Recurrence of Positive Cultures for Carbapenem-resistant Enterobacteriaceae (CRE) in Atlanta

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Background

- Duration of colonization with CRE after initial acquisition remains unclear
- Prior studies have shown that 48-78% of patients with a history of a positive CRE culture remain colonized for at least 3 months
- A history of clinical infection with CRE may increase the risk of subsequent prolonged colonization
- The impact of persistent colonization with CRE on the risk of future CRE infections and patient outcomes has not been studied
- We therefore assessed risk factors for recurrent CRE in patients with a history of a positive urine or sterile site culture and evaluated time to new positive culture
- Identification of factors that are predictive of recurrent infection may offer potential prevention targets

Objectives

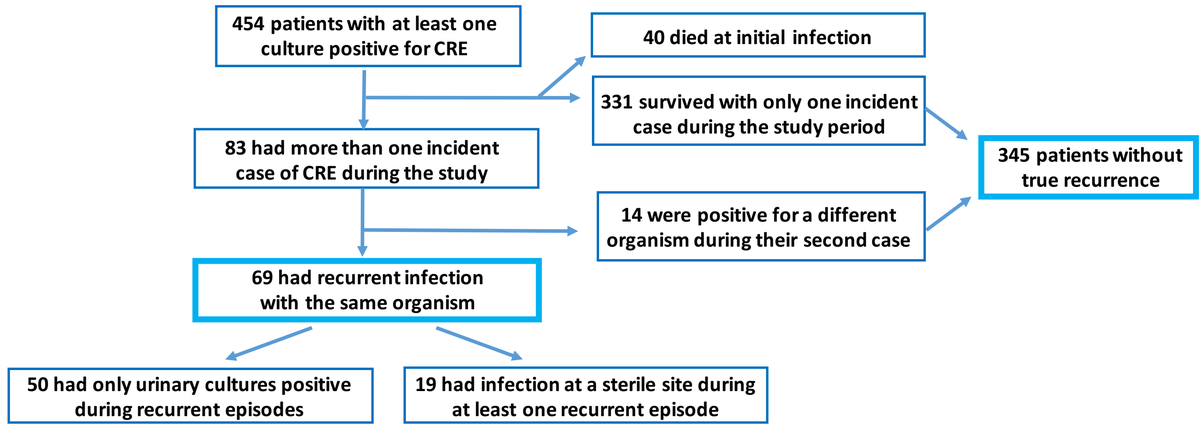
1. To compare baseline demographic characteristics of patients who had recurrent infection with CRE and those who survived without recurrence
2. To evaluate for differences in CRE risk factor prevalence between these two groups
3. To determine if particular risk factors are predictive of recurrent CRE infection after an initial positive culture

Methods

- Georgia Emerging Infections Program (EIP) conducts surveillance for incident CRE cases in the 8-county Atlanta metropolitan area
- CRE= carbapenem-nonsusceptible (excluding ertapenem); resistant to all tested 3rd generation cephalosporins
- Retrospective chart reviews performed for CRE cases identified from 8/2011-12/2014
- Incident case = first positive CRE culture in the urine or at a sterile site for an individual patient
- Patients considered to have recurrence with isolation of the same CRE organism more than 30 days later
- Mean number of recurrences, time to recurrence, and time from first to last positive culture assessed
- Prevalence of demographic and risk factors compared between patients with recurrence and those who survived without recurrence, with chi-square analysis for categorical variables and t-tests for continuous variables
- Risk factors assessed with univariable and multivariable logistic regression to evaluate predictors of a recurrent positive CRE culture

Results

Recurrent Positive Cultures in Patients with a History of CRE in Atlanta, 2011-2014



Comparison of Demographic Information and Risk Factor Prevalence in Patients With and Without CRE Recurrence

	Overall Number (%) N = 414	Recurrent Infection Number (%) N = 69	No Recurrence Number (%) N =345	p-value*
Race				
Caucasian	135 (32.6)	18 (26.1)	117 (33.9)	0.21
African-American	216 (52.2)	46 (66.7)	170 (49.3)	0.008
Organism				
Klebsiella pneumoniae	234 (56.5)	67 (97.1)	167 (48.4)	<0.0001
Escherichia coli	83 (20.0)	2 (2.9)	81 (23.5)	<0.0001
Enterobacter cloacae	57 (13.8)	0 (0)	57 (16.5)	0.0003
Enterobacter aerogenes	32 (7.7)	0 (0)	32 (9.3)	0.008
Klebsiella oxytoca	8 (1.9)	0 (0)	8 (2.3)	0.36
Hospitalized in the last year	244 (58.9)	56 (81.2)	188 (54.5)	<0.0001
Follow-up time (in days)	641.5 ±373.5	792.4 ±345.3	611.4 ±372.1	0.0002
Central venous catheter present	191 (46.1)	43 (62.3)	148 (42.9)	0.003
Urinary catheter present	191 (46.1)	43 (62.3)	148 (42.9)	0.003
Carbapenemase testing positive	54 (13.0)	16 (23.2)	38 (11.0)	0.006
Other indwelling device present	126 (30.4)	30 (43.5)	96 (27.8)	0.01
Immunocompromised	235 (56.8)	47 (68.1)	188 (54.5)	0.04
ICU stay after positive culture	77 (18.6)	19 (27.5)	58 (16.8)	0.04
Invasive infection	54 (13.0)	12 (17.4)	42 (12.2)	0.24
Hospitalized for ≥3 days	74 (17.9)	15 (21.7)	59 (17.1)	0.36
Surgery in the last year	101 (24.4)	17 (24.6)	84 (24.4)	0.96

Univariable and Multivariable Logistic Regression Analysis of Risk Factors For CRE Recurrence

	Crude Odds Ratio+	95% Confidence Interval	Adjusted Odds Ratio+	95% Confidence Interval
Hospitalized in the last year	3.60	1.90 – 6.82	3.04	1.58 – 5.85
Central venous catheter present	3.13	1.82 – 5.40	2.46	1.39– 4.34
Carbapenemase positive	2.42	1.26 – 4.66	---	---
Urinary catheter present	2.20	1.29 – 3.75	---	---
Other indwelling device present	2.00	1.17 – 3.39	---	---
Immunocompromised	1.78	1.03 – 3.09	---	---
Invasive infection	1.52	0.75 – 3.06	---	---
Any ICU stay	1.36	0.77 – 2.38	---	---
Hospitalized ≥ 3 days	1.35	0.71 – 2.55	---	---
Surgery in the last year	1.02	0.56 – 1.85	---	---
Follow-up time (in days)	1.001	1.001 – 1.002	1.001	1.000-1.002

Immunocompromised = patient history of diabetes, renal failure, cirrhosis or liver failure, hematologic malignancy, solid tumor malignancy, solid organ transplant, AIDS, or connective tissue disorder; Other indwelling device = tracheostomy, gastrostomy or NG tube, or nephrostomy.
*Chi-square tests performed to calculate p-values for comparisons of recurrent and non-recurrent groups with the exception of follow-up time, for which a t-test was utilized. +Univariable logistic regression was performed using each risk factor as the sole predictor of CRE recurrence for calculation of a crude odds ratio. Multivariable logistic regression was performed with backward selection using a significance level of p<0.05 to identify predictors of recurrent infection that remained significant; only significant adjusted odds ratios are listed in the table.

Results (continued)

~15% of patients with CRE had recurrent infection, with:

- Mean of 1.87 recurrent cases
- Mean time to first recurrence of 4.4 months
- Mean time from first to last positive culture of 8.3 months (range 1-36 months)

Discussion

- CRE recurrence seen over a prolonged time period, correlated with length of follow-up
- Implications for a potential need to extend duration of contact isolation and for selection of empiric antibiotic therapy in patients with a CRE history
- Potential for impact on CRE transmission in a variety of care settings, including LTCFs
- Need to further evaluate the role of antibiotic administration in CRE recurrence
- If effective methods for eradicating CRE colonization are identified, it may be beneficial to target them to patients at highest risk for recurrent infection

References

1. Reno J, Schenck C, Scott J, et al. Querying automated antibiotic susceptibility testing instruments: a novel population-based active surveillance method for multidrug-resistant gram-negative bacilli. *Infect Control Hosp Epidemiol* 2014;35(4):336-341.
2. Zimmerman FS, Assous MV, Bdolah-Abram T, Lachish T, Yinnon AM, Wiener-Well Y. Duration of carriage of carbapenem-resistant Enterobacteriaceae following hospital discharge. *American journal of infection control* 2013;41(3):190-194.
3. Feldman N, Adler A, Molshatzki N, et al. Gastrointestinal colonization by KPC-producing Klebsiella pneumoniae following hospital discharge: duration of carriage and risk factors for persistent carriage. *Clin Microbiol Infect* 2013;19(4):E190-196.
4. Trick WE, Weinstein RA, DeMarais PL, et al. Colonization of skilled-care facility residents with antimicrobial-resistant pathogens. *J Am Geriatr Soc* 2001;49(3):270-276.
5. Snitkin ES, Zelazny AM, Thomas PJ, et al. Tracking a hospital outbreak of carbapenem-resistant Klebsiella pneumoniae with whole-genome sequencing. *Sci Transl Med* 2012; 4(148):148ra116.
6. Lerner A, Adler A, Abu-Hanna J, Meitus I, Navon-Venezia S, Carmeli Y. Environmental contamination by carbapenem-resistant Enterobacteriaceae. *J Clin Microbiol* 2013;51(1):177-181.
7. Weber DJ, Rutala WA, Kanamori H, Gergen MF, Sickbert-Bennett EE. Carbapenem-resistant Enterobacteriaceae: frequency of hospital room contamination and survival on various inoculated surfaces. *Infection control and hospital epidemiology* 2015; 36(5):590-593.
8. Lerner A, Adler A, Abu-Hanna J, Cohen Percia S, Kazma Matalon M, Carmeli Y. Spread of KPC-producing carbapenem-resistant Enterobacteriaceae: the importance of super-spreaders and rectal KPC concentration. *Clin Microbiol Infect* 2015; 21(5):470 e471-477.
9. Ciobotaro P, Oved M, Nadir E, Bardenstein R, Zimhony O. An effective intervention to limit the spread of an epidemic carbapenem-resistant Klebsiella pneumoniae strain in an acute care setting: from theory to practice. *American journal of infection control* 2011; 39(8):671-677.
10. Guh A et al. Epidemiology and prevention of carbapenem-resistant Enterobacteriaceae in the United States. *Expert Rev. Anti Infect. Ther* 2014;12(5):565-580.
11. Trick WE, Lin MY, Cheng-Leidig R, et al. Electronic Public Health Registry of Extensively Drug-Resistant Organisms, Illinois, USA. *Emerging infectious diseases* 2015; 21(10):1725-1732.
12. Montassier E, Al-Ghalith GA, Ward T, et al. Pretreatment gut microbiome predicts chemotherapy-related bloodstream infection. *Genome Med* 2016; 8(1):49.
13. Dethlefsen L, Huse S, Sogin ML, Relman DA. The pervasive effects of an antibiotic on the human gut microbiota, as revealed by deep 16S rRNA sequencing. *PLoS Biol* 2008; 6(11):e280.
14. Halpin AL, de Man TJ, Kraft CS, et al. Intestinal microbiome disruption in patients in a long-term acute care hospital: A case for development of microbiome disruption indices to improve infection prevention. *American journal of infection control* 2016; 44(7):830-836.

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