Rates of Acute Kidney Injury in Vancomycin + Piperacillin/Tazobactam (Extended Infusion, Traditional) vs Vancomycin + Cefepime

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BACKGROUND

- SSM Health St. Mary's Hospital St. Louis (SM-SL) implemented the change from traditional piperacillin/tazobactam dosing to extended-infusion in 2019 and the question has been raised about whether this has affected incidence of acute kidney injury (AKI) in combination with vancomycin.
- The main goal of this study is to compare the rates of AKI in patients treated with vancomycin in combination with piperacillin/tazobactam extended infusion (PT - Extended infusion), piperacillin/tazobactam traditional dosing (PT - Traditional), or cefepime.
- Many studies have shown the risk of AKI is increased with the combination of vancomycin and piperacillin/tazobactam over vancomycin and cefepime, but information on the difference in AKI rate between vancomycin combined with extended infusion vs traditional dosing of piperacillin/tazobactam vs cefepime is lacking.[1-4]

METHODS

Study Design: Single-center, retrospective, cohort study

Enrollment: Patients were collected from August 1, 2017 to September 1, 2020

Inclusion Criteria:

- Age ≥ 18
- Combination therapy of trough-based vancomycin therapy and either piperacillin/tazobactam or cefepime for > 48 hours (antibiotics to be initiated ≤ 24 hours apart)
- ≥ 1 documented vancomycin trough
- Baseline SCr (to be obtained within 24 hours of initiation of antibiotic therapy)

Exclusion Criteria:

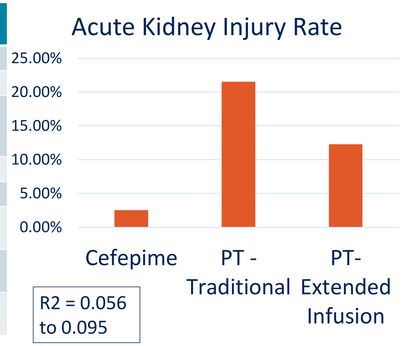
- Pregnancy
- Renal replacement therapy required before antibiotic initiation
- Structural kidney disease including: kidney cysts, transplant, renal cell carcinoma, and any other structural kidney disease present in the patient chart review.
- SCr >1.5 at baseline

RESULTS

Primary Outcome

- Rate of AKI in patients on the various combinations of antibiotics during hospitalization.
  - Increase in SCr by > 0.3 mg/dL OR 1.5x baseline SCr, within 7 days of antibiotic initiation
- AKI was 2.53% in the cefepime group, 21.54% in the PT- Traditional group (95% CI: 0.9 – 3.818, p = 0.001), and 12.28% in the PT- Extended infusion group (95% CI: 0.07 – 3.3 , p = 0.04)

Baseline Characteristics	Cefepime (n = 79)	PT-Traditional (n = 246)	PT- Extended Infusion (n = 57)
Age (years)	59.4	59.6	59.2
Female (%)	48.1	51.6	35.1
Nephrotoxic Drugs (average/patient)	1.13	1.06	1.88
ICU (%)	16.5	16.3	17.5
SCR (mg/dL)	0.97	0.97	0.93
Combo duration (days)	3.74	3.95	3.73
Vanco duration (days)	4.68	4.48	4.12
Avg Vanco trough (mcg/mL)	14.5	15.6	15.3



Secondary Outcomes

Outcome	Cefepime (Control)	PT- Traditional (95% CI)	PT- Extended Infusion (95% CI)
Length of Stay (days)	9.504	9.1 (-2.482 to 1.582)	9.1 (-3.088 to 2.372)
Readmission rate within 30 days (%)	15.2	13 (-0.9 to 0.5)	14 (-1.06 to 0.88)
In-hospital mortality (%)	2.5	2.03 (-1.9 to 1.4)	1.8 (-2.8 to 2.05)
Required RRT (%)	0	0.01 (-2.6 to 3.6)	0 (-3.6 to 4.3)
Time from 1st dose of combination to AKI (days)	1.82	2.65 (-1.85 to 3.5)	3.04 (-1.77 to 4.2)

CONCLUSION

- Acute kidney injury was significantly higher in the PT- Traditional and PT- Extended Infusion vs cefepime (95% CI: 0.9 – 3.818, p = 0.001 and 95% CI: 0.07 – 3.3 , p = 0.04 respectively)
- There were more nephrotoxic medications used on average in the PT- Extended Infusion group vs the cefepime group (1.88 vs 1.13)
- No secondary outcomes were significantly different
- Clinical significance unclear due to wide confidence intervals
- Takeaways/Moving Forward:
  - Continuing PT- Extended Infusion is a reasonable decision for St. Mary's at this time, however, cefepime in combination with vancomycin still remains the combination of choice for patients with need for MRSA and pseudomonas coverage

LIMITATIONS

- Small, single-center retrospective study
- Much larger cohort in the PT- Traditional group leading to potential skew of the data
- Unmatched data
- R2 is low indicating a poor fit of the data although significant difference was found.
- No statistical comparison for baseline characteristics

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