Retrospective Cohort Study of *Clostridium difficile* Infections and Carbapenem Use in Fraser Health Acute Care Sites

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Background

- Clostridium difficile infection (CDI) is a significant source of morbidity and mortality in hospitalized patients.
- Antimicrobial therapy is associated with an increased risk of CDI.
- There is a gap in the literature on the comparative risk of CDI between broad spectrum antibiotics
- Disproportionally high and potentially inappropriate carbapenem use at certain Fraser sites may be associated with more CDI.

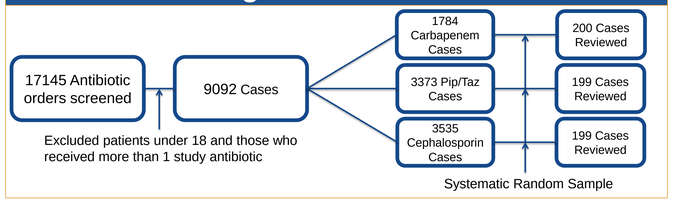
Objectives

- Primary: Compare the incidence of hospital acquired CDI associated with carbapenems, 3rd generation cephalosporins, and piperacillin/tazobactam.
  - CDI defined as 2 or more documented unformed or watery stools in 24 hours and positive toxin B stool assay. Confirmed by infection control.
  - Association defined as occurring within 6 weeks of antibiotic therapy.

Methods

- Retrospective chart review at Burnaby Hospital, Surrey Memorial Hospital, and Royal Columbian Hospital during April 1, 2012 to March 31, 2013.
- Patients identified via Meditech drug use records and split into three cohorts:
  - Meropenem and Imipenem
  - Ceftriaxone, Ceftazidime, and Cefotaxime
  - Piperacillin/tazobactam
- Data collection: Patient characteristics and outcomes gathered from electronic medical records.
- Inclusion: Inpatients with exposure to one of the above antibiotics.
- Exclusion: Patients under 18 years old and patients that received more than 1 of the above antibiotics during hospitalization.
- Power calculation: 2525 cases in each arm required to detect an OR of 1.4 with a baseline outcome rate of 5%.
- Convenience sample of 200 per arm.

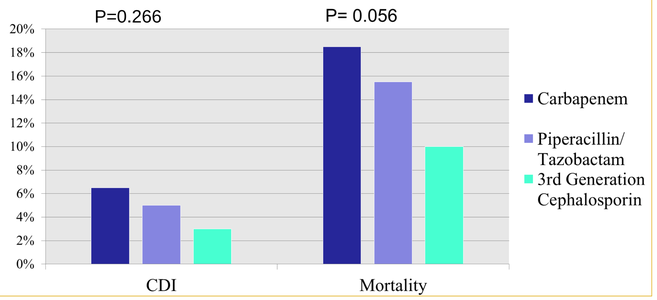
Patient Flow Diagram



Patient Characteristics

Variable	Carbapenem N=200	3rd Generation Cephalosporins N= 199	Piperacillin/ Tazobactam N=199	P value
Median Age (years)	73	68	69	0.048
Gender (male)	94 (47%)	88 (44%)	101(51%)	0.484
Median length of stay (days)	11	9	12	0.054
Median length of therapy (days)	5	5	6	0.571
Horn's Index (disease severity)	2.6	2.3	2.5	0.004
PPI or H2RA	128 (64%)	91 (46%)	123 (62%)	0.001
Received other antibiotic therapy	126 (63%)	122 (61%)	100 (50%)	0.018
Medical Ward Surgical Ward ICU	89.5% 8.5% 2.0%	93.5% 5.5% 1.0%	81.4% 16.1% 2.5%	

Results:



Odds Ratio for CDI

	Carbapenem Vs. Cephalosporin	Carbapenem Vs. Pip/Taz	Cephalosporin Vs. Pip/Taz
OR	2.22 (0.83-6.00)	1.31 (0.56-3.07)	0.58 (0.21-1.65)
P	0.102	0.527	0.307

Results of other studies

	Loo et al. 2005	Baxter et al. 2008	Pepin et al. 2005
Subjects	237 Cases 237 Controls	1142 Cases 3351 Controls	293 Cases 7421 Controls
Piperacillin/Tazobactam	1.2 (0.7-2.3)	1.23 (0.83-1.83)	1.88 (1.35-2.63)
Carbapenems	1.4 (0.3-6.3)	1.14 (0.6-2.14)	1.52 (0.79-2.94)
3rd Generation Cephalosporins	3.0 (1.4-6.8)	1.49 (1.15-1.93)	1.56 (1.15-2.39)

Available literature comparing risk of CDI for antibiotics vs. no exposure. 3rd generation cephalosporins significantly more CDI than no exposure, but not carbapenems. No comparisons were made between antibiotics.

Discussion

- Overall CDI rate of 5% similar to predicted.
- No difference found in incidence of CDI between any antibiotic arm.
- Patients who received carbapenems older and greater severity of illness.
- Trend for higher CDI and all cause mortality with carbapenems, but unable to account for baseline differences.
- Results consistent with prior research that development CDI is related to age, and underlying disease severity.

Strengths

- CDI cases clinically and microbiologically confirmed by infection control.
- Cohort design allows direct comparison between antibiotics.
- Able to qualitatively discuss differences in baseline risk factors.

Limitations

- Retrospective, non-randomized data with unblinded collection.
- Did not meet required sample size; unable to perform planned regression.
- Unable to account for outpatient antibiotic exposure.

Conclusions

- We did not find a significant difference in rate of CDI associated with carbapenems, piperacillin/tazobactam, or 3rd generation cephalosporins.
- Future studies with larger sample size and multiple regression analysis to account for baseline differences are required.

References
1. Loo VG, Poirier L, Miller MA, Oughton M, Libman MD, Michaud S, et al. A predominantly clonal multi-institutional outbreak of Clostridium difficile–associated diarrhea with high morbidity and mortality. New England Journal of Medicine. 2005;353(23):2442–9.
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3. Pépin J, Saheb N, Coulombe M-A, Alary M-E, Corriveau M-P, Authier S, et al. Emergence of fluoroquinolones as the predominant risk factor for Clostridium difficile–associated diarrhea: a cohort study during an epidemic in Quebec. Clinical Infectious Diseases. 2005;41(9):1254–60.

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