Complex Outpatient Oral Antimicrobial Therapy (COpAT) Program at a Rural Academic Medical Center: Evaluation of First 100 Patients

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ABSTRACT

Background: Literature shows early intravenous (IV) to oral (PO) antimicrobial transition for infective endocarditis (IE) and bone and joint infection (BJI) is noninferior to prolonged IV antimicrobial therapy. COVID-19 pandemic peaks resulted in critical shortages of staffed hospital beds spurring innovation. Outpatient parenteral antimicrobial therapy (OPAT), a well-established program using prolonged IV antimicrobials, faces challenges such as infusion resource needs and social circumstance limitations. Complex outpatient antimicrobial therapy (COpAT) uses PO in place of IV antimicrobials. We hypothesized rapid adoption of COpAT would decrease hospital length of stay and open beds while retaining satisfactory clinical outcomes.

Methods: COpAT protocols and guidelines by infection type and isolated organism were created. Hospitalized patients including persons who inject drugs (PWID) were evaluated for IV to PO antimicrobial transition by an infectious diseases (ID) physician and then followed by an ID physician-pharmacist team. Demographic, ID, and clinical outcome data for the first 100 COpAT patients between December 2020 and February 2022 were obtained by retrospective chart review.

Results: PWID accounted for 78% of COpAT patients. BJI followed by mixed infection (IE and BJI) was most prevalent with bacteremia in 53% of cases. *Staphylococcus aureus* was most frequently isolated. Oral linezolid and fluoroquinolones, often in combination, were most commonly used. IV and PO antimicrobials were taken for a median 28 and 14 days, respectively. The COpAT program saved 1425 IV antimicrobial and 1363 hospital days. Assuming daily inpatient cost of $2050, cost avoided was $2,794,150. COpAT patients participated in ID follow-up and adhered to PO antimicrobials with low 30-day readmission rates.

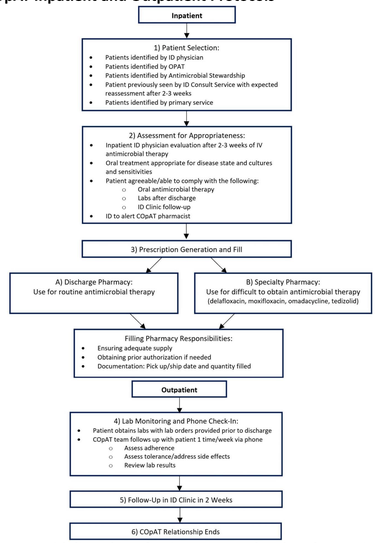
Conclusions: In a sample of 100 COpAT patients including PWID, IV to PO antimicrobial transition safely saved hospital days and mitigated critical bed shortages during pandemic peaks. A successful COpAT program requires a multidisciplinary group: close ID physician-pharmacist collaboration extending to OPAT and antimicrobial stewardship teams. With a COpAT program in place, even earlier IV to PO antimicrobial transitions should be studied.

BACKGROUND

- Literature supports early IV to PO transition for infections historically treated with prolonged IV antimicrobial therapy: IE and BJI.
- COVID-19 pandemic peaks resulted in critical shortages of staffed hospital beds, spurring innovation to decrease length of stay and open bed capacity.
- OPAT is a well-established program used to ensure safe and effective outpatient IV antimicrobial therapy.
- OPAT challenges include need for vascular access and infusion resources as well as social circumstance limitations such as injection drug use.
- From an antimicrobial use standpoint, there has been a movement in clinical ID toward earlier IV to PO transition.
- COpAT is defined as using PO antimicrobials with adequate bioavailability and infection site penetration for extended periods (requiring monitoring) in place of IV antimicrobials.
- We hypothesized rapid adoption of COpAT would decrease hospital length of stay and open bed capacity while retaining satisfactory clinical outcomes.

METHODS

- **Figure 1. COpAT Inpatient and Outpatient Protocols**



- **Figure 2. COpAT Guidelines by Infection Type and Isolated Organism**

Endocarditis				
Organism	**Antimicrobial Selection**	**Dose**	**Comments**	**Duration of Therapy**
MSSA	Dicloxacillin + rifampin	1 gm Q6H + 600 mg Q12H	- May replace dicloxacillin with cephalexin 1 g Q6H if dicloxacillin is not able to be obtained - May replace linezolid with tedizolid 200 mg Q24H if drug interactions or concern for cytopenias - Review drug interactions with rifampin - May consider rifampin 300 mg Q8H instead of 600 mg Q12H - Monitor K+ with TMP/SMX - Avoid fluoroquinolones (except delafloxacin) if QTc > 500 ms - Adjust all agents for renal function as needed	Total **6 weeks** combining IV and PO therapy
	Linezolid + rifampin	600 mg Q12H + 600 mg Q12H		
	TMP/SMX	2 DS (160/800 mg) Q12H OR 1 DS Q6H		
MRSA	Linezolid + rifampin	600 mg Q12H + 600 mg Q12H		
	TMP/SMX	2 DS (160/800 mg) Q12H OR 1 DS Q6H		
Enterococcus faecalis	Amoxicillin + moxifloxacin	1 gm Q8H + 400 mg Q24H		
	Amoxicillin + linezolid	1 gm Q8H + 600 mg Q12H		
Streptococcus spp.	Amoxicillin + rifampin	1 gm Q8H + 600 mg Q12H		
	Linezolid + rifampin	600 mg Q12H + 600 mg Q12H		
	Moxifloxacin + rifampin	400 mg Q24H + 600 mg Q12H		
Gram (-)	Levofloxacin	750 mg Q24H		

Bone and Joint Infections				
Organism	**Antimicrobial Selection**	**Dose**	**Comments**	**Duration of Therapy**
Gram (+), MSSA/MRSA	Linezolid	600 mg Q12H	- May replace linezolid with tedizolid 200 mg daily if drug interactions or concern for cytopenias - Add rifampin for prosthesis - Consider addition of rifampin in chronic *Staph aureus* osteomyelitis when using TMP/SMX - Average TMP/SMX dose is 7-8 mg/kg of TMP/day - Monitor K+ with TMP/SMX - Avoid fluoroquinolones (except delafloxacin) if QTc > 500 ms - Adjust all agents for renal function as needed	Total **6 weeks** combining IV and PO therapy
	TMP/SMX	2 DS (160/800 mg) Q12H		
	Clindamycin	300 - 450 mg Q6H - Q8H		
Gram (-), *Pseudmonas* spp. coverage	Ciprofloxacin	500 mg - 750 mg Q12H		
	Levofloxacin	750 mg Q24H		
	Moxifloxacin	400 mg Q24H		
Gram (-), no *Pseudmonas* spp. coverage	Amoxicillin-clavulanate	875/125 mg Q8 - 12H		
	TMP/SMX	1-2 DS (160/800 mg) Q12H		
Gram (+) (including MRSA) + Pseudomonas + Anaerobes	Delafloxacin	450 mg Q12H	- No data is available outside of SSTI	
Gram (+) (including MRSA) + Gram (-) (no Pseudomonas) + Anaerobes	Omadacycline	300 mg Q24H	- Post-marketing, real-world data outside of SSTI/CAP is available	

COpAT Guidelines were used as a reference with actual COpAT regimens tailored to patients.

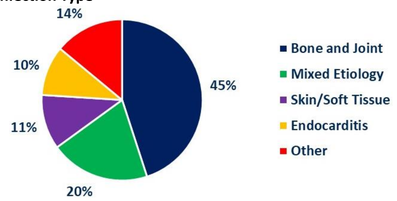
Retrospective chart review:
First 100 COpAT patients Dec. 2020-Feb. 2022

RESULTS

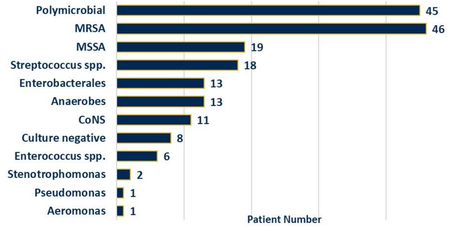
- **Table 1. Demographics**

N = 100	
Male, n (%)	57 (57)
Median Age, years (IQR)	41 (16.5)
Injection Drug Use, n (%)	78 (78)
Bacteremia, n (%)	53 (53)

- **Figure 3. Infection Type**



- **Figure 4. Isolated Organism**



- **Table 2. Antimicrobial Agents**

Targeted IV Therapy, n		COpAT, n	
Vancomycin	55	Linezolid	71
Daptomycin	17	Ciprofloxacin	13
Cefepime	14	Amoxicillin-clavulanate	12
Ceftriaxone	14	Metronidazole	12
Cefazolin	8	Levofloxacin	10
Ampicillin-sulbactam	6	TMP-SMX	8
Ceftaroline	3	Doxycycline	7
Oxacillin	3	Fluconazole	4
Clindamycin	2	Rifampin	4
Meropenem	2	Cephalexin	2
Piperacillin-tazobactam	2	Cefpodoxime	1
Other	5	Moxifloxacin	1

- **Table 3. Antimicrobial Duration**

Regimen	Median Days (IQR)
Targeted IV Therapy	28 (14)
COpAT	14 (0.5)
Total Therapy	42 (12.5)

RESULTS

- **Figure 5. Financial Outcomes**

1425 IV Antimicrobial Days Avoided → $42,684 IV Antimicrobial Cost Savings

1363 Hospital Admission Days Avoided → $2,794,150 Hospital Admission Cost Savings

- **Table 4. Clinical Outcomes**

N = 100	
Infectious Diseases Follow-Up, n (%)	56 (56)
Outpatient Labs, n (%)	42 (42)
Phone Check-In, n (%)	41 (41)
≥1 Missed Dose, n (%)	9 (9)
Adverse Event, n (%)	6 (6)
Side Effect, n (%)	5 (5)
Readmission ≤30 Days, n (%)	10 (10)
Readmission ≤30 Days COpAT-Related, n (%)	4 (4)

DISCUSSION

- The COpAT program matured into a multidisciplinary team providing monitoring and adherence counseling for select patients receiving PO antimicrobials.
- Of the first 100 COpAT patients, a majority were PWID
- Bacteremia occurred in more than half of cases, and MRSA was most frequently isolated, highlighting the inclusion of severe infections and resistant organisms.
- Antimicrobials with high bioavailability including linezolid and fluoroquinolones, often in combination, were most commonly used.
- The COpAT program reduced IV antimicrobial use and decreased hospital length of stay, resulting in significant cost savings.
- COpAT patients participated in ID follow-up and adhered to PO antimicrobials with few adverse events or side effects and low 30-day readmission rates.

CONCLUSIONS

- In a sample of 100 COpAT patients including PWID, IV to PO antimicrobial transition safely saved hospital days and mitigated critical bed shortages during pandemic peaks.
- The purpose of COpAT extends beyond facilitating hospital discharge to also include preventing hospital admission, avoiding vascular access, and optimizing overall patient care.
- A successful COpAT program requires a multidisciplinary group: ID physician-pharmacist collaboration extending to OPAT and antimicrobial stewardship teams.
- With a COpAT program in place, even earlier IV to PO antimicrobial transitions should be studied.

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Declaration of Interest:
Authors have no conflicts of interest or financial disclosures.