A Retrospective Review of Treatment Appropriateness and Outcomes of Enterobacteriaceae (with Inducible ampC β-lactamase) Bacteremias at a Large Academic Medical Centre: Opportunities and Implications for Antimicrobial Stewardship

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BACKGROUND

• Timely administration of appropriate empiric antimicrobial therapy is associated with reduced mortality
• Certain Enterobacteriaceae have chromosomal ampC β-lactamase genes (may be induced upon exposure to β-lactams and lead to clinical treatment failure)
• Avoiding unnecessary broad-spectrum antibiotics is an important component of antimicrobial stewardship
• There is a lack of published clinical data supporting use of non-carbapenem treatment for serious infections due to Enterobacteriaceae with inducible ampC-β-lactamases

OBJECTIVE

Describe current practice:
• Provide clinical characteristics and outcomes of patients with bacteremia caused by selected Enterobacteriaceae with inducible ampC-β-lactamase genes at a large, tertiary academic hospital
• Assess appropriateness of empirical and definitive antibiotic regimens chosen to treat these bacteremias

METHODS

• Included all patients with bacteremia caused by Enterobacteriaceae with inducible ampC-beta-lactamase genes over a 2 year period (2013-2014) at St. Michael’s Hospital
• One organism per patient per admission was included (multiple isolates of the same organism were included if collected on separate admissions)
• Patient characteristics and treatment details included: patient demographics, comorbidities, allergies, laboratory and blood culture and sensitivity results, empiric and definitive antimicrobial therapy against gram negative bacilli (GNB) and clinical outcomes (Table 1)
• Appropriateness of empiric and definitive therapy was assessed by 2 independent reviewers (JY, EL)
• Antimicrobial therapy was considered appropriate if the organism was reported as susceptible to the chosen agent

RESULTS

Table 1. Patient Characteristics.

Characteristic | Total patients (n = 49)
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Clinical Characteristics | 49 (100%)
Male, % | 39 (80)
Female, % | 10 (20)
Average age (min,max) | 60 (18,86)
ICU on day of bacteremia, n (%)
| 12 (24)
Comorbid medical conditions, n (%)
• Cancer | 17 (34)
• Cardiac disease | 27 (55)
• Renal disease | 20 (41)
• Liver disease | 25 (51)
• Mechanical ventilation | 13 (27)
• Invasive central line | 14 (29)
• Malignancy | 10 (20)
• Diabetes mellitus | 12 (24)
Laboratory results, mean (SD)
• WBC count | 11.17 (7.90)
• Creatinine clearance | 75.64 (34.76)
Pathogen isolation, n (%)
• Enterobacter cloacae | 32 (65)
• Enterobacter aerogenes | 7 (14)
• Serratia marcescens | 8 (16)
• Citrobacter freundii | 2 (4)
• Citrobacter koseri | 1 (2)
• AmpC producing | 6 (12)
• Non-β-lactams (i.e. clavulanate/amoxicillin, piperacillin/tazobactam) | 3 (6)
Clinical Outcomes | 49 (100%)
Survived during hospitalisation, n (%)
• 0-4 days | 23 (47)
• 5-10 days | 18 (37)
• 11-40 days | 10 (20)
Mean hospital length of stay in days, mean (SD) | 38.85 (50.53)

Table 2. Microbiological Outcomes.

Outcome | Total patients (n = 49)
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No cultures from other sources present during hospitalization | 46 (94)
Repeate blood cultures during hospitalization, n (%)
| 3 (6)
If repeat cultures collected, positive for the same organism, n (%)
| 5 (10)

DISCUSSION AND CONCLUSIONS

• The majority of patients received appropriate empiric and definitive antimicrobial therapy
• Some patients received definitive therapy with a carbapenem, but many received a non-carbapenem agent with similar outcomes
• Non-β-lactams (i.e. sulfamethoxazole-trimethoprim, ciprofloxacin) should be considered as carbapenem-sparing treatment options for these Enterobacteriaceae infections
• Limitation: retrospective study with limited sample size
• Future work: ongoing data collection to monitor trends over time

Legend of Abbreviations:
• carbapenem (IM, IV): meropenem, ertapenem (3), doripenem (1), imipenem (1), ertapenem (1)
• β-lactam: piperacillin (7), ticarcillin (4), cefazolin (2), cephalosporins (2), third generation cephalosporins (2), amoxicillin (2), amoxicillin-clavulanate (2), teicoplanin (2), vancomycin (1)
• fluoroquinolone (1)
• macrolide: macrolides (2), azithromycin (1)
• aminoglycoside: aminoglycosides (5), tobramycin (1), gentamicin (1)
• non-β-lactam: clavulanate/amoxicillin (1), piperacillin/tazobactam (1), sulfamethoxazole-trimethoprim (3), colistin (1)
• oral: doxycycline (1), sulfamethoxazole-trimethoprim (2), metronidazole (1)
• other: nafcillin (1)

References

Figure 1. Percentage of Total Patients with Polymicrobial Bacteremia

Figure 2. Percentage of Patients given Appropriate Empiric and Targeted Antimicrobial Therapy

2013 Antimicrobial Data

2014 Antimicrobial Data

Percentage of Patients who Survived During Hospitalization in Relation to Empirical and Targeted Antimicrobial Therapy

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[Graph]