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Frequency of Vancomycin-Associated Acute Kidney Injury and Healthcare Utilization among Veterans' Affairs Patients with Skin and Skin Structure Infections

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ABSTRACT

Background: Studies have described an increased risk of acute kidney injury with vancomycin (V) use. However, there are scant data of the risk of vancomycin-associated acute kidney injury (V-A AKI) among hospitalized adults with skin and skin structure (SSSI) infections. This study quantified the incidence of V-A AKI and characterize healthcare utilization among patients with SSSIs receiving V.

Materials/Methods: A retrospective cohort study was performed among hospitalized Veterans' Affairs patients between 2009 and 2015. Inclusion criteria: age ≥ 18; V ≥ 48h; V within 2 days of admission; serum creatinine (SCr) data (pre-V and on-treatment with V). Exclusion: chronic dialysis; osteomyelitis; life-threatening skin infections. Outcomes: VA-AKI, defined as 0.5g/L increase in SCr or 50% decline in creatinine clearance (CrCl) from baseline. Secondary outcomes were total length of stay (LOS), need for specialty physician consultation (infectious diseases or nephrology) and acute dialysis after experiencing V-A AKI.

Results: Among 218 patients, 207 (95%) were male with a mean ¬± standard deviation (SD) age of 65.2 ± 12.0 years. Most (75.2%) patients had cellulitis. Median (interquartile range, IQR) baseline CrCl was 76.6 (58.1 – 97.4) ml/min. Among the 191 patients with V concentrations, median (IQR) V concentration was 11.7 (9.3 – 15.7) mg/mL. Concomitant nephrotoxic medication use was 3.2%. The overall incidence of VA-AKI was 9.2%. Median (IQR) time to V-A AKI was 5 (4 – 6) days. Of the patients with V-A AKI, 25% required a specialty physician consultation after occurrence of post V-A AKI occurrence and 15% required acute dialysis. Median (IQR) LOS was significantly long for patients with V-A AKI vs those with no V-A AKI (12 (7 – 17) versus 7 (5 – 10) days, respectively, p = 0.001).

Conclusion: Among patients with SSSIs, V-A AKI incidence was 9.2%. LOS was significantly longer for patients V-A AKI. Many patients with V-A AKI had a specialty physician consultation and required acute dialysis.

BACKGROUND

- Acute bacterial skin and skin structure infections (ABSSSIs) remain one of the leading causes of infection-related emergency room visits and hospital admissions.
- Vancomycin is one of the commonly prescribed empiric antimicrobial agents for ABSSSIs.
- Acute kidney injury (AKI) is frequently associated with vancomycin therapy.
  - Patients who experience vancomycin-associated AKI have an increased risk of death, have extended hospital length of stay (LOS), and often require additional levels of care such as a specialty physician consultations and acute dialysis sessions
- Among vancomycin-recipients with ABSSSIs, the association between empiric vancomycin use and AKI is not well understood.
  - The use of excess healthcare resources (i.e. specialty physician consultations and acute dialysis sessions) have not been quantified in ABSSSI patients.
- Given the ubiquity of use, it is imperative to understand AKI rates and associated outcomes among patients with ABSSSI.

OBJECTIVES

- Determine the incidence of vancomycin-associated AKI among patients with skin and skin structure infections receiving empiric therapy with vancomycin.
- Compare hospital length of stay (LOS) between patients with and without vancomycin-associated AKI.
- Quantify use of specialty physician consultation and acute dialysis in patients with vancomycin-associated AKI

METHODS

Study Design

- Retrospective cohort study

Study Population

- The population was hospitalized, non-dialysis dependent Veterans Affairs patients with skin and skin structure infections (SSSIs) receiving empiric treatment with vancomycin within the Upstate New York Veterans Healthcare Administration between 2009 and 2015

Inclusion Criteria

1. Age ≥ 18 years
2. Required hospitalization
3. Received intravenous vancomycin within 48 hours of hospitalization
4. Non-dialysis dependent
5. Documented SSSI in physician clinical progress note

Data Collection

- Demographics
  - Age, sex, height/weight, race
- Comorbidities
  - Diabetes mellitus, heart failure, chronic obstructive pulmonary disease, hypertension, hepatic or renal dysfunction (defined by need for renal replacement therapy), transplanted organ, active malignancy or cancer, immunosuppressive drugs (prednisone > 20mg/day or equivalent corticosteroid ≥ 14 days prior to culture, or the receipt of any antineoplastic chemotherapy in the 3 months prior to culture), decubitus ulcers, human immunodeficiency virus (HIV) infection, history of cerebrovascular accident, alcoholism, and surgery requiring > 48 hours of hospitalization in the 30 days preceding the initiation of antibiotic therapy
- Course of hospitalization
  - Length of hospital stay (LOS), hospital unit residence (ICU versus non-ICU) at time of diagnosis of ABSSSI, and vital status at discharge
- Laboratory values
  - Where available, the following were collected: serum creatinine, complete blood count, vancomycin serum concentrations and all microbiologic culture and susceptibility data
  - Creatinine clearance (CLCR) estimated by the Cockcroft-Gault formula.
  - All laboratory data will be collected 5 days prior to the start vancomycin therapy and ended 2 days after the completion of therapy.

Outcomes

- Acute kidney injury (AKI):
  - Defined as increase in serum creatinine by ≥ 0.5 mg/dL or decline in creatinine clearance by ≥ 50% from baseline
- Hospital LOS between patients with and without vancomycin-associated AKI
- Use of specialty (infectious diseases or nephrology) physician consultation after occurrence of vancomycin-associated AKI
- Acute dialysis after occurrence of vancomycin-associated AKI and specialty physician consultation

Statistical Analyses

Bivariate Analyses

- Categorical variables assessed using the Pearson $\chi 2$ or Fisher's exact test.
- Continuous variables assessed using Student's t or Mann-Whitney *U* test.
  - Classification and Regression Tree (CART) analyses, to identify breakpoints within the distribution of continuous variables where the probability of vancomycin-associated AKI is distinctly different between the resulting groups.
- Kaplan Meier survival plots were generated
  - Survival distributions were compared using the log rank test.
- All analyses were performed in SPSS (v24, Armonk, NY) and CART (Salford Systems, San Diego, CA).

RESULTS

Table 1: Bivariate Relationship Between Clinical/Demographic Covariates and Vancomycin-Associated Acute Kidney Injury Among Veterans Affairs Patients With Skin And Skin Structure Infections

Covariate	Without Vancomycin-Associated AKI (n = 198)	With Vancomycin-Associated AKI (n = 20)	P-value
Age, years	64.9 ± 12.9	68.3 ± 11.0	0.23
• Age ≥ 65 years*	90 (45.5)	14 (70.0)	0.04
Sex, male	188 (94.9)	19 (95.0)	1.00
Race • Caucasian • Black • Hispanic • Other	 175 (88.4) 17 (8.6) 1 (0.5) 5 (2.5)	 18 (90.0) 0 (0) 0 (0) 2 (10.0)	0.17
Weight, kg	103.8 ± 53.5	106.1 ± 32.7	0.85
BMI ≥ 30	107 (54.0)	11 (55.0)	0.94
Baseline creatinine clearance • >50 ml/min • 30-50ml/min • <30 ml/min	 166 (83.8) 23 (11.6) 9 (4.5)	 16 (80.0) 3 (15.0) 1 (5.0)	0.89
Hypertension	145 (76.3)	14 (70.0)	0.73
Diabetes	91 (46.4)	9 (45.0)	0.62
Heart failure	29 (14.6)	4 (20.0)	0.52
COPD	36 (18.2)	4 (20.0)	0.77
Hepatic dysfunction	22 (11.1)	5 (25.0)	0.07
HIV	2 (1.0)	0 (0)	1.00
Active malignancy or cancer	18 (9.1)	4 (20.0)	0.12
Surgery in preceding 60 days	40 (20.2)	4 (20.0)	1.00
History of healthcare exposure in preceding 180 days	92 (46.5)	12 (60.0)	0.25
Concomitant nephrotoxic agents	7 (3.5)	0 (0)	1.00
Concomitant immunosuppressant drug use	4 (2.0)	2 (10.0)	0.09
Concomitant piperacillin/tazobactam	109 (55.1)	15 (75.0)	0.09
APACHE-II score, median (IQR)	6 (5 – 10)	7 (5 – 10)	0.30
• APACHE-II ≥ 9.5*	51 (25.8)	9 (45.0)	0.07
Cellulitis	148 (75.1)	16 (80.0)	0.79
Vancomycin serum concentration obtained	173 (87.4)	18 (90.0)	1.00
• First vancomycin serum concentration obtained, median (IQR)	11.6 (9.3 – 15.4)	16.0 (10.5 – 18.1)	0.02
Duration of therapy, median (IQR)	5 (3 – 7)	6 (5 – 11)	0.02

All data presented as n (%), mean ± standard deviation (SD) or median (interquartile range).
Abbreviations: AKI – acute kidney injury; APACHE – acute physiology and chronic health evaluation; BMI – body mass index; COPD – chronic obstructive pulmonary disorder; HIV – human immunodeficiency virus

Table 2: Overall Frequency And Subpopulation Frequencies Of Vancomycin-Associated Acute Kidney Injury

Population	Point Estimate
Overall frequency vancomycin-associated AKI	9.2%
• Patients with diabetes mellitus	9.0%
• Patients with diminished renal function (CLCR 30 – 50 ml/min)	11.5%
• Patients with body mass index ≥ 30	9.3%
• Patients with previous history of vancomycin-associated AKI	16.7%

Figure 1: Median Hospital Length of Stay Between Patients With and Without Vancomycin-Associate Acute Kidney Injury

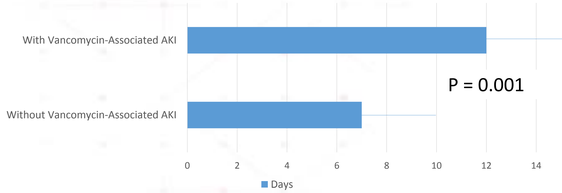


Figure 2: Excess Utilization Of Healthcare Services Among Patients With Acute Kidney Injury

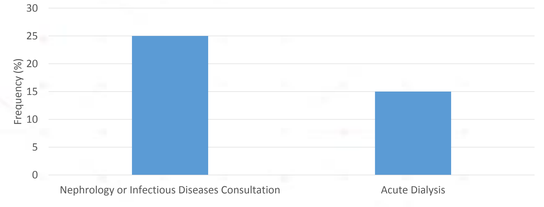
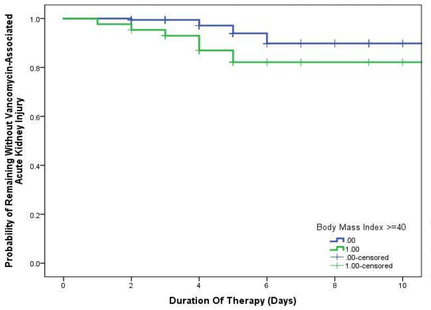


Figure 3: Kaplan Meier Curve of Probability of Remaining Without Vancomycin-Associated Acute Kidney Injury, Stratified by BMI ≥ 40



P = 0.06

CONCLUSIONS

- Among patients with skin and skin structure infections treated with vancomycin, the overall incidence of acute kidney injury (AKI) was 9.2%.
- Hospital length of stay and healthcare utilization (specialty physician consultation and acute dialysis) was higher among patients with vancomycin-associated AKI than those without.

DISCLOSURES

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