Uptake in newly approved antibiotics in patients with Carbapenem Resistant Enterobacteriaceae (CRE) infections

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Background[1,2]

- CRE is classified as an "urgent threat" to public health
- Historically, colistin and tigecycline had been considered the drugs of choice for CRE infections, along with agents such as aminoglycosides and carbapenems for adjunctive therapy
- FDA approval of ceftazidime-avibactam in 2015, meropenem-vaborbactam in 2017, and plazomicin in 2018 has expanded treatment options

Study Objective:

- To assess trends in CRE treatment for "new" antibiotics (ceftazidime-avibactam, meropenem-vaborbactam and plazomicin) in the VA setting as compared with other antibiotics with CRE activity.

Methods

Study Design:

- Retrospective cohort study using the National VA Corporate Data Warehouse
  - 134 VA facilities were included
- Inclusion Criteria:
  - Adult patients (18+) treated at any VA facility from 2012 to 2018
  - Positive culture for CRE
  - Received at least 24 hours of specified anti-CRE treatment within 2 days before to 5 days after the date of the positive CRE culture
- Additional data collected by manual review of the electronic health record
- Additional analysis conducted on Blood stream infection (BSI) group vs combined group (Non-BSI)

Definitions:

- "New antibiotics": ceftazidime-avibactam, meropenem-vaborbactam and plazomicin[3]
- CRE: *E. coli*, *Klebsiella* spp., or *Enterobacter* spp. isolates that were either resistant to doripenem, imipenem, or meropenem
- Combined group (Non-BSI): Respiratory, urinary, or other cultures

Statistical Analysis:

- Categorical data was assessed with a Fisher's exact test or Chi-square test
- Trends test and logistic regression determined changes in CRE treatment over time
- SAS version 9.4 (Cary, NC) was used for data and statistical analyses

Results

Table 1: Specimen Type

Specimen Type	N (%)
Urine (Non-BSI)	4744 (61.1%)
Blood	724 (9.3%)
Respiratory (Non-BSI)	1220 (15.7%)

Table 2: Demographics

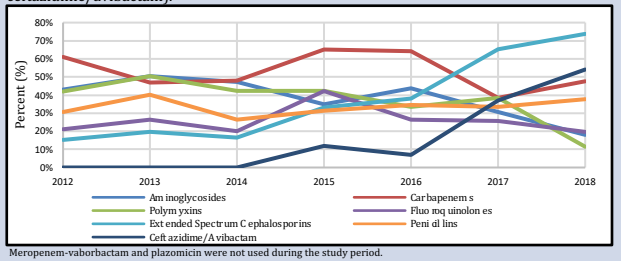
Variable	Overall (n=7766)	BSI (n=724)	Non-BSI (n=7024)	p-value
Age (mean, std)	71.4 (11.9)	71.5 (11.8)	70.4 (12.1)	0.0163
Charlson Comorbidity Index (mean)	3.6	3.6	3.6	0.95
Gagne Index (mean)	11.5	12.7	11.36	0.16
White (Race)	3350 (43.1%)	229 (31.6%)	3121 (44.4%)	<0.0001
Black (Race)	1831 (23.6%)	172 (23.7%)	1659 (23.6%)	0.0013
Hispanic (Race)	2235 (28.8%)	280 (38.6%)	1955 (27.8%)	<0.0001

Table 3: Frequency of CRE Cultures by Year

Year	Total	BSI	Non-BSI
2012	1323 (17%)	112 (8.5%)	1211 (91.5%)
2013	1273 (16.4%)	122 (9.6%)	1151 (90.4%)
2014	1144 (14.7%)	143 (12.5%)	1001 (87.5%)
2015	1174 (15.1%)	111 (9.5%)	1063 (90.5%)
2016	1161 (14.9%)	90 (7.8%)	1071 (92.2%)
2017	1003 (12.9%)	79 (7.9%)	924 (92.1%)
2018	689 (8.9%)	67 (9.7%)	622 (90.3%)

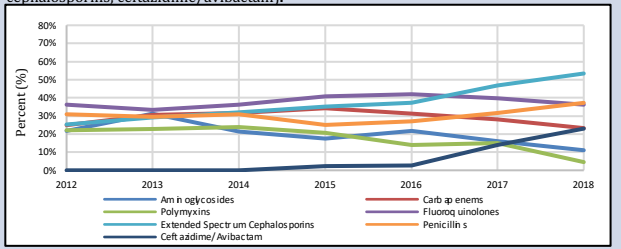
2014 p-value:0.011

Figure 1: Trends in CRE Antibiotic Use in the BSI Culture Group (p<0.01 for decrease in aminoglycosides and polymyxins; increases in extended spectrum cephalosporins and ceftazidime/avibactam).



Meropenem-vaborbactam and plazomicin were not used during the study period.

Figure 2: Trends in CRE Antibiotic Use in the Non-BSI Culture Group (p<0.0001 for decrease in aminoglycosides and polymyxins; increases in extended spectrum cephalosporins, ceftazidime/avibactam).



Discussion

- Regardless of culture source, aminoglycoside and polymyxin use decreased while ceftazidime/avibactam and extended spectrum cephalosporin use increased.
- The highest utilization for ceftazidime/avibactam was observed in 2018 for BSI (54%), which is still lower than the anticipated first line positioning estimates.[2]
- Increased utilization of extended spectrum cephalosporins was a surprising finding and could be due to empiric use prior to confirmed CRE cultures.

References

1. Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2013.
2. Clancy CJ, et al. Open Forum Infect. Dis. 2019; 6(8).
3. Infectious Diseases Society of America. CID. 2010;50:1081-823.

Conclusion

- Utilization of "older" agents such as aminoglycosides and polymyxin for the treatment of CRE infections is decreasing in VA patients.
- While the number of cultures positive for CRE decreased, utilization of ceftazidime-avibactam increased significantly over the study period.
- Antibiotics newly approved to treat CRE experienced uptake by clinicians.

Disclosures:

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