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Successful Management of ESBL Infections in Physician Outpatient Infusion Centers (POICs)

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Abstract

Objective: Infections with extended-spectrum β-lactamase (ESBL)-producing pathogens present treatment challenges with higher costs of care. Hospitalized patients (pts) with ESBL infections often require outpatient antimicrobial therapy (OPAT) following discharge. An Infectious Disease (ID) physician can facilitate optimal management in both the inpatient and outpatient setting, particularly when a POIC is an option. The increase of ESBL incidence led us to evaluate management and outcomes of genitourinary (GU) and intra-abdominal infections (IAI), the top two ESBL diagnoses treated in POICs.

Methods: Records were queried for pts hospitalized with ESBL infection and discharged to a POIC between 2019 and 2020. Primary outcome was completion of OPAT. Non-successful completion was defined as premature discontinuation of OPAT including hospital readmission. Adverse events (AEs) and re-treatment within 30 days were captured.

Results: A total of 112 pts (mean age: 59±17 years, 50% female) from 14 POICs were identified (93 GU, 19 IAI). Of these, 51% had their first ESBL infection and 52% were community-acquired prior to hospitalization. A total of 38% presented with concomitant bacteremia. ESBL *E. coli* was the predominant Gram-negative pathogen in both infection types (Table 1). Mean hospital LOS was 6±4 days (5±2 days GU, 11±6 days IAI) followed by 13±9 days of OPAT (12±7 days GU, 16±11 days IAI). Carbapenems were most frequently used as treatment (89% ertapenem, 7% meropenem). Overall, 106 pts (95%) successfully completed OPAT. Six pts (5%) discontinued due to hospital readmission. AEs were reported in 15 pts (13%), the majority of which were mild. Re-treatment in the POIC within 30 days post OPAT completion occurred in 6 GU pts. None were lost to follow-up. Table 1 summarizes primary outcome by clinical characteristics. Both GU and IAI pts had 95% successful OPAT completion.

Conclusion: Outpatient treatment of ESBL infections in POICs post-hospitalization showed high completion rates with low occurrence of readmissions and re-treatments. Consistent with a rise in ESBL infections, our incidence of community-acquired ESBL infections prior to hospitalization were high at 52%. Once ESBL infections were identified in the hospital, the ID physicians with a POIC rapidly facilitated discharge to OPAT.

Objectives

Infections with extended-spectrum β-lactamase (ESBL)-producing pathogens have been on the rise in both acute care and outpatient settings.[1-4] Data from our own POIC setting showed a 36% increase in ESBL genitourinary (GU) and intra-abdominal infections (IAI) from 2018-2020.[4] These are the top 2 ESBL diagnoses treated in our POICs, with a majority coming from the hospital.

The objective of this study was to evaluate ESBL GU and IAI infections treated with OPAT post-hospital discharge.

Methods

Study design: Retrospective, multicenter cohort study including 14 ID POICs
Study population: Previously hospitalized pts with ESBL infections discharged to a POIC for OPAT with GU or IAI infections
Data collection: Medical records were queried between 2019 and 2020 and the following data collected:

- Demographics (age, gender, comorbidities, underlying pathology)
- ESBL infection type characteristics
- Length of therapy prior to hospitalization
- OPAT management (therapy regimen, adverse events(AEs), length of OPAT)

Primary Outcome:

- Success (completion of OPAT as prescribed)
- Non-success (early discontinuation of OPAT for any reason)
- Risk factors for non-success

Statistical Analysis: Descriptive statistics were used. Bivariate comparison of ESBL risk factors between success and non-successful outcomes was performed using Chi-Square test or Fisher's exact test with *P*-values <0.05 considered statistically significant.

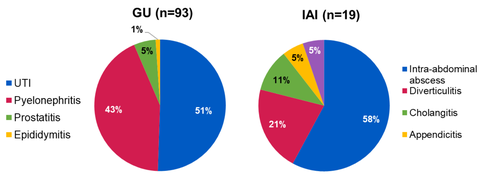
Study Cohort

- Data from 14 POICs revealed 112 pts with ESBL-producing pathogens

Demographics

Variable	All Patients n=112
Age, mean±SD	58±17
>65 years	41 (26%)
Gender, female	58 (50%)
Body mass index, mean (mg/kg^2)	29 ± 11
>30	41 (36%)
Infection Type	
Genitourinary infection (GU)	93 (83%)
Intra-abdominal infection (IAI)	19 (17%)
Pre-existing medical condition	50 (44%)
Malignancy	34 (30%)
Diabetes mellitus	30 (26%)
Heart disease	24 (21%)
Chronic renal disease	19 (16%)
Chronic liver disease	10 (9%)
Transplant	5 (4%)
Charlson comorbidity index, mean (SD)	4.7 ± 3
>2	83 (72%)
Other risk factors	
Prior antibiotic use	77 (67%)
History of recurrent disease	57 (50%)
Hospitalization in last 3 months	43 (37%)
Concomitant bacteremia	40 (35%)
Invasive procedure in last 30 days	32 (28%)
Underlying pathology	
Urinary catherization/stent	22 (19%)
Urinary obstruction/kidney stones	19 (17%)
Intestinal/bowel obstruction	10 (9%)

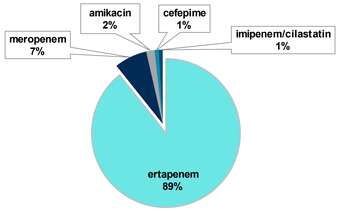
ESBL Infection Type Characteristics



- 4 pts overall had ESBL infection mixed with Gram-positive organisms
- 8 pts overall had multiple Gram-negative pathogens
- 58 pts (52%) had community onset infections prior to hospitalization including 52 in the GU group and 6 in the IAI group
- All pts were discharged from a hospital with an overall mean LOS of 6±4 days (5±2 days GU, 11±6 days IAI)

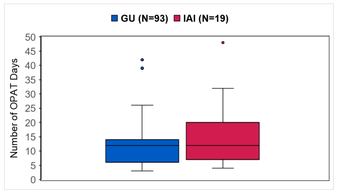
Therapy Characteristics

OPAT Management of ESBL Infections



- Carbapenems were most frequently used as treatment (89% ertapenem, 7% meropenem, 1% imipenem/cilastatin).
- Treatment-related mild to moderate AEs were reported in 15 pts (13%), not resulting in early discontinuations most commonly nausea (n=4) and fatigue (n=2)

Length of OPAT[6,7]



- Average OPAT duration was 13±9 days or a median of 12 days (IQR 7,15)

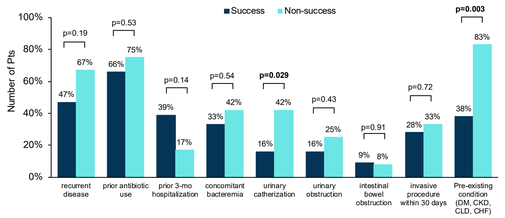
Treatment Outcomes

Variable	All Patients n=112	Successful Treatment n=106	Non-Successful Treatment* n=6
Genitourinary infection	**93 (100%)**	**88 (95%)**	**5 (5%)**
UTI	47 (50%)	43	4
Pyelonephritis	40 (43%)	39	1
Prostatitis	5 (5%)	5	-
Epididymitis	1 (1%)	1	-
Initial ESBL infection	46 (49%)	45	2
Community-acquired infection	52 (56%)	51	1
Concomitant bacteremia	37 (40%)	32	5
ESBL pathogen			
E. coli	83 (89%)	79	4
Klebsiella pneumoniae	9 (10%)	8	1
Proteus mirabilis	1 (1%)	1	-
Intra-abdominal infection	**19 (100%)**	**18 (95%)**	**1 (5%)**
Intra-abdominal abscess	11 (58%)	11	-
Diverticulitis	4 (21%)	4	-
Other[1]	4 (21%)	3	1
Initial ESBL infection	11 (58%)	10	1
Community-acquired infection	6 (32%)	6	-
Concomitant bacteremia	5 (26%)	4	1
ESBL pathogen			
E. coli	18 (95%)	17	1
E. coli and *Klebsiella oxytoca*	1 (5%)	1	-

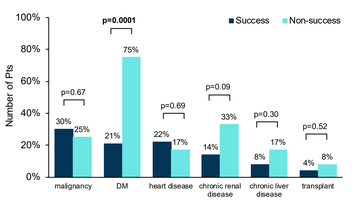
*; premature discontinuation of OPAT due to readmission to hospital.
1; successful = cholangitis (n=2), appendicitis (n=1); non-successful = peritonitis (n=1)

- Overall, 95% in each diagnostic group successfully completed OPAT
- 52% had a community acquired ESBL infection upon admission to the hospital
- Six pts (5%) did not complete treatment and were readmitted to the hospital
- 5 pts (4%), all GU, had recurrence within 30 days with re-treatment following successful OPAT. Underlying conditions present were diabetes mellitus (n=3), nephrolithiasis (n=2), BPH (n=1), liver transplant (n=1), urinary stents (n=1)

ESBL Risk Factors and Clinical Outcome



- Urinary catheterization/stents (p=0.029) and pre-existing medical condition (p=0.003) were significant ESBL risk factors associated with a non-successful outcome.



- Further analysis of pre-existing conditions revealed DM being a significant risk factor for non-success of ESBL infections (p = 0.0001)

Discussion

- Overall, 121 pts hospitalized with ESBL infections were discharged with OPAT to be received through an ID POIC. Only GU and IAI infections were captured, with the majority GU infections.
- Hospital LOS was 6±4 days followed by 13±9 days of OPAT.
- Ertapenem (89%) was the most common treatment, and a preferred antibiotic for treatment of ESBL *Enterobacterales*.[5] All antibiotics were well tolerated overall.
- ESBL *E. coli* was the predominant pathogen at 90% (83% GU, 95% IAI)
- Overall, 95% of pts had successful OPAT treatment of ESBL infections post-hospitalization.
- Over half (52%) had community-onset ESBL infection prior to hospitalization, with all but 1 pt successfully treated with OPAT.
- Six pts (5%) discontinued due to hospital readmission with non-successful treatment of OPAT.
- Re-treatment within 30 days of successful OPAT occurred in 5 pts with underlying conditions.
- Risk factors identified as significant for non-successful treatment outcomes were: urinary catheterization/stents, overall pre-existing medical conditions and diabetes.

Conclusion

- A high treatment success rate was demonstrated in ESBL infected GU and IAI patients receiving OPAT post-hospital discharge.
- Over half of the patients had a confirmed ESBL infection upon admission to the hospital, indicating a spread of ESBL organisms in the community. Clinicians should consider this potential for community-onset disease in pts who are not responding to traditional therapies.
- Patients identified at significant risk for non-successful outcomes with ESBL infections are those with comorbid conditions, particularly diabetes and those with urinary catheterization or stents.
- With the consistent rise in ESBL infections, management of these infections remains a high priority for ID physicians and pharmacists. The POIC setting can facilitate rapid discharge and OPAT treatment for hospitalized patients including complex patients with multidrug resistant organisms like ESBLs.

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