Association of Infection Recurrence with Oral Step-Down vs Continued Intravenous Antimicrobial Therapy in Patients with Complicated Intra-Abdominal Infection

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BACKGROUND

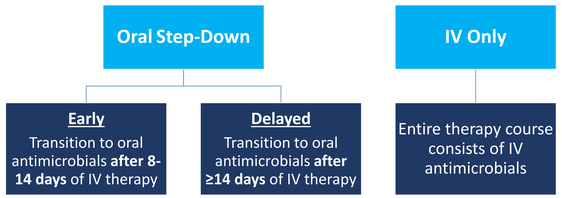
- Optimal management of complicated intra-abdominal infections (cIAIs) requires source control and appropriate antimicrobial therapy.[1,2,3]
- The Surgical Infection Society (SIS) recommends a short antimicrobial course of 4 to 7 days for cIAIs once source control is achieved.[1,2] However, several factors (e.g. inadequate source control, immunosuppression) may warrant longer duration to be completed either inpatient or outpatient.
- Outpatient parenteral antimicrobial therapy (OPAT) can carry risks, such as line-associated thromboses and infection. Data are currently limited on efficacy and safety of oral step-down therapy versus intravenous (IV)-only antimicrobial therapy in cIAIs.

OBJECTIVES

- To evaluate differences in infection recurrence between oral step-down and continued IV antimicrobial therapy for the treatment of cIAI's requiring an extended antimicrobial therapy

METHODS

- Single-center, retrospective review of electronic medical records (EMR) from March 20, 2017 to October 18, 2021
- **Intervention Groups**



- **Inclusion criteria**: Adults (≥18 y) admitted to The University of Texas Southwestern Medical Center (UTSW) with a diagnosis of intra-abdominal infection (ICD-10 codes) who received intravenous antimicrobials during hospitalization for > 7 days
- **Exclusion criteria**: 1) Diagnoses of primary peritonitis, peritoneal dialysis catheter peritonitis, necrotizing pancreatitis, or fistulizing inflammatory bowel disease; 2) Repeat hospitalizations during the study period; 3) Transferred from another acute facility after receiving care for > 24 hours
- **Primary Outcome**: Infection recurrence (defined as re-initiation of antimicrobial treatment with the same or broader-spectrum regimen after a treatment-free period of ≥ 3 days)
- **Secondary outcomes**: 1) Treatment escalation; 2) Repeat source control; 3) Treatment-related complications such as line-related infection or thromboembolism, *Clostridioides difficile* infection, or antimicrobial-related adverse effects; 4) 28-day and 90-day mortality

RESULTS

Figure 1. Oral antimicrobial agents used in oral step-down group

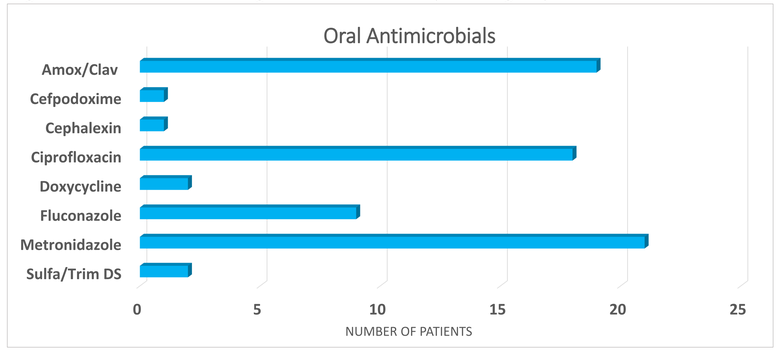


Table 1. Baseline Characteristics and Hospitalization Data

	IV Only (n = 199)	Oral Step-Down (n = 49)	P-value
Age, years, median (IQR)	67 (58-73)	62 (54.5-70.5)	0.135
Male, n (%)	103 (51.8)	16 (32.7)	**0.017**
Race, n (%)			0.111
Asian	6 (3.0)	2 (4.1)	
Black or African American	33 (16.6)	16 (32.7)	
Caucasian	140 (70.4)	32 (61.2)	
Other	21 (10.0)	1 (2.0)	
Charlson comorbidity index, median (IQR)	7 (5-11)	6 (4-9.5)	0.086
End-stage liver disease, n (%)	25 (12.6)	3 (6.1)	0.312
Chronic kidney disease, n (%)	39 (19.6)	9 (18.4)	0.845
Diabetes mellitus, n (%)	63 (31.7)	21 (42.9)	0.138
GI malignancy, n (%)	37 (18.6)	9 (18.4)	0.971
Immunocompromised, n (%)	59 (29.6)	11 (22.4)	0.316
Hospital length of stay, days, median (IQR)	19 (12-30)	13 (8.5-19)	**< 0.0001**
Infectious disease consult, n (%)	76 (38.2)	24 (49.0)	0.168
Oral intolerance, n (%)	36 (18.1)	--	

Table 2. Source Control and Antimicrobial Therapy Data

Source control procedure, n (%)	158 (79.4)	41 (83.7)	0.501
Procedure type, n (%)			0.857
Open	114 (72.2)	29 (70.7)	
Percutaneous	44 (27.8)	12 (29.3)	
Time to 1st source control, days, median (IQR)	2 (0-7)	1 (0-5)	0.226
Number of source control procedures, median (IQR)	1 (1-2)	1 (1-2)	0.208
Duration of overall therapy, days, median (IQR)	13 (9-21)	23 (16-37)	**< 0.0001**
Discharged on OPAT, n (%)	31 (15.6)	4 (8.2)	0.252
Positive intra-abdominal culture, n (%)	67 (33.7)	21 (42.9)	--

Figure 2. Infection Organ of Origin

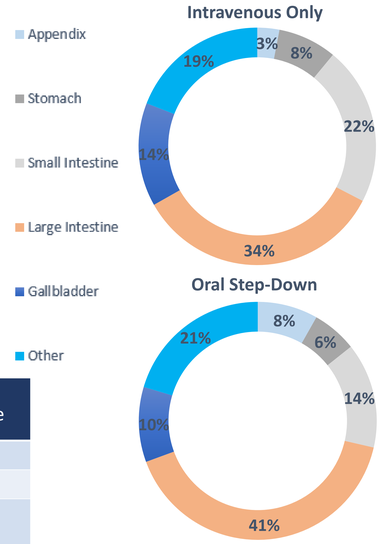


Table 3. Microbiologic Data

Organism	IV Only (n = 199)	Oral Step-Down (n = 49)
Staphylococcus spp.	8 (11.9)	2 (9.5)
MRSA	2 (3.0)	1 (4.8)
Streptococcus spp.	6 (9.0)	4 (19.0)
Enterococcus spp.	9 (13.4)	4 (19.0)
VRE	2 (3.0)	--
Escherichia coli	17 (25.4)	3 (14.3)
Klebsiella spp.	2 (3.0)	2 (9.5)
ESBL	4 (6.0)	1 (4.8)
Pseudomonas aeruginosa	3 (4.5)	3 (14.3)
Bacteroides spp.	3 (4.5)	4 (19.0)
Other bacteria*	8 (11.9)	1 (4.8)
Candida albicans	5 (7.5)	3 (14.3)
Other fungus^	6 (9.0)	1 (4.8)
Polymicrobial (≥3 organisms)	24 (35.8)	3 (14.3)

*Other bacteria: *Aeromonas* spp., *Clostridium tertium*, *Diphtheroids*, *Enterobacter cloacae* complex, *Eubacterium* spp., *Mycobacterium avium* complex, *Proteus mirabilis*, *Raoultella ornithinolytica*
^Other fungus: *Candida glabrata*, *Candida krusei*, *Candida lusitaniae*, *Aspergillus* spp.

Table 4. Primary and Secondary Outcomes

	IV Only (n = 199)	Oral Step-Down (n = 49)	P-value
Infection recurrence, n (%)	26 (13.1)	6 (12.2)	0.878
Time to infection recurrence, days, median (IQR)	10 (6-12)	8.5 (5-12)	0.828
Treatment escalation, n (%)	82 (41.2)	21 (42.9)	0.834
Repeat source control, n (%)	74 (37.2)	15 (30.6)	0.390
Mortality			
28-day mortality	19 (9.5)	1 (2.0)	0.138
90-day mortality	25 (12.6)	6 (12.2)	0.952
Treatment-related complication, n (%)			
OPAT complication	1 (0.5)	--	--
C. difficile infection	8 (4.0)	3 (6.1)	0.458
Adverse drug event*	6 (3.0)	5 (10.2)	**0.044**

*Adverse drug events: dermatologic reaction, gastrointestinal upset, diarrhea, nausea/vomiting, fatigue, thrombocytopenia, and kidney injury

CONCLUSION

Transition to oral step-down after initial IV antimicrobial therapy may be an alternative strategy for the management of cIAIs; however, larger non-inferiority studies are warranted to confirm the safety and efficacy of this approach.

REFERENCES

1) Solomkin et al. Surg Inf Soc & Inf Dis Soc of Amer. 2010;11(1):79-109. 2) Mazuski et al. Surg Inf Soc. 2017;18(1):1-76. 3) Rhodes et al. Surv Sepsis Camp. 2017;43(3):304-377. 4) Sartelli et al. Wld J Emer Surg. 2014;9-37. 5) CDER. FDA. 2018;(1):1-17. 6) Inui et al. Surg. 2009146(4):654-662. 7) Tellor et al. Surg Inf. 2015;16(6):785-793. 8) Wacha et al. Lang Arch Surg. 1999;384(1):24-32