ACUTE KIDNEY INJURY ASSOCIATED WITH VANCOMYCIN AND BETA-LACTAMS:
PIPERACILLIN-TAZOBACTAM VERSUS CEFEPIME
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BACKGROUND
Common empiric antibiotic regimens for severe or mixed infections often include vancomycin and a broad-spectrum beta-lactam to cover drug-resistant Gram-positive and Gram-negative organisms, respectively. Studies have begun to investigate the combination of vancomycin and beta-lactams as an independent risk factor for AKI after practitioners perceived a clinically noticeable increase in incidence of AKI with the combination of vancomycin plus piperacillin-tazobactam.

Meaney et al., found the rate of AKI with vancomycin plus piperacillin-tazobactam to be 5.36 times higher than with vancomycin alone.
Burgess et al., saw a two-fold higher incidence of AKI with vancomycin plus piperacillin-tazobactam compared to vancomycin monotherapy. 16.3% versus 8.1%, respectively.
Moenster et al., found the rate of AKI approximately doubled from 13.3% with vancomycin plus cefepime to 29.3% with vancomycin plus piperacillin-tazobactam.

Increasing weight and vancomycin trough concentrations were determined to be independent risk factors for AKI.
Similarly, Gomes et al., found the rate of AKI with vancomycin plus piperacillin-tazobactam to be nearly double that of vancomycin plus cefepime, 34.8% versus 12.5%, respectively.

Due to a recent national piperacillin-tazobactam shortage, our facility restricted its use and largely replaced it with cefepime between April and August 2015, providing a unique opportunity to compare AKI rates with the combination of vancomycin plus piperacillin-tazobactam to vancomycin plus cefepime in two isolated timeframes.

PURPOSE
To investigate the incidence of AKI with the combination of vancomycin and piperacillin-tazobactam versus the combination of vancomycin and cefepime.
To assess risk factors for vancomycin and beta-lactam associated AKI.

METHODS
Retrospective, single center study.

Study population: Patients receiving vancomycin plus piperacillin-tazobactam between April 1, 2014, and August 31, 2014, and patients receiving vancomycin plus cefepime between April 1, 2015, and August 31, 2015.

Inclusion:
> 18 years of age
Received either vancomycin plus piperacillin-tazobactam or vancomycin plus cefepime for at least 48 hours
Study drugs initiated no more than 48 hours apart

Exclusion:
Stage 5 CKD or renal replacement therapy at baseline
AKI prior to study drug initiation
Active cancer on IV chemotherapy
Active rhabdomyolysis at baseline
Study drugs started at another facility
Pregnancy

OUTCOMES
Primary outcome:
AKI, defined by the KDIGO/AKIN criteria, occurring during combination antibiotic therapy or within 72 hours of discontinuation of combination therapy.
Increase in serum creatinine by >0.3 mg/dL within 48 hours
Increase in serum creatinine ≥1.5 times baseline
Urine output <0.5 mL/kg/h for >6 hours

Secondary outcomes:
Time from initiation of combination therapy to AKI
Incidence of initiation of renal replacement therapy
Status of AKI at discharge
Hospital length of stay
ICU length of stay
Incidence of ICU admission
Disposition at discharge
Averages of daily mg/kg vancomycin dose
Predefined possible AKI risk factors:
Age >65 years
Initial vancomycin trough ≥20 mg/L
Average daily vancomycin dose >4 g
Duration of therapy >7 days
Body mass index (kg/m²)
Weight ≥101.4 kg
Use of vasopressors
Number of concomitant nephrotoxins:
Aminoglycosides
Amphotericin B
IV Contrast
Angiotensin converting enzyme inhibitors
Angiotensin II receptor antagonists
Loop diuretics

STATISTICAL ANALYSIS
Estimated power of 80% to detect a 20% difference in AKI with 72 patients in each group.
A p-value <0.05 will be considered significant.
Fisher exact test or χ² test will be used for categorical data and Wilcoxon rank sum test for continuous data.
Logistic regression will be performed to determine risk factors for AKI.

GOALS
Clarify potential differences in rates of AKI between two commonly used broad-spectrum antibiotic regimens.
Aid in appropriate selection of antibiotic therapy, especially in patients with risk factors for AKI.

REFERENCES

DISCLOSURES
Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have direct or indirect interest in the subject matter of this presentation.
Frances E. Aune, PharmD: Nothing to disclose.
Sarah B. Blackwell, PharmD, BCPS: Nothing to disclose.
Rebecca A. Maxson, PharmD, BCPS: Nothing to disclose.