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Protocol analysis of an antimicrobial renal dose protocol at a large, tertiary medical center

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Background

- Infection-related morbidity and mortality remains high among critically ill patients.
- Despite early and targeted use of antimicrobials, adequate exposure of some agents is difficult to accomplish.
- Regulatory requirements for renal dose adjustments are intended for those with chronic kidney disease (CKD).
 - Not studied in patients with an acute kidney injury (AKI) or the critically ill
- A retrospective study examined prevalence of AKI in 18,000 patients and showed that renal function recovered more often than impairment persisted.
 - Overall rate of AKI on admission was 17.5%.²
 - AKI resolved within 48 hours in 57.2% of patients.²
- It may be beneficial to reserve dose adjustment for antimicrobials with a wider safety margin and fewer toxicities (ex. beta-lactams) until AKI persists for 48 hours after.
- Critical care pharmacy in collaboration with intensivists at the institution implemented a protocol in July 2021 as part of continuing quality improvement to delay dose adjustment in patients admitted to the intensive care unit (ICU) with AKI.

Purpose

- Analyze the clinical effect of delaying antimicrobial adjustment for the first 48 hours for patients admitted to the ICU with an AKI or patients who developed an AKI during their ICU stay.

Objectives

- Primary outcome
 - Number of patients receiving full dose antimicrobial therapy for the first 48 hours of an AKI in patients that were admitted to or reside in the ICU
- Secondary outcomes
 - Mortality rate of patients with AKI in the ICU
 - Time to resolution of AKI [<0.3 mg/dL increase from baseline serum creatinine (SCr)]
 - Length of stay in the ICU

Methods

- Institution review board (IRB)-approved
- Electronic health record (EHR)-based quasi-experimental pre and post implementation study of those with an AKI in the ICU at a tertiary medical center
- Inclusion criteria:
 - Patients ≥ 18 years old
 - Patients admitted to or residing in the ICU that were admitted with or develop an AKI (SCr ≥ 0.3 mg/dL from baseline)
- Received an approved antimicrobial
 - Beta-lactam/beta-lactamase inhibitors, carbapenems, cephalosporins, clindamycin, penicillins, fluconazole
- Exclusion criteria
 - Renal replacement therapy
 - Intermittent HD (iHD), intraperitoneal hemodialysis (PD), or continuous renal replacement therapy (CRRT)
 - Extracorporeal membrane oxygenation (ECMO)
 - Urine output (UOP) of <0.5 mL/kg/hr in preceding 24 hours prior to assessment
 - History of CKD (chart documentation of CKD Stage 3 or higher or an eGFR <60 ml/min/1.73m² for ≥ 3 months)
- Study period
 - Pre-implementation: January 2020 to June 2021
 - Post-implementation: July 2021 to November 2021

Results

Table 1. Patient Demographics and Characteristics

Characteristic	Pre-implementation (n=23)	Post-implementation (n=0)
Mean age (years) \pm SD	65 \pm 15.9	0
Mean weight (kg) \pm SD	75.6 \pm 20.9	0
Mean height (cm) \pm SD	166 \pm 12.5	0
Mean BMI (kg/m ²) \pm SD	27.5 \pm 7.4	0
Female (no., % of patients)	12, 52.2	0
Mean baseline SCr (mg/dL) \pm SD	0.88 \pm 0.18	0
Mean peak SCr (mg/dL) \pm SD	3.09 \pm 1.41	0

Figure 1. Indications for Prescribed Antimicrobials

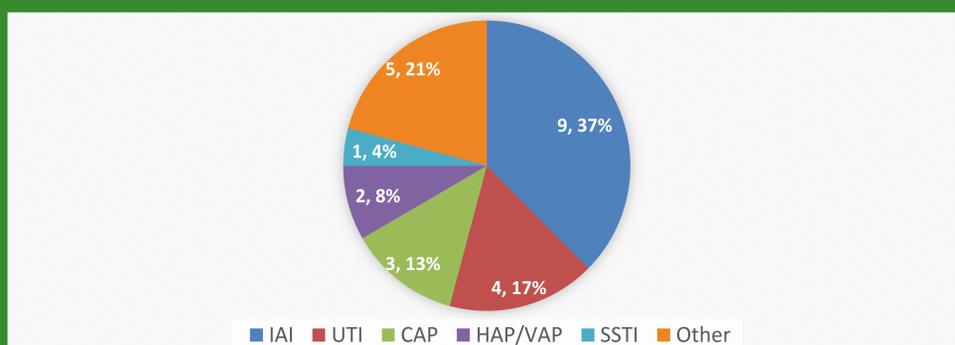


Figure 2. Antimicrobials Prescribed by Indication

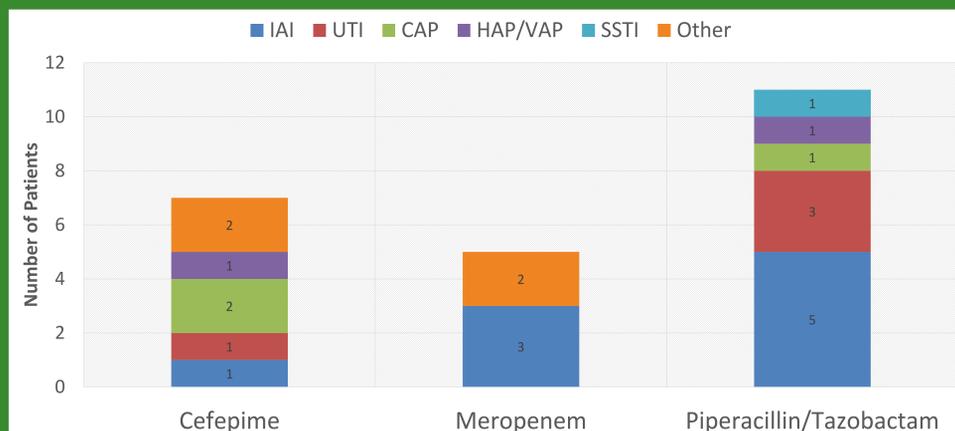


Table 2. Clinical Outcomes

Outcome	Pre-implementation (n=23)	Post-implementation (n=0)
Number of patients receiving full-dose antimicrobial therapy (no., % of patients)	3, 13.0	0
Mortality rate of patients with AKI in the ICU (no., % of patients)	3, 13.0	0
AKI resolution (no., % of patients)	19, 82.6	0
Cefepime (FEP)	7, 100	0
Meropenem (MEM)	5, 100	0
Piperacillin/tazobactam (TZP)	7, 63.6	0
Time to resolution of AKI (days) \pm SD	4.8 \pm 2.6	0
Cefepime (FEP)	4.8 \pm 3.1	0
Meropenem (MEM)	3.4 \pm 1.3	0
Piperacillin/tazobactam (TZP)	5.6 \pm 2.5	0
Length of stay in the ICU (days) \pm SD	5.9 \pm 5.0	0

Discussion

Patient Population

- A total of 23 patients from 1400 total encounters met inclusion criteria during the pre-implementation period, with none meeting inclusion criteria after protocol implementation in July 2021
- Collection period January 2020 through November 2021.
- Average age of 65 years, range 18-88
- Over half of patients (58.3%) with overweight or obesity (average BMI 27.5, range 15.0-44.2)

Clinical Outcomes

- Comparison between groups on clinical outcomes could not be conducted with only pre-implementation data available.
- Most common indications for antimicrobial therapy were intra-abdominal infection (IAI), urinary tract infection (UTI), community-acquired pneumonia (CAP), hospital- and ventilator-acquired pneumonia (HAP/VAP), and skin and soft tissue infections (SSTI)
 - Others include febrile neutropenia, bacteremia, and meningitis
- All but 3 patients in the pre-implementation period were dose adjusted on the first day that criteria for renal dose adjustment was met, meaning that 13.0% received full-dose antimicrobial therapy for the first 48 hours of AKI.
- There appears to be a trend with use of TZP and a longer time to resolution of AKI (nearly 1 day longer than FEP and 2 days longer than MEM), and all 4 patients whose AKI did not resolve received TZP.
- Difficult to evaluate outcomes since post-implementation period data is absent but based on the results it appears that delaying renal dose adjustment in patients with AKI in the ICU has low utility with how few patients qualified.

Study Limitations

- Retrospective, non-randomized design
- Select data was pulled retrospectively from EHR and evaluated by a single reviewer.
- Unable to compare pre- and post-implementation of the protocol as no patients met inclusion criteria during the post-implementation data collection period.
- The protocol was implemented with the assumption that providers would utilize the sepsis order set, which includes cefepime.
 - There was rare use of the sepsis order set, TZP was overwhelmingly the most prescribed antimicrobial included in the protocol.
- The presence of COVID-19 during the data collection period led to many patients being excluded from the protocol due to ECMO or renal replacement therapy needs.
- The strict protocol led to many patients being excluded based on inadequate UOP, baseline CKD, and renal replacement therapy.

Going Forward

- May be worthwhile to collect data again for this protocol as the impact of COVID-19 lessens, particularly if cefepime is prescribed more often.
- The potential increased risk of slowed or lack of recovery from AKI with TZP could warrant further investigation.
- Overall, our use of a strict protocol and inclusion of very few cases may not make this protocol worthwhile to implement.

References

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