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Healthcare Facility-Associated *Clostridium difficile* Infection in Hospitalized Patients Receiving Intravenous Beta-Lactam Antibiotics in the Veterans Affairs Healthcare System

Brigid M. Wilson PhD[1], Federico Perez MD[1,2,3], Elie Saade MD[2] and Curtis J. Donskey MD[1,3]

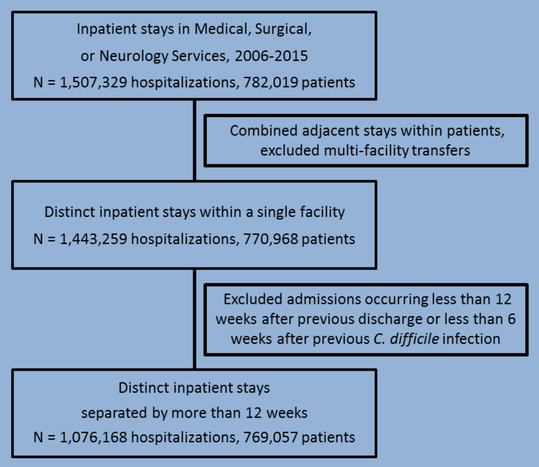
[1]Geriatric Research, Education and Clinical Center, Cleveland VA Medical Center; [2]Department of Medicine, University Hospitals Cleveland Medical Center, [3]Infectious Diseases Section, Cleveland VA Medical Center

Background

- Antibiotic exposure in the intestinal tract is the most important risk factor for *Clostridium difficile* infection (CDI)
- Oral administration of beta-lactamase enzymes such as SYN-004 (Synthetic Biologics, Inc) has been effective in eliminating the portion of intravenous beta-lactam antibiotics excreted into the intestinal tract, preserving the microbiota during therapy
- We examined patterns of use of beta-lactams and the relative frequency of healthcare facility-associated (HCFA)-CDI associated with them given alone or combined with other antibiotics

Methods

- Using nationwide databases, we identified systemic antibiotics administered for hospitalizations in the VHA from 2006-2015
- We identified CDI based on toxin/PCR/EIA test
- Rates of HCFA-CDI (cases per hospitalization) calculated for any antibiotic treatment and by selected beta-lactam and fluoroquinolone (FLQ) agents
- Additional risk factors for CDI assessed



Funding

Synthetic BIOLOGICS

Corresponding Author: curtis.donskey@va.gov

Results

Table 1. Percentage of hospitalizations associated with CDI, by antibiotic exposure

Antibiotics	N(%) hospitalizations	% CDI within 48 hours of admission	% CDI > 48 after admission <28 days after discharge
None	541893 (50%)	0.0%	0.1%
Antibiotics of interest	418050 (39%)	0.4%	1.3%
Other antibiotics	116221 (11%)	1.2%	0.9%

Figure 1. CDI in hospitalized patients receiving therapy with selected antibiotics

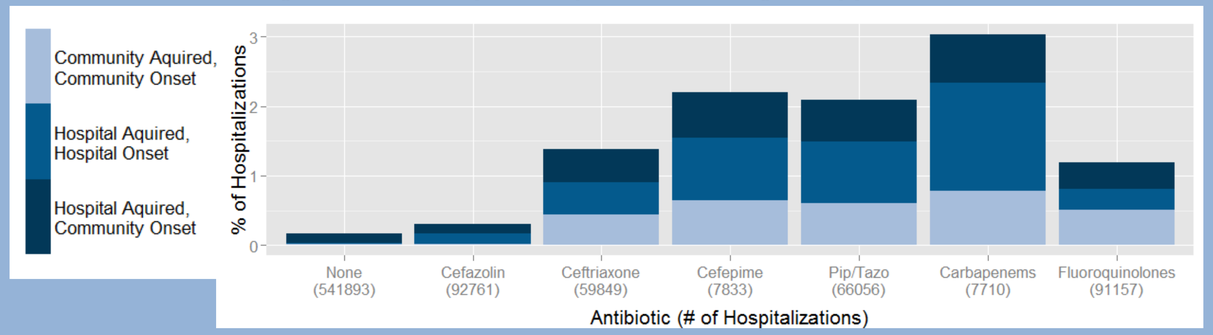


Figure 2. CDI in patients receiving selected antibiotics alone or in conjunction with other agents

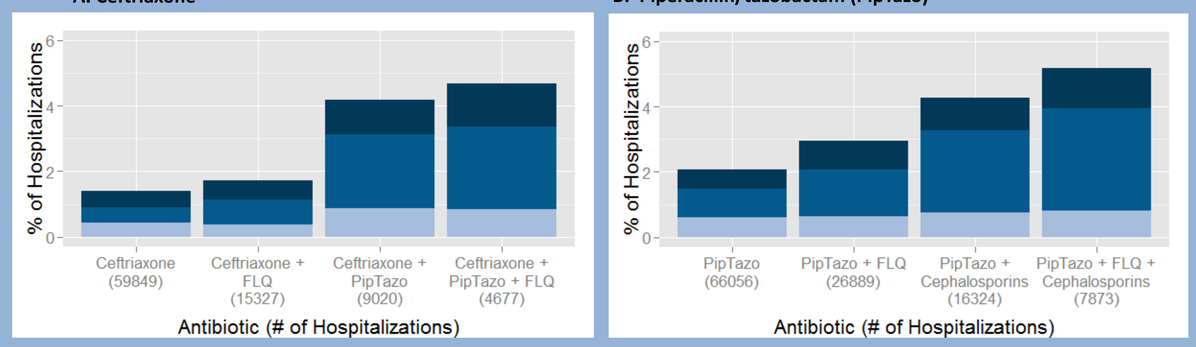


Figure 3. CDI by # of antibiotics and Braden score

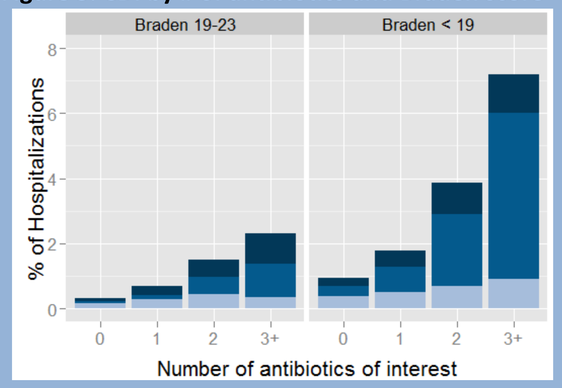


Figure 4. CDI in ceftriaxone-treated patients with or without additional risk factors

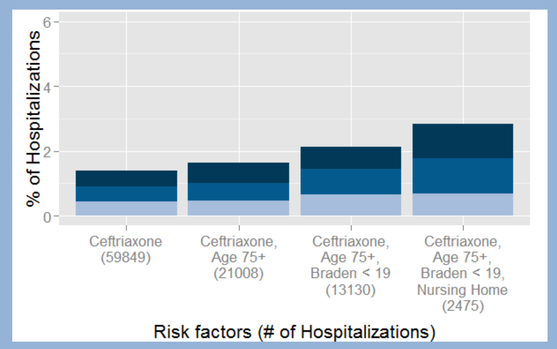


Table 2. Bivariate and multivariate analysis of risk factors for HCFA-CDI

Risk factor	Bivariate OR (95% CI)	Multivariate OR (95% CI)
Any antibiotics	8.7 (8.07, 9.37)	4.72 (4.36, 5.12)
Female	0.75 (0.67, 0.84)	1.11 (0.98, 1.25)
ICU	1.57 (1.46, 1.69)	1.04 (0.97, 1.13)
Prior outpatient antibiotics	1.1 (1.03, 1.17)	1.03 (0.97, 1.1)
Nursing home	4.11 (3.9, 4.34)	1.76 (1.66, 1.87)
Braden scale < 19	4.95 (4.68, 5.24)	1.79 (1.68, 1.9)
Charlson > 4	1.63 (1.56, 1.71)	1.22 (1.16, 1.28)
Length of stay > 4 days	7.32 (6.91, 7.77)	2.95 (2.76, 3.16)
Age 75+	1.55 (1.48, 1.63)	1.02 (0.96, 1.07)
Surgical admission	0.82 (0.77, 0.86)	0.79 (0.75, 0.84)
Creatinine > 1	1.49 (1.42, 1.56)	1.2 (1.14, 1.26)
Albumin > 3.5	0.21 (0.2, 0.23)	0.45 (0.42, 0.48)
Acid suppressants	2.3 (2.18, 2.42)	1.43 (1.35, 1.51)

NOTES: Braden scale is a tool for assessing pressure ulcer risk where scores <19 indicate increased risk; Charlson comorbidity index calculated from inpatient and outpatient ICD9 codes; univariate odds ratios generated using Mantel-Hanzel method; lab measures as the first after admission; multivariate odds ratios from a logistic model estimated in SAS 9.2 on hospitalizations with complete data.

Conclusions

- The beta-lactam antibiotics studied were prescribed in nearly a third of analyzed hospitalizations and were frequently associated with HCFA-CDI (>5,000 cases/year)
- Receipt of multiple antibiotics and non-antimicrobial factors may increase the risk for CDI in antibiotic-treated patients
- Interventions such as SYN-004 that prevent beta-lactam-induced disruption of the intestinal microbiota could reduce HCFA-CDI