Poster 1147

Carbapenem-Resistant Enterobacteriaceae (CRE) in a Pediatric Population: A Descriptive Analysis

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ABSTRACT

Background: The incidence of CRE in the US has been steadily rising since the first reported outbreak of carbapenem-resistant Klebsiella pneumoniae and Enterobacter species in 2003. Risk factors for CRE in adults have been well described, but data are lacking in pediatric populations.

Methods: A case-control study was performed among patients hospitalized at Children's National Medical Center between 8/2009 and 8/2011 for gastrointestinal (GI) complaints or underlying GI disease. Cases had one or more clinical or surveillance cultures confirmed positive for CRE by modified Hodge testing. Cases were individually matched to four control patients by age as defined by the American Academy of Pediatrics. Controls were randomly selected from patients without positive CRE cultures. Conditional logistic regression was conducted to identify independent risk factors for CRE, adjusted for underlying GI condition.

Results: Thirteen cases with CRE infection (46%) or colonization (54%) were identified. These patients ranged in age from 6 months to 18 years, with an average of 4.2 years. The most common CRE was *K. pneumoniae* (62%) followed by *Escherichia coli* (15%) and *Enterobacter cloacae* (15%). The majority (77%) of cases had GI disease. In the 12 months prior to onset of CRE, all cases had previous hospitalizations and 85% received three or more antibiotics. The most common sites of infection were intra-abdominal (39%) followed by urinary tract (31%). Analysis identified the following risk factors: 1) prior exposure to penicillin (Odds Ratio [OR]=44.2, p=0.002), 3rd generation cephalosporin (OR=14.8, p=0.012), carbapenem (OR=12.6, p=0.003), fluoroquinolone (OR=8.7, p=0.002) or trimethoprim/sulfamethoxazole (OR6.5, p=0.009); 2) prior colonization/infection history with a vancomycin resistant Enterococcus (OR=8.6, p=0.01) or an extended spectrum beta-lactamase (ESBL) producing Enterobacteriaceae family member (OR=9.5, p=0.007).

Conclusion: This study evaluated a large group of CRE colonized/infected pediatric gastroenterology patients and demonstrated that prior antibiotic exposure and a history of antibiotic resistant organisms are significant risk factors for CRE acquisition. Further studies are warranted to identify measures to ameliorate the risk of CRE.

INTRODUCTION

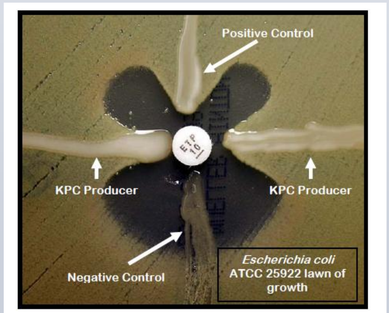
- Enterobacteriaceae are important pathogens in the setting of healthcare-associated infections.
  - Third generation cephalosporins have traditionally been effective therapy for these pathogens.
  - Carbapenems are reserved as an option for treatment of Enterobacteriaceae with ESBL production.
- Since the outbreak of carbapenem-resistant *K. pneumoniae* and *Enterobacter* species was first detected in Brooklyn, NY, USA in 2003, the incidence of CRE has increased.
- Published risk factors for CRE infection in adults include health care exposure and antimicrobials, however, data are lacking regarding the incidence of CRE in the pediatric population, as well as risk factors.
- Published data are limited to a few case reports, containing small numbers of clinical isolates, with minimal information regarding clinical presentation and risk factors for acquisition.

METHODS

•A 1:4 case-control study was conducted at Children's National Medical Center
•A case patient was defined as a patient with a CRE isolated from specimens collected between August 2009 and August 2011. The identity of a CRE was confirmed by the Modified Hodge Test (Figure 1).
• Four control patients for each case patient were randomly selected from patients of the same general age as case patients, who were treated during the same time period and who had no CRE identified.
•Medical records were reviewed to extract information on:
- Demographics
- Medical history and presentation
- Preceding hospitalization
- Preceding antimicrobial exposure
- Presence of foreign bodies, intravascular or other devices
- Administration of total parenteral nutrition
- Bacterial identification and susceptibility test results

•Descriptive statistical analysis and conditional logistic regression were performed to identify independent risk factors for CRE.

Figure 1. Modified Hodge Test



RESULTS

- The study identified 13 patients with CRE infection or colonization.
- Patient characteristics are shown in Table 1.
- Of the 13 CRE isolates, *K. pneumoniae* accounted for 61%, followed by *E. coli* (15%), and *Enterobacter cloacae* (15%).
- Most cases were considered colonization (54%) as opposed to true infection (46%) with CRE (Table 2).
- 77% had underlying gastrointestinal diseases.
- 77% had central venous catheters and /or gastrostomy tubes.
- All (100%) had a prior history of hospitalization.
- 85% received 3 or more antibiotics at the onset of CRE.
- Classes of antibiotics received Included: beta-lactams (100%), penicillins (100%), carbapenems (69%), aminoglycosides (77%), fluoroquinolones (61%), 3rd generation cephalosporins (61%), and folic acid antagonists (46%)

Table 1. Patient characteristics

Patient Characteristics	N	%
Age:		
<1 year	2	15%
1 year	4	31%
2-4 years	4	31%
5-11 years	2	15%
12-18 years	1	8%
Ethnicity:		
Black	9	69%
White	2	15%
Hispanic	2	15%
Underlying disease:		
Gastrointestinal	10	77%
Cardiovascular	1	8%
Transplantation	1	8%
None	1	8%

Table 2 . CRE site of isolation

CRE sites	N	%
Colonization		
Rectal swab	4	31%
GT drainage	3	23%
Total	**7**	**54%**
Infection:		
Blood culture	1	8%
Urine culture	3	23%
GT cellulitis	2	15%
Total	**6**	**46%**

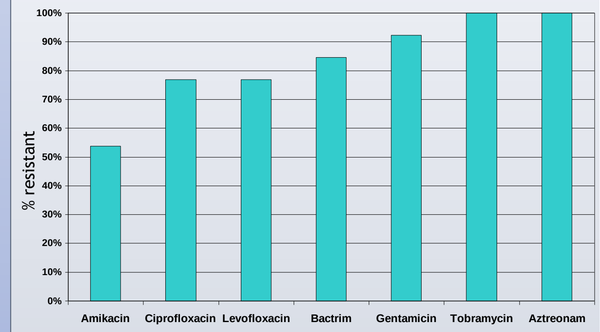
- 52 control patients were matched to individual case patients.
- Univariate analysis identified that exposure to antibiotics and prior history of resistant organisms significantly increased a patient's risk for acquiring CRE (Table 3).

Table 3 . Risk Factors

Risk factors	OR	p
Exposure to penicillins	44.2	0.002
Exposure to 3rd generation cephalosporins	14.8	0.012
Exposure to carbapenems	12.6	0.003
Exposure to fluoroquinolones	8.7	0.02
Exposure to folic acid antagonists	6.5	0.09
Prior history of VRE colonization/infection	8.6	0.01
Prior history of ESBL colonization or infection	9.5	0.007

- Antibiotic resistance patterns are shown in Figure 2.

Figure 2. Antimicrobial Resistance patterns for CRE isolates



CONCLUSIONS

- This study is the largest report of pediatric CRE to date.
- Similar to published risk factors for adults, prior hospitalization and exposure to multiple antibiotics are identified as common risk factors in children.
- In contrast to adults, residency in long term care facilities or intensive care units was not identified as a risk factor in this pediatric cohort with CRE.
- The majority of our study patients had underlying intra-abdominal disease, intravascular catheters, and/or gastrostomy tubes.
- Most cases were considered colonization and there was only one case of invasive infection.
- Identification of risk factors for CRE could assist in developing strategies to limit further emergence in the pediatric population.
- Active surveillance would assist in determining the true incidence in hospitalized pediatric patients and in guiding appropriate infection control measures.

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