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Outpatient Treatment of Infective Endocarditis (IE) at Physician Office Infusion Centers (POICs): A 2-Year Analysis of Clinical and Economic Outcomes

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Abstract

Background: : IE is life-threatening and requires prolonged intravenous (IV) antibiotics. Infectious Disease (ID) physician management of IE from the inpatient (IP) setting into ID-based POIC can provide closer monitoring and supervision compared to traditional outpatient (OP) settings with demonstrated improved outcomes, reduced/avoided IP stay, and associated cost savings. POICs provide a desirable alternative to home care, extended care facilities or other OP settings for treatment of IE. This study assesses clinical and economic outcomes of ID POIC-managed IE.

Methods: A multicenter, retrospective review was conducted of IE patients (pts) treated at 10 POICs in 2014-2015. Data collected were demographics, comorbidities, Charlson index (CI), IP stay, disease and therapy (tx) characteristics, clinical outcomes, readmissions and adverse events (AEs). Economic outcomes were measured from costs of total IP days saved by tx in the POIC and assessment of costs of other care settings. Costs were derived from a national database and published data. Student's *t*-test was used for analysis.

Results: 152 IE pts were included (97 native valve, 24 mechanical valve, 20 bioprosthetic valve, and 11 lead). Mean age was 58 years (38% ≥ 65 years), 72% male and 11% IV drug users. 95% had ≥ 1 predisposing factor for IE. Mean CI was 5. Average length of tx was 40.7 days, including 8.9 IP days. This compared with 12.5 mean IP days nationally, saving 3.6 IP days. Five pts received all tx in the POIC. Etiology included viridans streptococci (34%), *Staphylococcus aureus* (28%) and enterococci (14%). 86% of pts successfully completed IE tx with 5% hospitalized for valve replacement, all returning to the POIC for tx completion. Unplanned hospitalization occurred in 13% due to disease exacerbation or complications. Drug-related AEs occurred in 34 pts with 88% mild to moderate. Estimated costs for traditional care with 12.5 IP days were $5.2 million compared to $3.7 million for actual IP days of POIC pts, generating cost savings of $1.5 million (p<0.0001). Additionally, POIC care can result in cost savings of more than $1000 per day compared to other OP settings.

Conclusion: IE pts with considerable comorbidities were successfully managed by ID physicians through a POIC. IP stay was reduced or avoided; readmissions were low with significant cost savings compared to other settings of care.

Introduction

IE is a serious infectious disease with a high mortality. IE incidence has remained stable, however in recent years, *S. aureus* has become the most frequent causative pathogen.[1] Curative treatment requires prolonged therapy with parenteral, bactericidal antibiotics. Patients can be transitioned to outpatient parenteral antimicrobial therapy (OPAT) once they are stabilized and at lower risk of adverse events related to IE.[2] The enhanced supervision of a POIC may make this an ideal setting for the treatment of IE and provide cost savings through reduction of inpatient stay. A POIC can also provide coverage of therapy for Medicare recipients, with the potential for cost savings over other outpatient treatment settings.

Methods

Pts with confirmed diagnosis of IE infections treated with OPAT through 10 POICs during 2014 and 2015 were identified.

1. Data collection: demographics, anthropometrics, predisposing factors[5], comorbidities, IP stay, disease characteristics, microbiology, treatment, AEs, clinical outcome and hospital admissions
2. Charlson Index was calculated for all patients using standard definitions
3. Clinical outcomes:
   a) Successful completion of OPAT: Clinical signs/symptoms improved or resolved at end of OPAT, may include chronic suppressive antibiotic therapy
   b) Planned hospitalization: Pts who had an IE-related hospitalization scheduled during OPAT
   c) Unplanned hospitalization: Pts who had a therapy-related IE hospitalization
4. Economic outcomes:
   a) IP cost avoidance = (cost of national mean IP days) – (cost of study group mean IP days)
   b) POIC cost savings *vs.* Long Term Acute Care (LTAC) for study Medicare recipients = (LTAC cost per day) – (POIC cost per day)
   c) Total POIC cost savings for IE = IP cost avoidance + (POIC care cost – LTAC care cost)

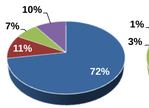
HCUP and CMS published data were used for cost estimates.[4-6] Student's *t*-test was used to determine statistical significance with p≤0.05 (MedCalc®, Ostend, Belgium).

Results

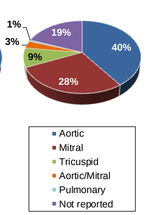
Demographics

Characteristics (n=152, 10 POICs)	N	%
Gender, male	110	72%
Age, mean years (range)	58 (23-93)	
Age ≥ 65	58	38%
Charlson Index, mean (range)	5 (0-18)	
Predisposing factor ≥1 for IE[3]	145	95%
Comorbidities per pt, mean (range)	4 (0-13)	
Intravenous drug use	16	11%
Hospitalized prior to OPAT	147	97%
Length of hospitalization, mean days (range)	8.9 (0-29)	

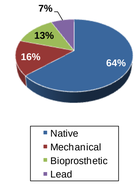
Location of IE



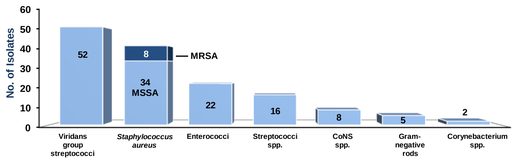
Anatomic Site of IE



Valve Type and Pacemaker Leads



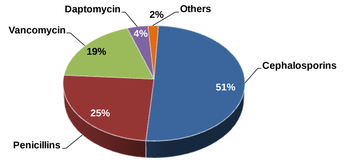
Microbiology



- A total of 147 isolates were reported in 135 pts
- Polymicrobial infections were present in 12 pts (9%)
- Culture negative infections were observed in 17 pts (11%)

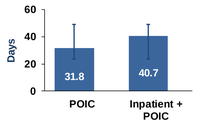
Organism	No. of Isolates								
	Anatomic Site					Valve Type and Pacemaker Leads			
	Mitral	Aortic	Tricuspid	Pulmonary	Unknown	Native	Mechanical	Pacemaker	Bioprosthetic
Viridans grp. streptococci	19	26	1	-	7	34	8	-	10
Staphylococcus aureus	11	12	7	-	13	31	3	6	2
CoNS spp.	1	3	1	1	2	3	1	2	2
Other streptococci spp.	5	6	1	-	4	10	4	1	1
Enterococci	6	11	2	-	4	9	7	2	4
Corynebacterium spp.	-	2	-	-	-	1	-	-	1
Gram-negative rods	-	3	1	-	1	3	2	-	-
Culture negative	9	9	-	-	1	13	1	1	2

Antimicrobial Use

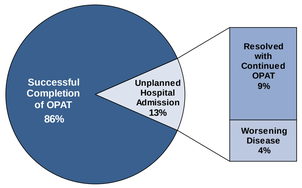


- Cephalosporins included ceftriaxone (36%), cefazolin (11%), cefotaxime (2%) cefepime (1%), and cefuroxime (1%)
- Penicillins included penicillin (11%), oxacillin (6%), ampicillin (5%), ampicillin/sulbactam (1%) and nafcillin (1%)
- Others included clindamycin (1%), ertapenem (1%), and aztreonam (1%)
- Dual therapy with gentamicin was used in 32 pts (21%) including penicillins (14 pts), ceftriaxone (12 pts), vancomycin (5 pts), and daptomycin (1 pt)

Mean Length of Therapy



Clinical Outcome



- 86% of pts (n=130) successfully completed OPAT
- 13% of pts (n=20) had unplanned hospital admissions, of which 9% (n=13) successfully continued OPAT following discharge
- 5% of pts (n=8) had planned admissions during OPAT for valve replacements followed by successful completion of therapy
- 1% of pts (n=2) were non-evaluable for outcomes at end of OPAT

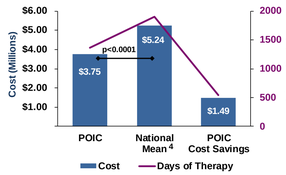
Safety

Adverse Event		Incidence No. of Pts (%)	Intervention/Outcome
Mild to Moderate	fatigue	9 (6%)	resolved
	rash	9 (6%)	antihistamines (n=4) drug changed (n=4) drug discontinued (n=1)
	diarrhea	5 (3%)	probiotics, resolved
	nausea and vomiting	3 (2%)	anti-emetics (n=2) drug changed (n=1)
	elevated serum creatinine	3 (2%)	drug changed (n=1) dose reduction (n=1) drug discontinued (n=1)
	shortness of breath	3 (2%)	drug changed (n=1) drug discontinued (n=1) fluid volume reduced (n=1)
	C. difficile infection	1 (0.6%)	metronidazole/resolved
	dizziness	1 (0.6%)	drug changed
	eosinophilia	1 (0.6%)	drug changed
	headache	1 (0.6%)	resolved
	yeast infection	1 (0.6%)	drug treatment/resolved
Serious	renal toxicity	2 (1.3%)	hospitalized
	pancytopenia	1 (0.6%)	drug changed
	leukopenia	1 (0.6%)	drug changed
	ototoxicity	1 (0.6%)	drug discontinued

- A total of 42 AEs were reported in 34 pts (22%) with 88% mild to moderate
- Overall incidence was 0.0103 AEs per patient day
- Hospitalizations for AEs were due to gentamicin (n=1) and vancomycin (n=1)
- 6 of 32 pts (19%) receiving gentamicin required discontinuation due to AEs
- Catheter complications occurred in 3 pts (2%), 2 requiring PICC replacement and one with DVT, all pts completed therapy

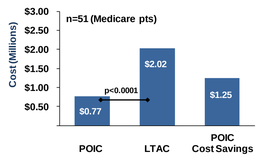
Economic Outcome

A. Inpatient Cost Avoidance through Transition to POIC

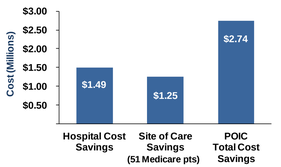


- Early discharge (n=117) or hospital avoidance (n=5) occurred in 122 pts (80%) for a reduction of 541 inpatient days . When compared to national IE inpatient stay, this led to significant cost savings of $1.49 million USD (p<0.0001)
- Transition of Medicare pts to a POIC rather than LTAC resulted in significant cost savings of $1.25 million USD (p<0.0001)

B. POIC Costs Savings vs. LTAC



C. Total POIC Costs Savings for IE



Discussion

This 2-year retrospective multicenter study of pts with IE has demonstrated:

- Successful treatment of native, mechanical, bioprosthetic and pacemaker lead IE in a POIC
- A variety of antimicrobials were successfully used, including those with multiple frequencies per day and dual therapies
- Therapy was completed with a low incidence of AEs (22%) and catheter complications (2%) with effective management by the ID physician in the POIC
- 86% had successful clinical outcomes. Of 20 pts with IE-related hospitalizations, 65% (n=13) returned to the POIC for completion of OPAT.
- 541 total inpatient hospital days were saved in 122 pts (80%) through early discharge to a POIC or avoidance of hospitalization
- Medicare IE pts in this study (34%) were successfully managed through a POIC avoiding treatment through a more costly site of care
- Early discharge resulted in cost savings of $1.49 million USD. Transition of Medicare pts to a POIC rather than LTAC resulted in cost savings of $1.25 million USD for a total projected cost savings of $2.74 million USD

Limitations to this study include:

- Costs utilized were published in 2009, 2012, and 2013 and may have underestimated the current costs of care in other outpatient settings, thereby lowering calculated cost savings through POICs. All Medicare recipients were evaluated for site of post-hospital care in either POIC or LTAC
- Discharge from hospital earlier than the average inpatient stay for IE was assumed to be related to availability to receive IV antibiotics through a POIC

Conclusions

- Management of IE through an ID-based POIC resulted in successful treatment of pts requiring long term IV antimicrobials
- Early discharge or hospital avoidance was achieved in 80% of pts.
- Hospital admissions related to therapy were low with 65% of pts returning to the POIC for successful completion of therapy following discharge
- Significant cost savings of $2.74 million USD were realized by treatment through a POIC due to early discharge or hospital avoidance and with treatment in the POIC versus LTAC

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