Incidence of Acute Kidney Injury in Pediatric Oncology Patients Receiving Combination Therapy with Vancomycin and Piperacillin-Tazobactam or Cefepime

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Background

One of the most common infectious complications in pediatric oncology patients is febrile neutropenia, with reported incidence rates greater than 80% in hematologic malignancies.[1,2] An important aspect of management for febrile neutropenia is prompt initiation of an anti-pseudomonal beta-lactam or carbapenem, such as cefepime or piperacillin-tazobactam.[1] The benefits of additional antimicrobial coverage vancomycin provides against viridans group streptococcal infections must be weighed against the risk of patients developing an acute kidney injury (AKI).

Piperacillin-tazobactam used as monotherapy is associated rarely with nephrotoxicity with an incidence of less than 1%.[3] However, recent literature has raised the concern of an increased incidence of AKI with vancomycin and piperacillin-tazobactam are used in combination, but most literature has been limited to adult patients without febrile neutropenia.[4-6]

Secondary to nationwide drug shortages, Children's Medical Center Dallas, transitioned from using piperacillin-tazobactam as the first-line empiric agent for febrile neutropenia to cefepime in May 2015. This change in practice provided an opportunity to compare the incidence of AKI in pediatric oncology patients receiving vancomycin in combination with either piperacillin-tazobactam (VPT) or cefepime (VC) within the same institution.

Primary Objective

Compare incidence of AKI, defined using Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines, in pediatric oncology patients receiving either VPT or VC combination therapy

Methods

Study Design

Retrospective, single center, IRB approved, study of AKI incidence with VPT or VC therapy in pediatric oncology patients

Inclusion Criteria

- Age ≤ 18 years old
- Received VPT or VC for ≥ 48 hours
- Antibiotic initiated within 48 hours of each other
- At least 2 serum creatinine values
- At least 1 vancomycin trough > 7 mcg/mL

Exclusion Criteria

- Pre-existing renal dysfunction
- AKI within 30 days of VC or VPT initiation
- Vasopressors within 48 hours of initiation or during therapy
- Tumor lysis syndrome
- Initial vancomycin dose > 4 grams/day

Statistical Analysis

Medians, ranges, and frequencies were used for descriptive analyses. Statistical testing was performed using chi-square and student t-test as appropriate. A p-value < 0.05 was considered to be statistically significant.

Results

Figure 1. Study Method

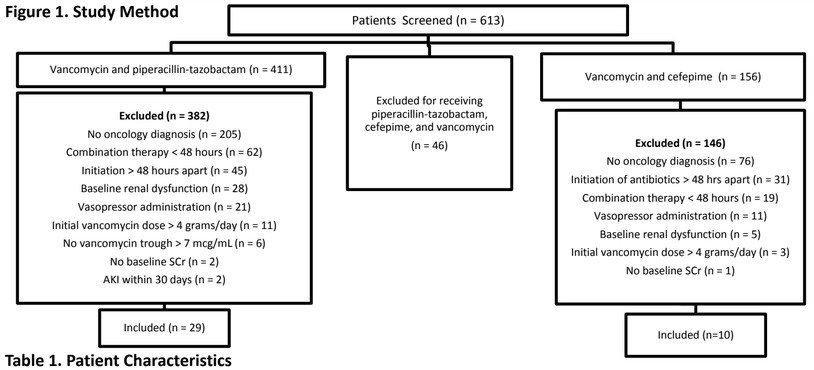

Table 1. Patient Characteristics

Characteristics	VPT (n= 29)	VC (n =10)	P value
Age (year), *median [IQR]*	10 [4 – 13]	6.5 [2.5 – 14]	0.634
Weight (kg), *median [IQR]*	32.4 [13.4 – 53.9]	24.6 [14.3 – 44.6]	0.319
Male gender, *n (%)*	17 (58.6)	1 (10)	0.007
ICU Admission, *n (%)*	8 (27.6)	2 (20)	0.646
Positive Culture during encounter, *n (%)*	15 (51.7)	5 (50)	0.925
Baseline SCr (mcg/dL), *median [IQR]*	0.4 [0.3 – 0.7]	0.4 [0.3 – 0.6]	0.293
Number of concurrent nephrotoxic medications, *median [IQR]*	1 [0 – 2]	0 [0 – 1]	0.162
Oncology Diagnosis, *n (%)*			
Acute lymphoid leukemia	8 (27.6)	5 (50)	0.888
Acute myeloid leukemia	9 (31)	2 (20)	
Other	12 (41.4)	3 (3)	

Table 2. Antibiotic Regimen Comparison

Characteristics	VPT (n = 29)	VC (n = 10)	P value
Beta-lactam regimen			
Duration (days)	6.9 [5 – 12.8]	6.6 [4.9 – 10.2]	0.554
Vancomycin Regimen			
Daily dose (mg/kg/day)	63.2 [51.9 – 74]	73.4 [61.4 – 84.4]	0.157
Number of dose changes	1 [1 – 3]	1 [1 – 2]	0.266
Duration (days)	2.8 [2 – 5.4]	2.2 [2 – 3]	0.831
Serum trough (mcg/mL)	12.3 [9.3 – 15.8]	9.2 [8.2 – 12.6]	0.215
Calculated AUC (mg-hr/L)	568.9 [529.3 – 699]	644.4 [553.7 – 743.6]	0.4523
Combination Therapy			
Duration (days)	2.2 [2 – 4.4]	2.2 [2 – 3]	0.819

**All values are reported as medians with interquartile ranges*

Table 3. Comparison of Acute Kidney Injury

Characteristics	VPT (n = 29)	VC (n = 10)	P value
Incidence, *n (%)*	10 (34.5)	2 (20)	0.406
Time to AKI (days), *median [IQR]*	1.5 [1 – 3.8]	1 [1 – 1]	0.442
Change in SCr (mg/dL)[a,b], *median [IQR]*	0.35 [0.2 – 0.4]	0.3 [0.2 – 0.4]	0.675
Return to baseline SCr (days)[b], *median [IQR]*	7 [3 – 9]	20.5 [2 – 40]	0.226

[a]*Change from baseline SCr to maximum SCr documented during combination therapy*
[b]*Only includes data from patients who developed an AKI*

Conclusions

The results of our study suggest pediatric oncology patients receiving VPT are at an increased risk of developing an AKI compared to patients receiving VC. The AKI incidence in our study is similar to published incidence of AKI seen in adult literature.[4-5] While a study with a larger sample size is needed to confirm these findings, consideration for increased risk of AKI should be made when selecting empiric antimicrobial regimens for pediatric oncology patients.

References

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