agents for LRTI caused by CRPA susceptible to traditional agents.
- Traditional agents may be considered for these infections.
- Further comparative studies are needed to guide treatment decisions for CRPA.
- Our results will help to optimize treatment approach and improve patient outcomes for this population.

References

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Disclosures

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