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

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Background

Acute kidney injury (AKI) has many short-term and long-term side effects. Short term side effects may include fluid overload, electrolyte imbalances, cardiac arrhythmias, and others. Many practitioners are familiar with its management; however, in the long term, even one episode of AKI can have a detrimental impact on patients. Long term risks include deterioration of renal function, cardiovascular events, and even death.

SSM Health St. Mary's Hospital St. Louis (SM-SL) implemented the change from traditional piperacillin/tazobactam dosing to extended-infusion in 2019. Recently, the question has been raised about whether this has affected incidence of AKI in combination with vancomycin. 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. 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, piperacillin/tazobactam traditional dosing, or cefepime.

Methods

Study Design: Single-center, retrospective, matched, cohort study.

Inclusion Criteria:

- Age $\geq$ 18
- Patients need to be on combination therapy of vancomycin and either piperacillin/tazobactam or cefepime for > 48 hours (antibiotics to be initiated $\leq$ 24 hours apart)
- $\geq$ 1 documented vancomycin trough
- Baseline Serum Creatinine (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 mg/dL at baseline

Primary Outcome:

- Rate of AKI in patients on the various combinations of antibiotics during hospitalization.
    - AKI is defined as an increase in SCr by > 0.3 mg/dL OR 1.5x baseline SCr, within 7 days of antibiotic initiation
    - AKI will be assessed up to 3 days following discontinuation of antibiotic therapy if they are stopped before day 7.
    - This definition is related most similarly to KDIGO and AKIN classifications without the inclusion of urine output as a factor.

Secondary Outcomes:

- Length of stay
- Readmission rate within 30 days
- Time from 1st dose of combination to AKI
- In-hospital mortality
- Percent of patients who required renal replacement therapy

Results

The total population included 382 patients and 16.4% of these patients experienced AKI. 2.53% experienced AKI in the cefepime group, 21.54% in the piperacillin/tazobactam traditional group (95% CI: 0.9 – 3.818, p = 0.001), and 12.28% in the piperacillin/tazobactam extended infusion group (95% CI: 0.07 – 3.3 , p = 0.04). Of note, there were more nephrotoxic medications used on average in the piperacillin/tazobactam extended infusion group vs the cefepime group (1.88 vs 1.13).

No secondary outcomes investigated resulted in significant differences when comparing piperacillin/tazobactam traditional dosing to cefepime and piperacillin/tazobactam extended-infusion to cefepime. This included length of stay (9.1 days vs 9.5 days (CI: -2.482 to 1.582) and 9.1 days vs 9.5 days (CI: -3.088 to 2.372) respectively), readmission rate within 30 days (13% vs 15.2% (CI: -0.9 to 0.5) and 14% vs 15.2% (CI: -1.06 to 0.88) respectively), mortality in the hospital (2.03% vs 2.5% (CI: -1.9 to 1.4) and 1.8% vs 2.5% (CI: -2.8 to 2.05) respectively), patients requiring renal replacement therapy (0.01% vs 0% (CI: -2.6 to 3.6), 0% vs 0% (CI: -3.6 to 4.3) respectively) and time from first dose to AKI (2.65 days vs 1.82 days (CI: -1.85 to 3.5) and 3.04 days vs 1.82 days (CI: -1.77 to 4.2) respectively).

Conclusions

Acute kidney injury rate was significantly higher in the piperacillin/tazobactam traditional and piperacillin/tazobactam extended-infusion when compared to cefepime. The clinical significance of these outcomes is unclear due to wide confidence intervals. However, continuing piperacillin/tazobactam extended infusion is a reasonable decision for St. Mary's at this time. Cefepime in combination with vancomycin still remains the combination of choice for patients with need for MRSA and pseudomonas coverage.