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Risk of acute kidney injury in patients receiving vancomycin and piperacillin-tazobactam compared to vancomycin and cefepime

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Disclosure Statement

The listed individuals have the following to disclose regarding financial or personal relationships with commercial entities (or their competitors) that may be referenced in this presentation:

Viktoria Andonova, Pharm.D. – Nothing to disclose

Kristin Boyar, Pharm.D., BCPS – Nothing to disclose

Boca Raton Regional Hospital

- Not-for-profit 400 bed advanced academic tertiary medical center
- **Recognized leader in:**
  - Cardiovascular Care
  - Oncology
  - Women's Health
  - Orthopedics
  - Emergency Medicine
  - Neurosciences
- Predominantly elderly patient population
- Highest ranked hospital in Palm Beach County
  - Listed by U.S. News & World Report 2019-2020
- Lynn Cancer Institute is one of the largest cancer programs in the state of Florida and accredited by the American College of Surgeons

Presentation Objective

Assess the risk of acute kidney injury in patients receiving vancomycin plus piperacillin-tazobactam compared to vancomycin plus cefepime

Background

- Vancomycin is a commonly used antibiotic to cover methicillin-resistant Staphylococcus aureus (MRSA)
- It is often used in combination with broad spectrum antibiotics such as piperacillin-tazobactam or cefepime for empiric therapy in commonly encountered hospital infections

Background

- The mechanism by which vancomycin causes renal injury is not well understood. Accumulation of vancomycin in the proximal renal tubule may lead to acute tubular necrosis and glomerular destruction.[1]
- Semisynthetic penicillins, such as piperacillin, exhibit high concentrations throughout the nephron and mechanism of nephrotoxicity is likely acute interstitial nephritis.[1]

1. Hammond DA, Smith MN, Li C, Hayes SM, Lusardi K, Bookstaver PB. Systematic review and meta-analysis of acute kidney injury associated with concomitant vancomycin and piperacillin/tazobactam. *Clin Infect Dis*. 2017;64(5):666-674.

Primary Literature

Trial	Outcome	Results
Hammond D. A. et al. *Clin Infect Dis*. 2017;64(5):666-674	The primary outcome was incidence of AKI	Concomitant vancomycin and piperacillin-tazobactam was associated with increased risk of AKI (OR 3.12; 95% CI, 2.04-4.78; P <0.001)
Luther M. K. et al. *Crit Care Med* 2018; 46:12-20	The primary outcome was AKI, as defined by the individual study (AKIN, RIFLE, KDIGO)	• Vancomycin plus piperacillin-tazobactam vs vancomycin monotherapy (OR, 3.40; 95% CI, 2.57–4.50) • Vancomycin plus cefepime or carbapenem vs vancomycin plus piperacillin-tazobactam (OR, 2.68; 95% CI, 1.83–3.91)

KDIGO – AKI Definition

Stage	Serum creatinine	Urine output
1	1.5 – 1.9 times baseline OR ≥ 0.3 mg/dL increase	< 0.5 mL/kg/hour for 6 – 12 hours
2	2 – 2.9 times baseline	< 0.5 mL/kg/hour for ≥ 12 hours
3	3 times baseline OR Increase in serum creatinine to ≥ 4 mg/dL OR Initiation of renal replacement therapy OR, In patients < 18 years, decrease in eGFR to < 35 mL/min/1.73 m^2	< 0.3 mL/kg/hour for ≥ 24 hours OR Anuria for ≥ 12 hours

Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract* 2012; 120:179–184.

Purpose

Compare the incidence of acute kidney injury in patients receiving vancomycin plus piperacillin-tazobactam compared to vancomycin plus cefepime in our institution

Methods

Retrospective, single center, observational study

Conducted between January 1st, 2019 and December 31st, 2019

Patients were identified by a computer-generated report through Discern Analytics Reporting Portal Program

Statistical Analysis

- N-1 Chi-squared test was used for evaluation of nominal data
- Comparison between continuous data was performed using Student's *t* test

Inclusion and Exclusion Criteria

Inclusion

- Patients ≥ 18 years of age
- Patients on vancomycin plus piperacillin-tazobactam or vancomycin plus cefepime for more than 48 hours

Exclusion

- Patients already experiencing an AKI
- Patients with stage 4 CKD
- Patients on renal replacement therapy
- Patients with allergies to any of the study medications

Study Outcomes

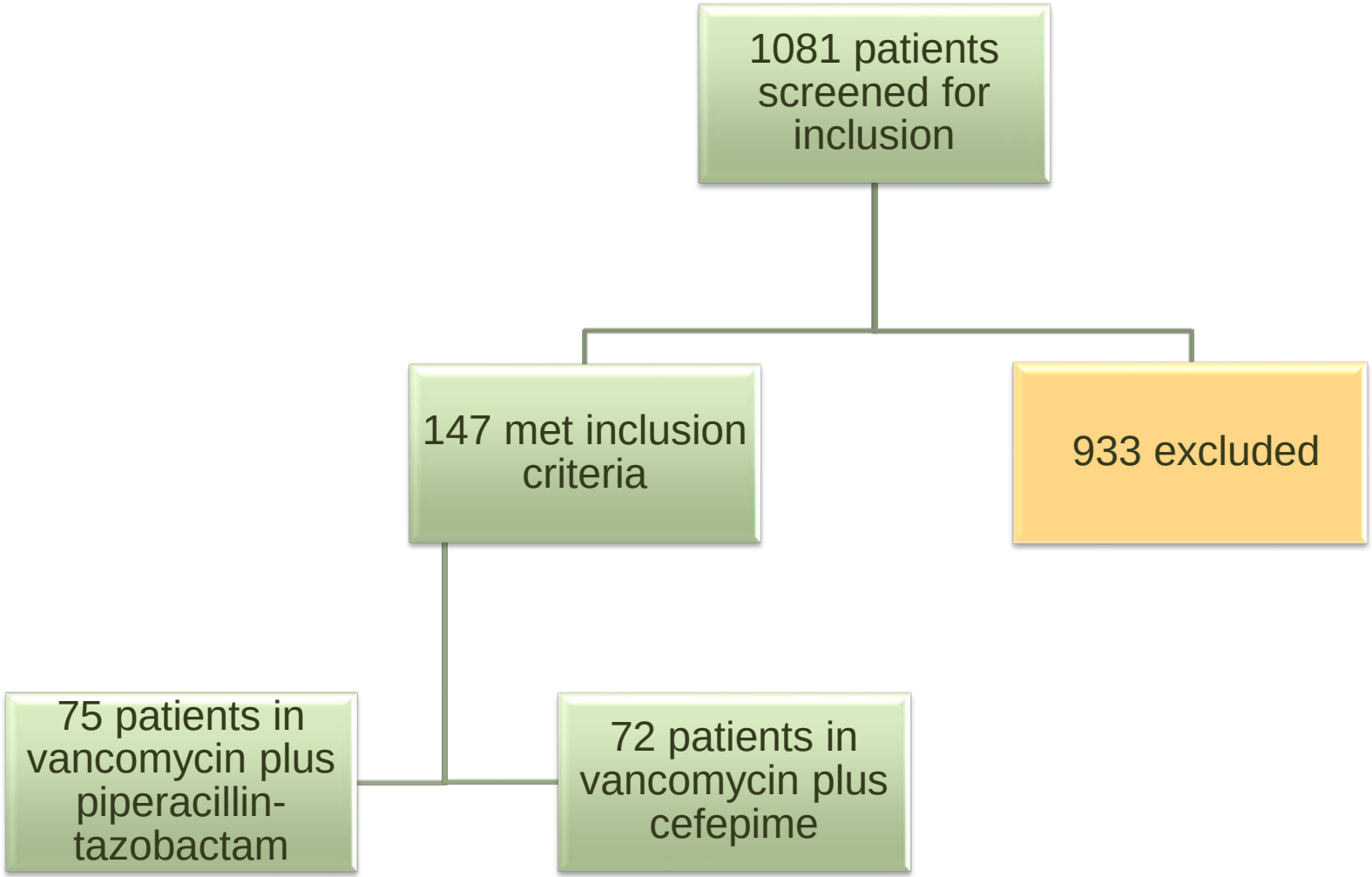
Primary Endpoint

- The incidence of acute kidney injury in patients receiving vancomycin plus piperacillin-tazobactam compared to vancomycin plus cefepime

Secondary Endpoints

- Length of hospital stay
- Increase in creatinine to 2 times baseline
- Nephrology consult after AKI

Results


1081 patients screened for inclusion
147 met inclusion criteria
933 excluded
75 patients in vancomycin plus piperacillin-tazobactam
72 patients in vancomycin plus cefepime

Baseline Characteristics

Characteristics	vanc/pip-tazo (n=75)	vanc/cef (n=72)	*P* value
Male sex	39 (52%)	38 (53%)	0.93
Age (years)	67.3 ± 19.59	71.03 ± 15.17	0.19
Baseline SCr (mg/dL)	0.91 ± 0.3	0.9 ± 0.9	0.92
ICU	12 (16%)	10 (14%)	0.72
Duration of antibiotic therapy (days)	5.6 ± 2.5	5.3 ± 2.6	0.45
Comorbidities			
CDK	6 (8%)	5 (7%)	0.81
Diabetes	15 (20%)	13 (18%)	0.76
COPD	10 (13%)	6 (8%)	0.33
CHF	6 (8%)	2 (3%)	0.16
Malignancy	17 (23%)	25 (35%)	0.11

ABBREVATIONS: CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CHF, chronic heart failure; vanc, vancomycin; pip-tazo, piperacillin-tazobactam; cef, cefepime

Primary Type of Infection

Type	vanc/pip-tazo (n=75)	vanc/cef (n=72)	*P* value
Bacteremia	4 (5%)	2 (3%)	0.44
Cellulitis	13 (17%)	14 (19%)	0.74
Other*	9 (12%)	14 (19%)	0.22
Osteomyelitis	2 (3%)	4 (6%)	0.38
Pneumonia**	36 (48%)	21 (29%)	0.02
Sepsis-empiric	10 (13%)	15 (21%)	0.23
SSTI	1 (1%)	3 (4%)	0.29

*Meningitis, neutropenic fever, UTI, joint infection, other
**HAP/VAP, CAP, Aspiration pneumonia

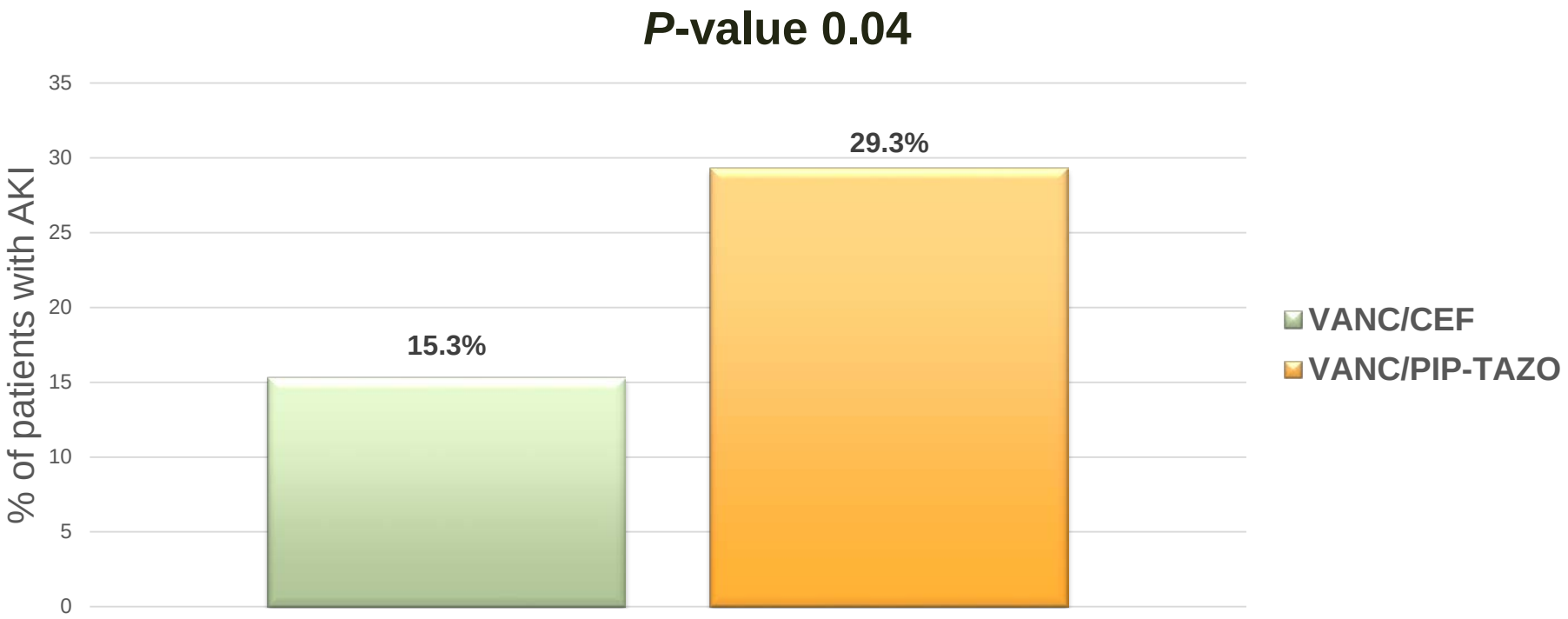
ABBREVATIONS: SSTI, skin and soft tissue infection; vanc, vancomycin; pip-tazo, piperacillin-tazobactam; cef, cefepime

Concomitant Nephrotoxic Medications

Medication	vanc/pip-tazo (n=75)	vanc/cef (n=72)	*P value*
ACEi/ARB	13 (17%)	10 (13%)	0.57
Acyclovir	1 (1%)	1 (1%)	1.00
Loop diuretics	21 (28%)	13 (18%)	0.15
NSAIDs	3 (4%)	5 (7%)	0.43
Vasopressors	4 (5%)	4 (6%)	1.00
Radiocontrast media	3 (4%)	0 (0%)	0.09

ABBREVATIONS: vanc, vancomycin; pip-tazo, piperacillin-tazobactam; cef, cefepime; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; NSAID, nonsteroidal anti-inflammatory

Primary Outcome



Secondary Outcomes

Outcome	vanc/pip-tazo (n=75)	vanc/cef (n=72)	*P* value
Length of hospital stay (days)	14.28 ± 17.9	11.76 ± 9.2	0.28
SCr ≥ 2 times baseline	6 (8%)	0 (0%)	0.02
Nephrologist consult	2/22 (9%)	0/11 (0%)	0.54

ABBREVATIONS: vanc, vancomycin; pip-tazo, piperacillin-tazobactam; cef, cefepime

Conclusion

- This study showed that concomitant use of vancomycin plus piperacillin-tazobactam puts patients at an increased risk for AKI
- The severity of AKI was worse in the vancomycin plus piperacillin-tazobactam group compared to vancomycin plus cefepime group
- Clinicians should be aware of this potential risk and be cautious when prescribing this regimen

Limitations

- Retrospective observational study
- Single center
- Small sample size

Self-Assessment Question

The use of vancomycin plus piperacillin-tazobactam is associated with an increased risk of acute kidney injury

a. TRUE

b. FALSE

Acknowledgment

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