3-12-2024

# Project #21: Leveraging stewardship to promote ceftriaxone use in severe infections with low- and no-risk AmpC Enterobacterales

Megan Hardy
*Henry Ford Health*

Rachel Kenney
*Henry Ford Health*

Amy Beaulac
*Henry Ford Health*

Tricia Stein
*Henry Ford Health*

Erin Eriksson
*Henry Ford Health*

*See next page for additional authors*

## Authors

Megan Hardy, Rachel Kenney, Amy Beaulac, Tricia Stein, Erin Eriksson, Vivek Kak, Asgar Boxwalla, Shaina Vincent, Nasir Husain, Anita B. Shallal, Robert Tibbetts, Kathy Callahan, Allison Weinmann, Geehan Suleyman, and Michael Veve

# Leveraging stewardship to promote ceftriaxone use in severe infections with low- and no-risk AmpC Enterobacterales

Megan Hardy, PharmD (HFH), Rachel Kenney, PharmD (HFH), Amy Beaulac, PharmD (HFWB), Tricia Stein, MD (Infectious Diseases, HFWB), Erin Eriksson, PharmD (HFJH), Vivek Kak, MD (Infectious Diseases & Internal Medicine, HFJH), Asgar Boxwalla, MD (Infectious Diseases, HFWH), Shaina Vincent, PharmD (HFMH), Nasir Husain, MD (Infectious Diseases, HFMH) Anita Shallal, MD (Infectious Diseases, HFH), Robert Tibbetts, PhD, D(ABMM) (Microbiology, Pathology and Laboratory Medicine, Henry Ford Health), Kathy Callahan, BS MT (ASCP) (Microbiology, Pathology and Laboratory Medicine, Henry Ford Health), Allison Weinmann, MBBS, FRACP (Infectious Diseases, Henry Ford Health), Geehan Suleyman, MD (Infectious Diseases, HFH, Henry Ford Health), Michael Veve, PharmD, MPH (HFH)

## Aim

- To implement and evaluate the impact of a stewardship intervention on the antibiotic treatment of severe infections due to low- and no-risk Enterobacterales
- The historical standard of care for the treatment of infections due to these organisms was broad-spectrum intravenous antibiotic therapy with cefepime or a carbapenem such as ertapenem or meropenem. More recent evidence suggests that ceftriaxone, a narrower spectrum antibiotic, is an appropriate choice
- Therefore, we aimed to change prescribing practices across Henry Ford Health hospitals to use narrower spectrum therapy to achieve the same patient outcomes

## Changes Implemented

Eliminated an AmpC comment in the electronic medical record microbiology report for *Citrobacter koseri*, *Citrobacter amalonaticus*, *Serratia marcescens*, *Morganella morganii*, and *Providencia* species (22 March 2022).

Revised Tier 1: Rapid blood polymerase chain reaction (PCR) identification guideline and modified blood PCR microbiology comment for *Serratia marcescens* recommending ceftriaxone as the treatment of choice (29 June 2022).

Developed a one-page guidance document and provided education in person and electronically for pharmacists and prescribers (2nd quarter 2022)

- The AmpC comment eliminated had stated, "*This organism is known to harbor an inducible AmpC β-lactamase and may develop resistance during prolonged therapy with third-generation cephalosporins such as cefoxitin, ceftriaxone, cefotaxime. Therefore, isolates that are susceptible in vitro may develop resistance following 3 to 4 days of therapy...*"

**Serratia microbiology comment before:**

```
!
Anaerobic bottle Serratia marcescens Susceptibility to follow Presumed AmpC
beta-lactamase producer.  Drugs of choice = Cefepime or Ertapenem.
```

**Serratia microbiology comment after intervention:**

```
Aerobic bottle Serratia marcescens Susceptibility to follow Drug of choice = Ceftriaxone !
```

## Study Design

**Pre-period:** Antibiotics received prior to AmpC comment removal

**Post-period:** Antibiotics received after AmpC comment removal

**Intervention:** Removal of AmpC comment for low or no risk AmpC-harboring isolates

- Single pre-test, single post-test quasi-experiment with a non-equivalent dependent variable (oral antibiotic switch)
- Primary endpoint: definitive ceftriaxone (CRO) prescribing
- Secondary endpoints: patient outcomes including safety and efficacy

## Results

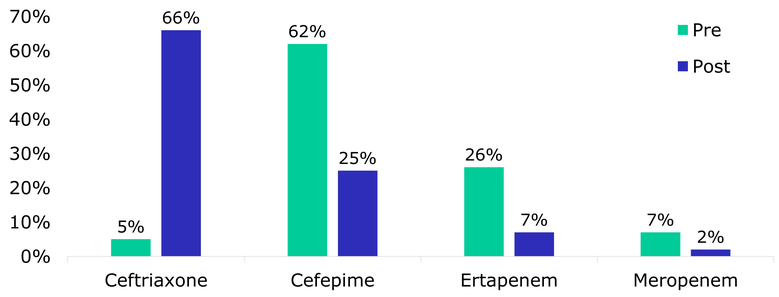
### Patient Baseline Characteristics

| *n* (%) or Median (IQR) | Pre-intervention (*n*=115) | Post-intervention (*n*=109) | *P*-value |
|---|---|---|---|
| Age (yrs) | 66 (58-74) | 67 (57-73) | 0.66 |
| Male sex | 78 (68%) | 70 (64%) | 0.57 |
| Race | | | |
| White/Caucasian | 70 (61%) | 56 (51%) | 0.15 |
| Black/African American | 33 (29%) | 42 (39%) | 0.12 |
| Comorbidities | | | |
| CHF | 39 (34%) | 33 (30%) | 0.57 |
| CKD (moderate-severe) | 33 (29%) | 38 (35%) | 0.39 |
| CCI score | 5 (3-7) | 5 (3-8) | 0.20 |
| Any immunosuppression | 17 (15%) | 9 (8%) | 0.15 |
| ID consult | 88 (77%) | 76 (70%) | 0.25 |
| ICU admission | 66 (57%) | 51 (47%) | 0.11 |
| COVID-19 infection | 21 (18%) | 5 (5%) | 0.001 |

### Infection Characteristics

| | Pre-intervention (*n*=115) | Post-intervention (*n*=109) | *P*-value |
|---|---|---|---|
| Bacterial isolate | | | |
| *Serratia marcescens* | 67 (58%) | 64 (59%) | 0.95 |
| *Morganella morganii* | 19 (17%) | 24 (22%) | 0.30 |
| *Citrobacter koseri* | 21 (18%) | 12 (11%) | 0.13 |
| *Providencia* spp. | 9 (8%) | 11 (10%) | 0.55 |
| *Citrobacter amalonaticus* | 0 (0%) | 1 (1%) | 1.0 |
| Infection source | | | |
| Pneumonia | 51 (44%) | 39 (36%) | 0.19 |
| Bone and joint | 18 (16%) | 21 (19%) | 0.48 |
| ABSSSI | 19 (17%) | 19 (17%) | 0.86 |
| Intra-abdominal | 14 (12%) | 11 (10%) | 0.62 |
| UTI with bacteremia | 8 (7%) | 12 (11%) | 0.29 |
| Infective endocarditis | 2 (2%) | 2 (2%) | 1.0 |
| Bacteremia | 0 | 2 (2%) | 0.24 |
| Other | 3 (3%) | 3 (2%) | 1.0 |
| Any bloodstream infection | 45 (39%) | 34 (31%) | 0.21 |

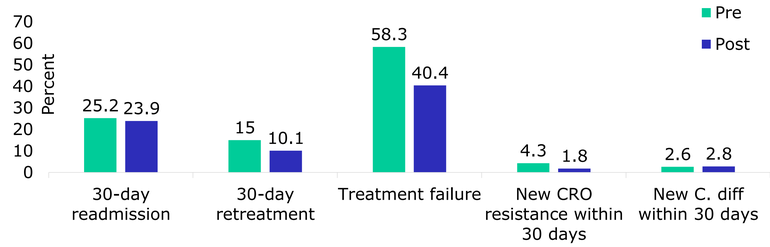
### Treatment Characteristics



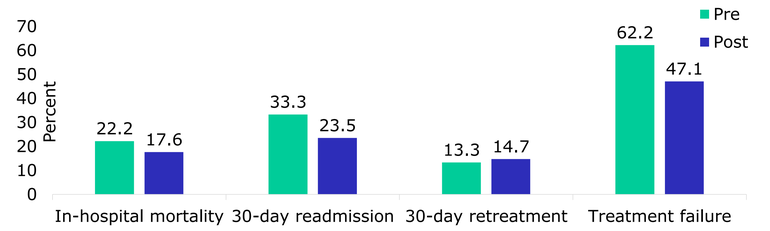

| *n* (%) or Median (IQR) | Pre-intervention (*n*=115) | Post-intervention (*n*=109) | *P*-value |
|---|---|---|---|
| Switch to oral antibiotics | 33 (29%) | 33 (30%) | |
| Ciprofloxacin | 18 (55%) | 10 (30%) | 0.14 |
| TMP/SMX | 14 (42%) | 17 (52%) | 0.46 |
| Duration of therapy | 7 (7-17) | 10 (7-18) | 0.46 |

- Ceftriaxone prescribing significantly increased, *P*<0.001. In multivariable logistic regression, after adjustment for Charlson Comorbidity Index and Infectious Diseases Consultation, the intervention was associated with a 35-fold increase in odds of ceftriaxone prescribing [35.4 (14.2-88.0)]

### Patient Outcomes




### Patient Outcomes – Subgroup Analysis Bloodstream




## Cycles of Learning

Plan: Opportunity for improvement identified in the treatment of low-risk AmpC organisms after the November 2021 publication of the Infectious Diseases Society of America (IDSA) Guidance on the Treatment of Antimicrobial Resistant (AMR) Gram-Negative Infections

Do: An AmpC intervention was developed and implemented in quarter 1-2, 2022

Check: Narrower antibiotic spectrum prescribing with ceftriaxone was statistically increased after the intervention. Patient efficacy and safety outcomes were comparable

Act: An ongoing study of patients with bloodstream infection due to low-risk AmpC organisms (*Serratia marcescens*, *Morganella morganii*, or *Providencia spp*.) was designed to evaluate a patient-focused outcome, treatment success, as the primary endpoint

## Keys to Success and Spread

- Collaboration by infectious diseases physicians, pharmacists and clinical microbiology was essential to implement and measure the intervention
- Leveraging clear, actionable microbiology comments builds on prior published success of our antibiotic stewardship program (Musgrove M et al. 2018 and Arena CJ et al. 2023).
  - Microbiology comments are an efficient and reliable approach to drive best-practice antibiotic prescribing
- Spread: Ongoing work by the antibiotic stewardship team and microbiology involves implementation and measurement of the impact of another new microbiology comment for *Stenotrophomonas maltophilia* in the respiratory tract