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Knoxville Infectious Disease Consultants, P.C.

Serious Bacterial Infections: Successful Outpatient Management by Infectious Disease Physicians in Office Infusion Centers

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Abstract

Background: Patients (pts) with serious bacterial infections (SBI), identified as bone and joint infections (BJI), bacteremia/endocarditis, and central nervous system (CNS) infections are frequently discharged on outpatient parenteral antimicrobial therapy (OPAT). They account for 48% of all infections treated in our network of Infectious Disease (ID) physician office infusion centers (POICs). Care for these pts poses risks and challenges to ensure safe and successful outcomes while avoiding hospitalizations. This study examines clinical outcomes and complications of our SBI pts receiving OPAT in ID POICs.

Methods: All pts were identified with SBI receiving OPAT in 2017 from 14 POICs. A group of 250 pts were randomly selected by incidence of diagnosis and a retrospective chart review performed. Demographics, treatment regimen, clinical outcomes, adverse drug-reactions (ADRs) and unplanned hospitalizations during OPAT were collected. Clinical success was defined as clinical cure or improvement at completion of OPAT. Pts were included who were hospitalized for ≤7 days and subsequently completed OPAT. ADRs leading to hospitalization or discontinuation of OPAT were deemed serious. Descriptive statistics were used for distribution of variables.

Results: SBI pts included BJI (n=175), bacteremia/endocarditis (n=60) and CNS infections (n=15) as described in Table 1. Successful clinical outcomes were reported in 224 pts (89.6%) after a mean duration of OPAT of 32±20 days. Of these, 14 pts (6.2%) were hospitalized during OPAT and returned to the POIC for a successful clinical outcome. Clinical success rates for BJI, bacteremia/endocarditis and CNS infections were 89.1%, 91.6% and 86.7%, respectively. The primary reason for non-favorable outcomes was worsening of infection (16/26, 62%). Serious ADRs were reported in 12 pts (4.8%) with 6 (2.4%) leading to hospitalization. Unplanned hospitalizations during OPAT occurred in 33 pts (13.2%) with the majority (22/33, 67%) related to disease. ADRs and hospitalizations compare favorably to data previously reported.[3]

Background

Serious bacterial infections (SBIs) can pose both patient risks and therapy challenges with long durations of intravenous antimicrobial therapy required.[1] Frequently, these pts must be discharged from an acute care setting to continue OPAT. An Infectious Disease POIC provides a supervised setting for close monitoring of these patients, often facilitating early hospital discharge.[2] In our network of ID POICs, almost 50% of pts receiving OPAT have SBIs including BJI, bacteremia/IE, and CNS infections.[3] Outpatient studies regarding outcomes and complications in these pts are inconsistent, with data across multiple OPAT settings.[4-7]

This study evaluates our clinical outcome, serious adverse drug reactions (ADRs), and unplanned hospitalizations in SBI pts receiving OPAT in ID POICs.

Methods

This was a retrospective cohort study of pts receiving OPAT in 2017 for BJI, bacteremia/IE, and CNS infections across ID POIC sites nationwide (n=16).

Data collection included demographics, location prior to OPAT, Charlson comorbidity index, antimicrobial usage, duration of OPAT and clinical outcome stratified by type of infection. Complications collected were adverse drug reactions (ADRs), which included catheter infections and unplanned hospitalizations.

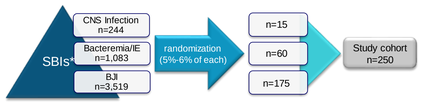
Data analysis:

- ADRs leading to hospitalization or early discontinuation of OPAT were deemed serious
- Successful clinical outcome was defined as completion of OPAT with signs of cure or improvement as indicated as reduction in inflammatory markers and/or negative cultures. Pts who were hospitalized but resumed OPAT within 7 days were included in the outcome assessment.
- Non-successful outcome was defined as early discontinuation of OPAT for any reason or hospitalization lasting more than 7 days.
- Descriptive statistics (mean, median, frequency) were used to describe distribution of variables. Multivariate analysis was used to evaluate predictors for unsuccessful OPAT outcome using odds ratio (OR) and 95% confidence interval (CI) with p<0.05 considered to be statistically significant. Analysis was performed using GraphPad Prism 7 software.

Results

Study Population

Selection of Study Population



*SBI; serious bacterial infections

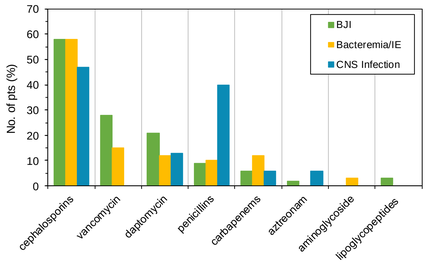
Patient Demographics & Baseline Characteristics

Variable	BJI	Bacteremia/ IE	CNS Infection
Age in years, median (range)	58 (21-83)	60 (28-97)	67 (40-82)
≥ 65 years	48 (27)	24 (40)	8 (53)
Male	111 (63)	38 (63)	8 (53)
Charlson index, mean (SD)*	2.8 (2.0)	3.7 (2.3)	3.8 (2.8)
Location prior to OPAT			
hospital	128 (73)	57 (95)	11 (73)
community	38 (22)	3 (5)	4 (27)
extended care	9 (5)	-	-

Data presented as No. of pts (%) unless otherwise indicated.
*; incl. comorbidities (total no. of pts) : 35% diabetes mellitus, 18% malignancy, 16% peptic ulcer, 10% CKD, 9% liver disease, 8% CHF or MI, 7% PVD, 6% COPD, and 2% dementia

- BJI: 98 osteomyelitis, 48 prosthetic joint infections, and 29 septic arthritis
- Bacteremia source: 20 IE, 13 genitourinary, 7 device infections, 6 surgical site, 5 skin, 5 of unknown source, and 4 respiratory
- CNS infections: 6 spinal infections, 4 neurosyphilis, 3 meningitis, and 2 cranial infections

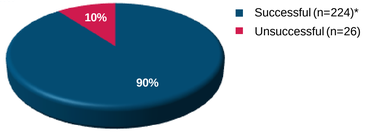
Antimicrobial Usage by Diagnosis



- 31 pts (12%) received concomitant antimicrobial therapies and 28 pts (11%) received consecutive therapies
- Average OPAT duration of BJI, bacteremia/IE, and CNS infections were 37±23 days, 20±10 days, and 26±18 days, respectively

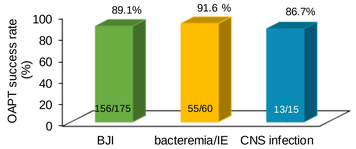
Clinical Outcome

OPAT Success



*; incl. 14 pts with hospitalizations ≤7 days and return to POIC with successful completion of OPAT

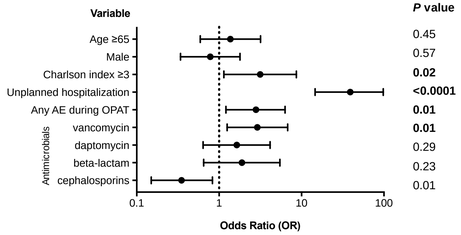
OPAT Success by Diagnosis



Reasons for unsuccessful OPAT included:

- worsening infection (n=16, 62%): 11 BJI, 5 bacteremia
- ADRs (n=4, 15%): 3 BJI, 1 CNS infection
- non-compliance (n=4, 15%): all BJI
- new infection (n=2, 8%): 1 BJI, 1 CNS infection

Risk Analysis for Unsuccessful OPAT

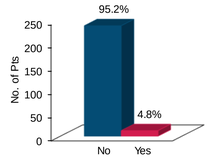


Variables associated with unsuccessful OPAT were:

- Charlson index ≥3 (OR: 3.2, CI: 1.14-8.65, *P*=0.02)
- Unplanned hospitalization (OR: 40.7, CI: 14.6-98.5, *P*<0.0001)
- Any adverse event during OPAT (OR: 2.8, CI: 1.21-6.31, *P*=0.01)
- Use of vancomycin (OR: 2.9, CI: 1.25-6.78, *P*=0.01)

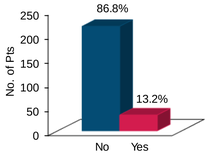
Complications

Adverse Drug Reactions



- Serious ADRs were reported in 12 of 250 pts (4.8%) and included: nephrotoxicity (n=4), rash (n=3), elevated CPK (n=2), catheter infection (n=1), intractable vomiting (n=1) and syncope (n=1)
- Serious ADRs resulted in 6 hospitalizations
- Other non-serious ADRs were reported for 77 pts (30.8%), most commonly gastrointestinal events (15%). All were managed through the POIC without the need for therapy discontinuation.

Unplanned Hospitalizations



Reason for Unplanned Hospitalization	No. of Pts (%)	Type of SBI (n)	Length of Hospital Stay (median, range)
Disease-related	22 (67%)	BJI (n=17) bacteremia (n=4) IE (n=1)	5 days (2 to 20)
Adverse drug reaction	7 (21%)	BJI (n=5) CNS infection (n=2)	6 days (2 to 13)
Catheter-related infection	4 (12%)	BJI (n=4)	3 days (1 to 8)

- Unplanned hospitalizations occurred in 33 of 250 pts (13.2%). Of those, 14 pts returned to the POIC within 7 days to successfully complete OPAT

Comparison of POIC vs. Other OPAT Populations

Reference	No. Pts	Successful Outcome	ADRs leading to D/C of OPAT	Hospitalization Rate
POIC study population	250	89.2%	4.8%	12.4% (during OPAT)
Townsend J. et al.[4]	107	80.4%	14.9%	15.9% (30-day)
Schmidt M. et al. [5]	2228	n.r	n.r.	18.5% (90-day)
Allison GM. et al.[6]	782	n.r	n.r.	26% (30-day)
Rehm S. et al.[7]	103	86.4%	7.8%	17.5% (during OPAT)

Abbreviations, D/C: discontinuation; n.r.: not reported.

Discussion

We studied adult patients receiving OPAT in POICs for serious bacterial infections to investigate clinical outcome and complications during OPAT.

- The study cohort of 250 pts was randomly selected from 16 ID physician office infusion centers and included 175 BJI, 60 bacteremia/IE, and 15 CNS infections
- Overall median age was 59 years (range, 21 to 97) with 63% being male and 78% of pts receiving OPAT following hospital discharge
- Cephalosporins (57%) were most frequently used antimicrobials for all SBIs followed by vancomycin for BJI and bacteremia (25%) and penicillins for CNS infection (40%). The average OPAT duration was 32±21 days.
- 90% of pts achieved successful clinical outcomes
- The most frequent reason for early OPAT discontinuation was worsening of infection (62%). Significant predictors associated with unsuccessful outcomes were Charlson index ≥3, unplanned hospitalization during OPAT, occurrence of an adverse event and the use of vancomycin.
- Complications, defined as ADRs and unplanned hospitalizations, occurred overall in 38 pts (15.2%). Of those, 18 pts continued OPAT, ultimately leading to a successful clinical outcomes. Serious ADRs were observed in 12 pts (4.8%) and unplanned hospitalizations in 33 pts (13.2%), with 7 pts reporting occurrence of both.
- OPAT outcomes in POICs compared favorably to those of other published studies, with the lowest rates of ADRs leading to discontinuation of therapy and unplanned hospitalizations.

Conclusions

- **OPAT treatment of serious bacterial infections provided to patients through an Infectious Disease POIC resulted in a high success rate.**
- **Low rates of serious ADRs and unplanned hospitalizations were observed.**
- **These results support successful management of serious bacterial infections by Infectious Disease specialists through physician office infusion centers.**

References

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