Risk Factors for OPAT-Related Adverse Drug Events: A Case-Control Study

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Background

Outpatient parenteral antimicrobial therapy (OPAT)

- Definition: the administration of parenteral antimicrobial therapy in at least two doses on different days without intervening hospitalization

Potential Benefits of OPAT	Potential Risks of OPAT
↓ Hospital length of stay	• Catheter-associated infection
↓ Risk of hospital-associated conditions	• Venous thrombophlebitis
↑ Patient satisfaction/quality of life	• Unplanned readmissions/ED visits
↓ Overall healthcare costs	• Adverse drug events (ADEs)

Significant OPAT-related ADEs are common

- Cumulative incidence ranges from 2-44%; varying study definitions
- Approximately 25% of unplanned 30-day readmissions are ADE-related
- Additional consequences of OPAT-related ADEs include: ED visits, diminished quality of life and satisfaction, increased costs, interruption of antimicrobial therapy, or selection of inferior alternative therapies

Study Purpose

- Understanding significant OPAT-related ADEs is crucial for the purposes of prevention, monitoring, and selection of therapy
- In January 2021, our institution's OPAT program began using a custom documentation template to routinely capture significant ADEs
- We sought to characterize the cumulative incidence, type, timing, and risk factors associated with significant OPAT-related ADEs

Methods

Retrospective case-control study from January 2021 – October 2021

Inclusion Criteria	Exclusion Criteria
• Adults (≥18 years of age) • Hospital discharge with at least one parenteral antimicrobial prescription • Enrolled in monitoring by our institution's OPAT program	• Loss to follow up • Readmission to an outside hospital during OPAT course

Source Population
All patients meeting inclusion criteria during study period

Case Group
All patients **with** a significant OPAT-related ADE

Control Group
Randomly selected patients (2:1) **without** a significant OPAT-related ADE

Significant OPAT-related ADE

- An ADE that occurred during OPAT which resulted in at least one of the following: ED visit, hospital readmission, antimicrobial dose adjustment, antimicrobial regimen change, early cessation of OPAT, other intervention (e.g. additional laboratory or diagnostic testing)

Methods

Data Collection

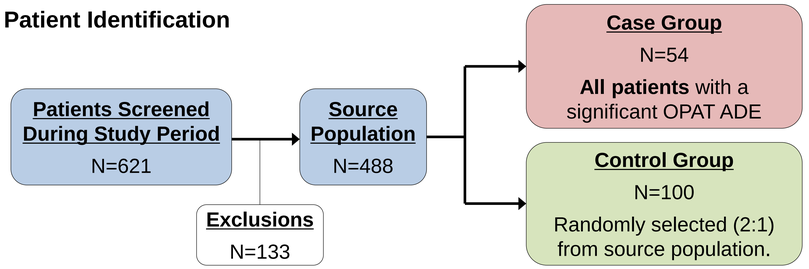
- Manual chart review was used to extract data relating to patient demographics and clinical characteristics, index hospitalization, infection characteristics, OPAT characteristics, and ADE-related information

Statistical Analysis

- Descriptive statistics to characterize ADE incidence, type, and timing
- Univariate analysis to compare case and control groups
  - Categorical variables: X2 or Fisher's exact test
  - Continuous variables: unpaired student's t-test or Mann-Whitney U test
- Multivariable logistic regression analysis to identify ADE risk factors
  - Variables with P<0.2 on univariate analysis considered as model input
  - Associations reported using adjusted odds ratios (aORs) with P≤0.05 considered significant in the final model

Results

Patient Identification



Descriptive Results

- Cumulative incidence of significant OPAT-related ADE was 11% (54/488)
- Median time-to-ADE was 13 days (range: 2 – 96 days) from discharge

ADE Type (N=58)[a]	n (%)
Acute kidney injury	29 (50.0)
Rash/hypersensitivity	8 (13.8)
Leukopenia	5 (8.6)
Anemia	4 (6.9)
Hepatotoxicity	4 (6.9)
Thrombocytopenia	3 (5.2)
Electrolyte abnormality	3 (5.2)
Nausea/vomiting	3 (5.2)
Diarrhea	2 (3.4)
Other[b]	6 (10.3)

[a]Several patients experienced >1 ADE
[b]Includes rhabdomyolysis, *C. difficile*-associated diarrhea, ototoxicity, chest pain

ADE Outcome (N=58)	n (%)[a]
Regimen change[b]	19 (32.8)
Dosage adjustment	17 (29.3)
Early OPAT cessation	12 (20.7)
Hospital admission	6 (10.3)
Additional lab monitoring	4 (6.9)
ED visit	3 (5.2)
Other[c]	4 (6.9)

[a]Several ADEs resulted in >1 outcome
[b]Switching offending agent to alternative
[c]Includes blood transfusion, addition of granulocyte colony stimulating factor, electrolye replacement, additional of oral vancomycin

Results

Select Variables[a]	ADE/Case (N=54)	No ADE/Control (N=100)	*P* Value
Age, mean years (SD)	61 (14)	57 (15)	0.080
Female, n (%)	24 (44)	46 (46)	0.853
Race/ethnicity, n (%)			
Caucasian	38 (70)	53 (53)	0.036
African American	12 (22)	43 (43)	0.010
Unknown/other	4 (7)	4 (4)	0.452
CCI, median (IQR)	4 (2-7)	4 (2-6)	0.303
Immunocompromised, n (%)	25 (46)	42 (42)	0.608
Index LOS, median (IQR)	9 (7-14)	8 (5-14)	0.273
Infection Type, n (%)			
Bacteremia	12 (22)	49 (49)	0.001
Genitourinary	0 (0)	13 (13)	0.004
Viremia/Transplant Infection	14 (26)	9 (9)	0.005
Empiric therapy/Culture-Negative, n (%)	10 (19)	6 (6)	0.015
Receipt of OPAT agent, n (%)			
Cefepime	14 (26)	11 (11)	0.017
Ceftriaxone	5 (9)	26 (26)	0.013
Vancomycin	24 (44)	10 (10)	<0.001
Multi-drug OPAT regimen, n (%)	19 (35)	15 (15)	0.004

SD: standard deviation; CCI: Charlson Comorbidity Index; LOS: length of hospital stay; IQR: interquartile range
[a]Not all variables reported due to space limitations

Multivariable Analysis: Significant OPAT-related ADE

Variable	aOR (95% CI)	*P* Value
Receipt of vancomycin OPAT	8.3 (2.98 – 22.88)	<0.001
Receipt of empiric therapy	6.7 (1.71 – 26.20)	0.006
OPAT duration ≥28 days	3.7 (1.54 – 8.78)	0.003
Receipt of ceftriaxone OPAT	0.2 (0.06 – 0.79)	0.021
African American race	0.4 (0.14 – 0.90)	0.03

aOR: adjusted odds ratio; CI: confidence interval; Hosmer-Lemeshow *P* value = 0.756

Conclusions

- Significant OPAT-related ADEs were common, occurring in approximately 1 in 9 patients and typically within the first two weeks of OPAT. Acute kidney injury and rash/hypersensitivity were most frequently observed
- Several modifiable ADE risk factors were identified and should be carefully considered prior to hospital discharge
- Based on these data, OPAT programs should consider employing vancomycin alternatives when possible, efforts to optimize culture-directed therapy, and strategies to minimize duration of parenteral treatment

References

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