Comparison of Colistin Non-Susceptible *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* Isolates in an Inner City Hospital

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Abstract

Background: The prevalence of infections due to colistin non-susceptible (CNS) gram-negative bacilli is increasing worldwide. We have had an increase of CNS *Klebsiella pneumoniae* (KP) and *Pseudomonas aeruginosa* (PA) isolates in our inner city medical center and have noted differences in patient factors and therapies.

Methods: Adult patients with infection or colonization due to CNS KP and/or PA (colistin MIC >2 mcg/mL) within a 6.5 year period were identified for inclusion in a retrospective study. Patient, microbiological, treatment, and outcome data parameters were collected from the hospital electronic medical record. The epidemiology and treatment outcomes of patients with cultures positive for CNS KP and PA were evaluated and compared using descriptive and univariate analysis.

Results: A total of 116 CNS isolates were included in the study – 69 KP isolates (59%) and 47 PA isolates (41%). The median colistin MIC was 6 µg/mL for CNS KP isolates and 4 µg/mL for CNS PA isolates. CNS PA was most commonly isolated from respiratory specimens (60%), while the majority of CNS KP (47%) was isolated from a urinary source. CNS KP bacteremia was observed in 18% of the study cohort, but no patients had CNS PA isolated from blood cultures. A comparable number of antimicrobials were used in both groups (mean of 2 in KP group vs. 1.9 in PA group). 78% of patients with CNS PA infection received appropriate antimicrobial therapy compared to only 59% of the CNS KP subgroup. Antibiotic treatment regimens most frequently included carbapenems, aminoglycosides and tigecycline (for KP isolates). 33% of patients in the KP group received colistin within the preceding year versus 11% in the PA group. Hospital mortality rates were similar between the 2 groups (38% in KP group vs. 40% in PA group).

Conclusion: KP isolates had higher colistin MICs and were more likely to be associated with urinary tract infections compared to CNS PA, which were commonly associated with respiratory tract infections. Combination antibiotic regimens, including carbapenems and aminoglycosides, were used to treat infections in both subgroups. Mortality rates were high (over 30%) in patients with CNS KP and PA infections.

Introduction

- Antibiotic resistance among gram-negative bacteria is an increasing public health concern, with significant negative consequences on patient outcomes and healthcare expenditures.
- Although most multi-drug resistant gram-negative pathogens have been susceptible to polymyxin antibiotics historically, resistance to this antibiotic class has been observed.
- At University Hospital, a growing incidence of colistin non-susceptible (CNS) gram-negative infections has been noted, mostly commonly resulting from *Klebsiella pneumoniae* (KP) and *Pseudomonas aeruginosa* (PA).
- Differences in management and outcomes of infections from CNS KP and PA have not been thoroughly evaluated.

Methods

- Retrospective chart review of all patients admitted to University Hospital between March 2007 and March 2014 with at least 1 colistin-non-susceptible KP and/or PA isolate
  - First colistin-non-susceptible isolate per bacterial species and culture site for each patient admission included in analysis
  - Colistin non-susceptible defined as MIC > 2 mcg/mL
  - Selective, reflexive colistin susceptibility testing conducted based on susceptibility results of isolated pathogen
- Approval from hospital's Institutional Review Board obtained
- Data collection included:
  - Patient demographics
  - Culture and susceptibility results
  - Systemic antimicrobial therapy
  - Prior exposure to colistin
  - Survival to hospital discharge
- Data analyzed using descriptive statistics

Objective

- To evaluate and compare the clinical presentation, management strategies and treatment outcomes of patients with colistin-non-susceptible *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* admitted to University Hospital

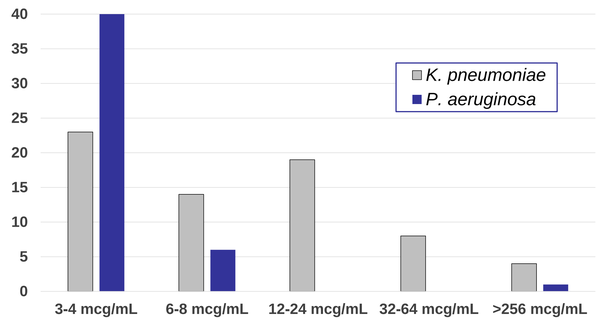


Figure 1. Distribution of Colistin MICs Among Study Isolates

Results

Table 1. Patient Demographics and Culture Results

Variable	*K. pneumoniae* Isolates	*P. aeruginosa* Isolates
Number of isolates identified	69	47
Age, mean years (range)	56.9 (12 - 90)	51.5 (5 - 92)
Gender, n (%)		
Male	32 (46.4)	19 (40.4)
Female	37 (53.6)	28 (59.6)
Race/ethnicity, n (%)		
African American	34 (49.3)	31 (66)
White/Hispanic	15 (21.7)	9 (19.1)
White/non-Hispanic	13 (18.8)	6 (12.8)
Other	7 (10.1)	1 (2.1)
Colistin MIC, median mcg/mL	6	4
Colistin use within prior 1 year, n (%)	23 (33.3)	5 (10.6)
Site of positive culture for colistin-non-susceptible gram-negative, n (%)		
Blood	12 (17.4)	0
Respiratory	18 (26.1)	28 (59.6)
Urine	32 (46.4)	9 (19.1)
Intra-abdominal	4 (5.8)	4 (8.5)
Other	3 (4.3)	6 (12.8)

Table 2. Patient Outcomes

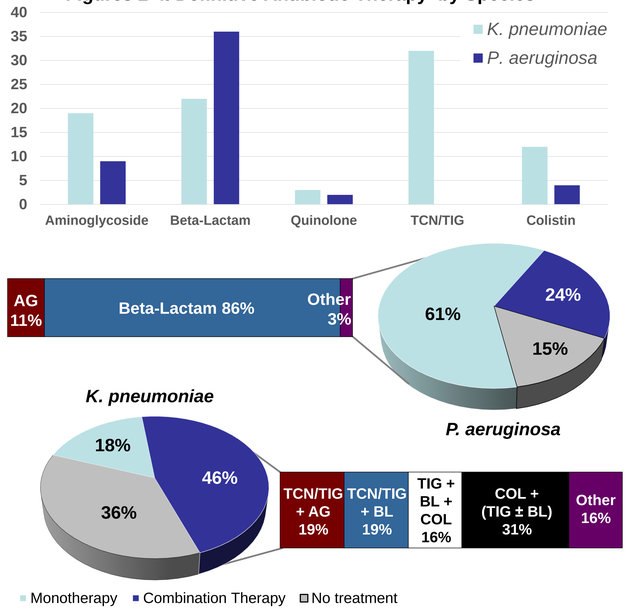
Variable	*K. pneumoniae* Isolates	*P. aeruginosa* Isolates
Duration of hospital stay, median days (range)	22 (2 – 198)	26 (1 – 572)
Survival to hospital discharge, n (%)	43 (62.3)	28 (59.6)

Table 3. Susceptibility Profiles of Organisms Isolated (% Susceptible)

Organism	AMK	AZT	CEF	CTZ	GEN	LEV	MER	P/T	TCN	TIG	T/S
KP isolates	20	1	1	3	49	4	7	3	32	77	3
PA isolates	77	23	32	43	36	21	17	55	-	-	-

Abbreviations: AG: aminoglycoside; AMK: amikacin; AZT: aztreonam; BL: beta-lactam; CEF: cefepime; COL: colistin; CTZ: ceftazidime; GEN: gentamicin; LEV: levofloxacin; MER: meropenem; P/T: piperacillin/tazobactam; TCN: tetracycline; TIG: tigecycline; T/S: trimethoprim/ sulfamethoxazole

Figures 2-4. Definitive Antibiotic Therapy by Species



Conclusion

- Colistin non-susceptibility has been identified in *K. pneumoniae* and *P. aeruginosa* isolates from University Hospital.
- KP isolates had higher colistin MICs and were more frequently found from a genitourinary source, but were associated with clinical outcomes similar to PA isolates.
- Various antibiotic regimens were used to treat infections due to colistin-non-susceptible bacteria. Monotherapy with a beta-lactam agent was most commonly used to treat CNS PA isolates compared to tetracycline/tigecycline-containing combination regimens for CNS KP isolates.
- Additional studies are needed to further elucidate the differences between CNS KP and PA isolates.