Effect of renal-preserving empiric antibiotic regimens on acute kidney injury

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Background

Acute kidney injury (AKI) is a common occurrence in the inpatient setting. AKI is associated with negative outcomes such as increased morbidity and mortality. The risk of AKI is compounded by the concomitant use of nephrotoxic medications, such as beta-lactam antibiotics.[1]

In patients presenting with sepsis or other critical infectious illness, empiric antibiotic regimens often target *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus*. As a result, treatment consists of vancomycin in combination with an anti-Pseudomonal beta-lactam. Individually, these are known nephrotoxins, and recent literature suggests additive nephrotoxicity with this combination. A higher incidence of nephrotoxicity has been observed with co-administration of vancomycin and piperacillin/tazobactam (VPT) specifically.[2-6]

Objective

To examine the effect of pharmacist intervention on AKI incidence following implementation and utilization of a renal-preserving empiric regimen guideline

Methods

An IRB-approved pre-post cohort study evaluated patients receiving the following combination regimens from January 15, 2019 to April 1, 2019:

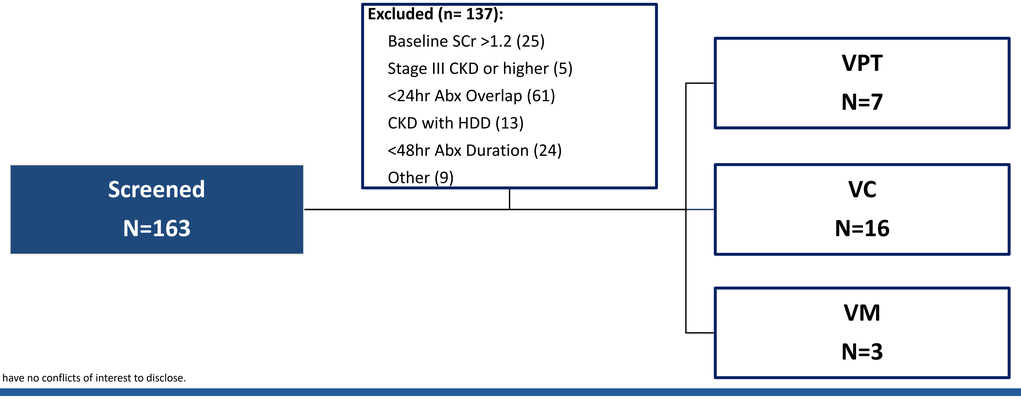
1. Vancomycin and piperacillin/tazobactam (VPT)
2. Vancomycin and cefepime (VC)
3. Vancomycin and a carbapenem (VM)

The following data was collected from patients' electronic health record: demographics; concomitant nephrotoxic medications; baseline serum creatinine (SCr) and creatinine clearance (CrCl); inpatient unit; length of stay; antibiotic dose, duration, and indication; renal function during antibiotic treatment; and comorbidities.

The primary endpoint was the rate of AKI as defined by AKIN criteria: (1) Stage 1, a rise in SCr by 1.5-fold or 0.3 mg/dL; (2) Stage 2, a rise in SCr by 2-fold; and (3) Stage 3, a rise in SCr by 3-fold or initiation of renal replacement therapy. Secondary endpoints include length of stay (LoS), initiation of hemodialysis, duration of antibiotic therapy, and time to AKI. Continuous data was analyzed using the student's t-test, and nominal data was analyzed using the chi-squared test.

Results

Figure 1. Study flow



The authors of this study have no conflicts of interest to disclose.

Results

One hundred and thirty-nine patients were compared to a prospective cohort of 26 patients following implementation of a renal-preserving protocol. Prior to pharmacist intervention, incidence of AKI was 27.3% vs 15.4% prospectively (OR 0.56, 95% CI 0.16-1.49, p=0.2). Mean time to AKI decreased from 4.5 days to 1.6 days prospectively (p=0.04).

Table 1. Baseline demographics

Variable	Pre-intervention (N=139)	Post-intervention (N=26)
Mean age (SD), years	64 (16.6)	64 (12.3)
ICU patients, No (%)	52 (37.4)	10 (38.5)
Mean baseline SCr (SD), mg/dL	0.82 (0.23)	0.80 (0.26)
Indication for antibiotics, No (%)		
Bacteremia	16 (11.5)	5 (19.2)
Sepsis	54 (38.8)	6 (23.1)
Pneumonia	41 (29.5)	8 (30.8)
ABSSSI	13 (9.4)	6 (23.1)
Other	15 (10.8)	1 (3.9)
Concomitant nephrotoxins, No (%)		
NSAIDs	29 (20.9)	1 (3.8)
Aminoglycosides	11 (7.9)	2 (7.7)
Loop diuretics	69 (49.6)	14 (53.8)
ACEI/ARBs	33 (23.7)	5 (19.2)
IV contrast	6 (4.3)	6 (23.1)
Other*	8 (5.8)	0 (0)

Figure 2. Rate of AKI (%)

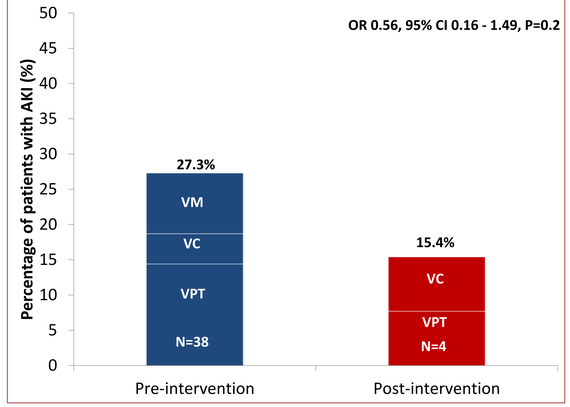
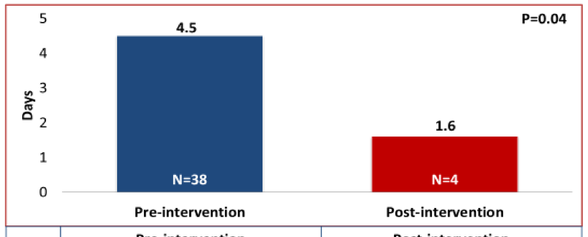
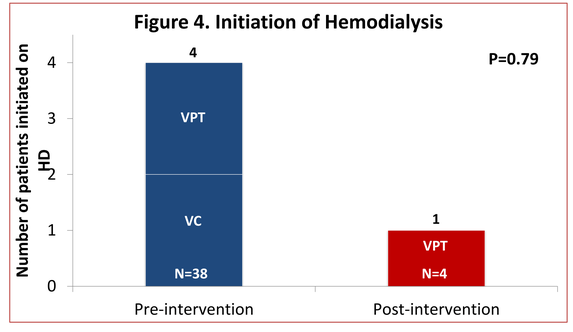


Figure 3. Mean time to AKI



	Pre-intervention	Post-intervention
VM	3.7	0
VC	3.6	2
VPT	5.4	1.5

Figure 4. Initiation of Hemodialysis



The mean duration of AKI was 5 days in our retrospective cohort and 10 days in our prospective cohort (p=0.21). The mean LoS was 16 days in our retrospective cohort and 17 days in our prospective cohort (p=0.7).

Conclusion

Renal-preserving antibiotic regimens are associated with a lower incidence of AKI. Continuous education and reassessment ensured success of pharmacist intervention and compliance with the renal-preserving protocol. An ongoing continuation of this study will collect a large enough sample size to power hypothesis testing.

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