IDWeek™ 2022
#610

Low Rates of Acute Kidney Injury (AKI) in Outpatient Vancomycin Managed by Pharmacists using Precision Dosing Software

Claudia P. Schroeder, PharmD, PhD[1] , Kimberly A. Couch, PharmD[1] , Joyce Gee, PharmD[1], Lucinda J. Van Anglen, BS, PharmD[1]
Healix Infusion Therapy, Sugar Land, TX

Abstract

Background: AKI is a complication of intravenous vancomycin (VAN) occurring in up to 43% of patients (pts) during hospitalization. Data on AKI in pts receiving VAN through outpatient parenteral antimicrobial therapy (OPAT) are limited. There is suggestion that VAN managed through precision dosing pharmacokinetic (PK) software may limit this occurrence. We evaluated the AKI rate of pts receiving VAN as OPAT through Physician Office Infusion Centers (POICs) over a 12-month period.

Methods: A review was conducted of OPAT VAN pts treated in 2021 with therapeutic drug monitoring (TDM) performed (InsightRX) and ≥2 VAN serum levels. These pts were then evaluated for AKI, defined as increase in serum creatinine (SCr) ≥1.5 times baseline. Pts on dialysis were excluded. Data included comorbidities, diagnosis, VAN regimen, concomitant medications, SCr, and VAN serum levels. PK parameters were collected with trough values and estimated 24-hr area under the curve (AUC_{24}). Outcome of therapy was assessed following identification of AKI.

Results: A total of 357 pts from 51 POICs had TDM performed. Of these, 27 (7.6%) developed AKI. Median age was 61 years, 67% were male, and baseline SCr was 0.8 mg/dL (IQR, 0.7-1.0). Most pts (89%) were on concomitant nephrotoxic medications. Median duration of OPAT was 34 days (IQR, 18-41) with onset of AKI after 16 days (IQR, 10-21). At time of AKI, the median SCr increase was 1.7 times baseline (IQR, 1.5-2.0) with a corresponding VAN trough of 21 mg/mL (IQR, 15-28) and AUC_{24} of 572 mg*h/L (IQR, 495-660). As a result, VAN was discontinued in 14 (52%), dose or frequency modified in 10 (37%) with completion of VAN, and no modifications performed in 3 (11%). One pt who discontinued VAN required hospitalization due to AKI with resolution.

Conclusion: VAN managed by pharmacists in an OPAT setting using precision dosing software resulted in a low rate of AKI. Median rise in SCr was <2 times baseline for those with AKI. Rapid identification of early AKI by the pharmacist resulted in changes to the regimen or VAN discontinuation, preventing serious patient sequelae. This supports the need for pharmacist-led monitoring in an outpatient setting with long VAN therapy durations.

Objectives

This retrospective study was designed:

- to evaluate the incidence of AKI in pts treated with VAN in POICs
- to determine characteristics of patients experiencing AKI
- to assess OPAT outcomes of AKI pts

Methods

Study Design and Patient Population:

- Retrospective cohort study of pts receiving VAN in POIC in 2021 with TDM
- Pt with ≥2 VAN trough level and PK analysis
- Excluded pts on hemodialysis and peritoneal dialysis from the AKI population

AKI Definition:[3]

- KDIGO (Kidney Disease: Improving Global Outcomes) classification:
  - Stage 1: SCr 1.5-1.9 times baseline or ≥0.3 mg/dL increase
  - Stage 2: SCr 2.0-2.9 times baseline
  - Stage 3: SCr 3.0 times baseline or ≥4.0 mg/dL increase or initiation of renal replacement therapy

PK analysis:

- VAN trough concentrations were used to perform PK analysis utilizing Bayesian PK analytic software (InsightRX®) to predict AUC_{24}

Data collection:

- Demographics, clinical characteristics of AKI pts, VAN regimen, VAN trough levels, fold increase in SCr from baseline, calculated AUC_{24}, concomitant nephrotoxic drug, OPAT outcomes

Data Analysis:

- Incidence of AKI in pts receiving VAN (%)
- Descriptive statistics

Study Population

- A total of 357 pts from 51 POICs were identified in 2021 with 27 pts developing AKI (7.6%)

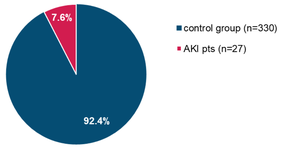


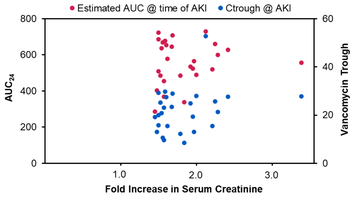
Table 1. Clinical Characteristics of AKI Pts by KDIGO Stage*

Characteristics	Total (n=27)	AKI Severity*		
		Stage 1 (n=18)	Stage 2 (n=8)	Stage 3 (n=1)
Age in years, median (IQR)	61 (54-72)	63 (55-72)	57 (52-71)	61
≥65	11 (41)	8 (44)	3 (38)	-
Gender				
Male	18 (67)	12 (67)	5 (62)	1 (100)
Female	9 (33)	6 (33)	3 (38)	-
Anthropometrics, median (IQR)				
BMI (mg/kg^2)	30 (25-33)	30 (25-33)	30 (25-33)	24
Ideal body weight (kg)	67 (61-72)	66 (58-70)	70 (67-74)	76
Total body weight (kg)	89 (73-105)	80 (71-104)	95 (76-105)	82
Charlson score, median (IQR)	6 (3-6)	6 (3-6)	5 (3-8)	6
Hospitalization prior to OPAT	17 (57)	12 (67)	4 (50)	1 (100)
SCr at baseline, median (IQR)	0.8 (0.7-1.0)	0.8 (0.7-1.0)	0.8 (0.6-1.0)	0.4
Comorbitidites				
Hypertension	21 (78)	13 (72)	7 (88)	1 (100)
Diabetes mellitus	12 (44)	10 (56)	1 (12)	1 (100)
Obesity (BMI >30 mg/kg^2)	12 (44)	8 (44)	4 (50)	-
Cardiovascular disease	10 (37)	6 (33)	4 (50)	-
Cancer	7 (26)	5 (28)	1 (12)	1 (100)
Chronic kidney disease	1 (4)	1 (6)	-	-
Diagnosis				
Bone and joint infection	20 (74)	15 (83)	5 (62)	-
Bacteremia/endocarditis	3 (11)	1 (6)	2 (25)	-
Intra-abdominal infection	2 (7)	1 (6)	-	1 (100)
Cardiac device infection	1 (4)	1 (6)	-	-
Cellulitis	1 (4)	-	1 (12)	-
Vancomycin regimen				
Daily dosing (mg)				
≤2000 mg	14 (52)	10 (56)	4 (50)	-
2001 - 3000 mg	10 (37)	6 (33)	4 (50)	-
≥3000 mg	3 (11)	2 (11)	-	1 (100)
Infusion device				
Ambulatory pump	15 (56)	9 (50)	6 (75)	
Elastomeric device	12 (44)	9 (50)	2 (25)	1 (100)

Data are presented as no. (%) unless otherwise indicated.
*: KDIGO (Kidney Disease Improving Global Outcomes) classification:
Stage 1: SCr 1.5-1.9 times baseline or ≥0.3 mg/dL increase
Stage 2: SCr 2.0-2.9 times baseline
Stage 3: SCr 3.0 times baseline or increase in SCr to ≥4.0 mg/dL or initiation of renal replacement therapy
Abbreviations: BMI; body mass index; IQR; Interquartile range

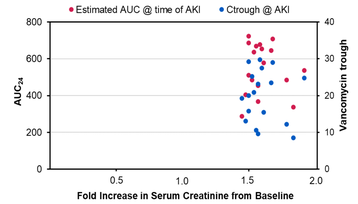
Results

Fig. 1. Overall: AKI relative to Trough and AUC (N=27)



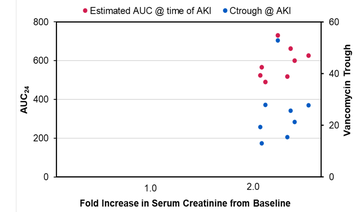
- 2 pts had vancomycin trough <10 and 15 pts had vancomycin trough >20
- 3 pts had AUC <400 and 11 pts had AUC >600
- Number of days to AKI, median (IQR) = 16 (10-21)
- Number of doses to AKI, median (IQR) = 24 (13-39)

Fig. 2. Stage 1: AKI relative to Trough and AUC (n=18)



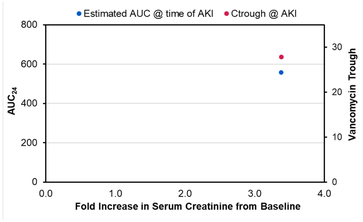
- 2 pts had vancomycin trough <10 and 9 pts had vancomycin trough >20
- 3 pts had AUC < 400 and 8 pts had AUC > 600
- Number of days to AKI, median (IQR) = 15 (9-21)
- Number of doses to AKI, median (IQR) = 16 (13-38)

Fig. 3. Stage 2: AKI relative to Trough and AUC (n=8)



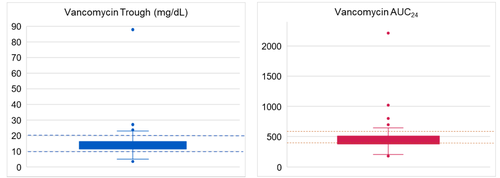
- No pt had vancomycin trough <10 and 5 pts had vancomycin trough >20
- No pt had AUC < 400 and 3 pts had AUC > 600
- Number of days to AKI, median (IQR) = 17 (14-21)
- Number of doses to AKI, median (IQR) = 35 (21-38)

Fig. 4. Stage 3 AKI relative to Trough and AUC (n=1)



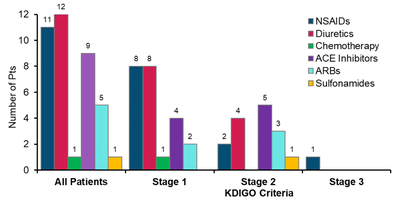
- This pt had vancomycin trough >25 and an AUC >550
- Number of days to AKI = 10
- Number of doses to AKI = 47

Fig. 5. Trough and AUC in Patients without AKI (N=330)



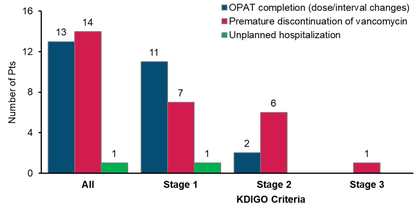
- 264 pts (80%) had therapeutic troughs of 10-20 mg/dL
- 50 pts (15.2%) had subtherapeutic vancomycin troughs < 10 mg/dL
- 16 pts (4.8%) had supratherapeutic vancomycin troughs (> 20 mg/dL)
- 216 pts (65.5%) achieved goal AUC 400-600
- 97 pts (29.4%) were below goal AUC with AUC < 400
- 17 pts (5.2%) exceeded goal AUC with AUC > 600

Fig. 6. Use of Concomitant Nephrotoxic Drugs in AKI Pts



- 9 pts with Stage 1 AKI had >1 nephrotoxic medication
- 5 pts with Stage 2 AKI had >1 nephrotoxic medication
- The pt with Stage 3 AKI had 1 nephrotoxic medication

Fig. 7. OPAT Outcome of Pts with AKI



- 14 pts (52%) had vancomycin therapy discontinued before the planned end of OPAT
- 13 pts (48%) were able to complete vancomycin therapy despite experiencing AKI
- 1 pt (4%) with Stage 1 AKI had premature discontinuation and hospitalization

Discussion & Conclusion

This study evaluated the annual rate of AKI in pts receiving VAN through OPAT in POICs. AKI severity was obtained through precision dosing PK software.

- **Pharmacist-managed VAN utilizing precision dosing software in POICs led to a low incidence rate of AKI at 7.6%.**
- **Early intervention by the pharmacist was made possible by rapid identification of AKI, thus leading to alterations in VAN regimen or discontinuation of VAN.**
- **Rapid identification led to a very low overall rate of hospitalization of 4% for AKI pts.**
- **Limitations: lack of demographics and concomitant medication data for the control group prevented determination of risk factors. The small sample size of AKI pts per severity stage makes final conclusions specific to each stage of AKI difficult.**

Further investigation into a larger population can identify specific risk factors for AKI in the OPAT population. This can assist clinicians in determining those patients who require close monitoring and early therapeutic intervention in order to mitigate AKI.

References

1. van Hal SJ, Paterson DL, Lodise TP. Antimicrob Agents Chemother 2013; 57:734–44.
2. Hamad Y, Nickel KB, Burnett Y, et al. Open Forum Infect Dis. 2020 Dec 31;7(Suppl 1):S366. doi: 10.1093/ofid/ofaa439.804. PMCID: PMC7777684.
3. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012;120(4):c179-84. doi: 10.1159/000339789. Epub 2012 Aug 7.
4. www.insight-rx.com

Healix
IDWeek