

Antibiotic stewardship for intra-abdominal infections: early impact on antimicrobial utilization and patient outcomes

Presentation #B1-188

Yanina Dubrovskaya PharmD¹, Sapna A. Mehta MD¹, Marco Scipione PharmD¹, Michael S. Phillips MD¹, Jerry Altshuler PharmD¹, John Papadopoulos PharmD^{1,2}
¹NYU Langone Medical Center, ²Arnold and Marie Schwartz College of Pharmacy

Contact Information
 Yanina Dubrovskaya, Pharm.D., BCPS
 Clinical Coordinator, Infectious Diseases
 Pharmacotherapy
 NYU Langone Medical Center
 550 First Avenue
 New York, NY 10016
 yanina.dubrovskaya@nyumc.org

Abstract (modified)

Background

After review of local susceptibilities, a multidisciplinary group developed guidelines for empiric therapy of complicated intra-abdominal infections (cIAI) in adults. These guidelines recommend cefazolin for mild to moderate cholecystitis, ceftiofur (CX) for mild to moderate extra-biliary infections and piperacillin-tazobactam (PTZ) or meropenem ± aminoglycosides ± vancomycin for severe community-acquired or health-care associated cIAI.

Methods

All patients admitted to general surgery over a four month period before guideline implementation (baseline group) and one month after guideline implementation (AGI group) were included. The primary endpoint was antimicrobial utilization measured in defined daily doses (DDD)/1000 patient (pt) days per standard methodology. Secondary endpoints included hospital-acquired *Clostridium difficile* infection (HA-CDI) rates, readmission to the surgical service within 30 days and length of stay (LOS).

Results

626 admissions to general surgery (304 baseline, 322 AGI) were reviewed. Among antimicrobials administered, ampicillin-sulbactam (AS) utilization was the highest, with a mean of 141 DDD/1000 pt days in baseline group and 130 DDD/1000 pt days AGI (p=0.8). CX utilization increased by 48 DDD/1000 pt days (p=0.001) AGI. Intravenous ciprofloxacin (CP) use decreased by 22.6 DDD/1000 pt days (p=0.003) AGI. PTZ utilization increased by 22 DDD/1000 pt days (p=0.41). Cefazolin use decreased from 32.8 DDD/1000 pt days to 13.8 DDD/1000 pt days AGI (p=0.006). The HA-CDI rate for all patients admitted to the general surgery decreased from 3.1 to 2.7/1000 pt days (p=0.65) AGI. Thirty-day readmission rate decreased by 1.8% (p=0.26) AGI. Mean LOS was 8.4 and 7.9 days (p=0.5) at baseline and AGI, respectively.

Conclusion

Implementation of guidelines for empiric coverage of cIAI combined with stewardship interventions increased CX utilization; however, continued high use of AS and CP and low use of cefazolin warrants further intervention. An early stage post-implementation review of adherence to inpatient guidelines helped our program identify areas to direct further stewardship education to improve the use of appropriate empiric antimicrobial therapy.

Background

- 2010 Infectious Diseases Society of America/Surgical Infection Society (IDSA/SIS) guidelines on "Diagnosis and Management of Complicated Intra-abdominal Infection in Adults and Children" emphasize the role of antimicrobial stewardship in identifying appropriate antimicrobial agents based on local susceptibilities and subsequent implementation of hospital specific guidelines.¹
- Previously, ampicillin-sulbactam (AS) and ciprofloxacin (CP) in combination with metronidazole were antimicrobials of choice at our institution for empiric coverage of intra-abdominal infections.
 - IDSA/SIS guidelines advise that fluoroquinolones should not be used for empiric therapy if hospital surveillance indicates > 10% resistance of *E. coli* to fluoroquinolones.¹
 - Rates of resistance of *Escherichia coli* to AS and CP were high: 2009:50% of *E. coli* intra-abdominal isolates resistant to AS; 39% resistant to CP.

- After review of local susceptibilities, a multidisciplinary group developed guidelines for empiric therapy of complicated intra-abdominal infections (cIAI) in adults. Our guidelines recommend :
 - Cefazolin for mild to moderate cholecystitis.
 - Ceftiofur (CX) for mild to moderate extra-biliary infections.
 - Piperacillin-tazobactam (PTZ) or meropenem ± aminoglycosides ± vancomycin for severe community-acquired or health-care associated cIAI.
 - Ciprofloxacin ± metronidazole only for patients with severe penicillin type 1-immEDIATE hypersensitivity.

- Guidelines were disseminated to clinicians as well as posted on our hospital's antibiotic stewardship website.

Objective

The objective of this study was to evaluate the early impact of these guidelines on antimicrobial utilization and clinical outcomes.

Disclosure: The authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities.

Methods

- All patients admitted to general surgery over a four month period before guideline implementation (baseline group) and one month after guideline implementation (AGI group) were included.
- Data on antimicrobial utilization were extracted from a pharmacy database of administered antimicrobials.
- Patient-specific data retrospectively collected from electronic medical records.
- Primary outcome:** Antimicrobial utilization measured in defined daily doses (DDD)/1000 patient (pt) days per standard methodology.^{2,3}
- Secondary outcomes:**
 - Hospital-acquired *Clostridium difficile* infection (HA-CDI) rates⁴
 - Readmission to the surgical service within 30 days
 - Length of stay (LOS)
- Data were analyzed using SPSS for Windows (version 19.0).
 - Chi-square or Fisher exact test were used for categorical variables, 2-tailed t-test or Mann-Whitney U test were used for continuous variables.
 - P-value < 0.05 was considered to be statistically significant

Results

Figure 1. Antimicrobial Utilization in DDD/1000 patient days

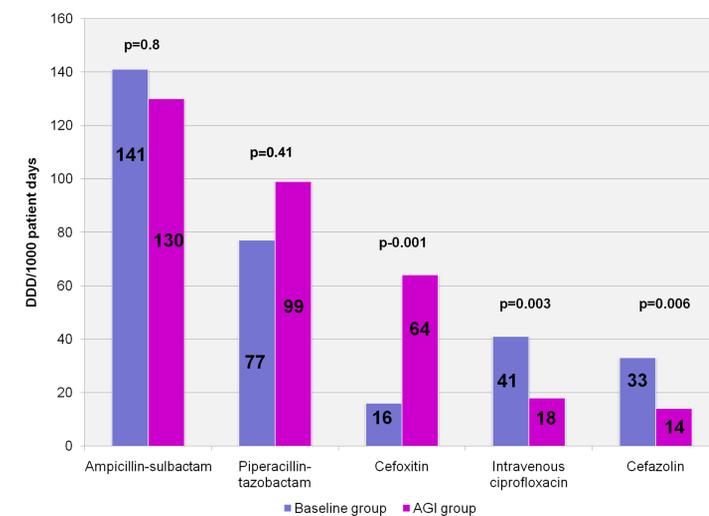


Table 1. Secondary Outcomes

	Baseline group n=304	AGI group n=322	p-value
Mean LOS ± SD, (range)	8.4 ± 10.5	7.9 ± 7.17	0.50
HA-CDI rate/1000 pt days	3.1 ± 2.3	2.7 ± 1.8	0.65
30-days readmission, n (%)	16 (5.3)	11 (3.4)	0.26

- A subgroup of 340 patients with cIAI (159 baseline and 181 AGI group) was identified based on clinical diagnosis.

- Baseline demographic and clinical characteristics were similar between both groups.
- The most common diagnosis was appendicitis followed by acute cholecystitis/cholangitis.
- There were significantly more patients with diverticulitis in the AGI group.

Results (cont'd)

Table 2: Clinical characteristics and antimicrobial use in patients with complicated intra-abdominal infections

	Baseline group n=159	AGI group n=181	p-value
Mean age ± SD, years	47 ± 20	51 ± 21	0.07
Male gender, n (%)	72(45)	86 (48)	0.68
Reported beta-lactam allergy, n (%)	29 (18)	24 (13)	0.21
anaphylaxis, n (%)	2 (1)	4 (2)	0.51
Intensive care unit stay during admission, n (%)	9 (6)	16 (9)	0.26
Malignancy, n (%)	14 (9)	13 (7)	0.58
Surgical procedures, n (%)	135 (85)	140 (77)	0.08
Diagnosis, n (%)			
appendicitis	79 (50)	76 (42)	0.16
acute cholecystitis/cholangitis	34 (21)	36 (20)	0.73
diverticulitis	11 (7)	26 (14)	0.03
intra-abdominal abscess	11 (7)	17 (9)	0.41
abdominal wound	14 (9)	11 (6)	0.34
peritonitis	9 (6)	15 (8)	0.35
necrotizing pancreatitis	1 (1)	0	0.29
Median LOS days (range)	3 (1-92)	4 (1-34)	0.32
30-days readmission, n (%)	12 (8)	7 (4)	0.14
Antimicrobial use ¹ , n, (%)			
ampicillin-sulbactam	106 (67)	101 (56)	0.04
ceftiofur	9 (6)	45 (25)	0.0001
intravenous ciprofloxacin	29 (18)	26 (14)	0.33
cefazolin	7 (4)	9 (5)	0.80
piperacillin-tazobactam	24 (15)	39 (22)	0.13
meropenem	10 (6)	8 (4)	0.44

¹ Patients who received at least one dose of selected antimicrobials

- Utilization of IV CP using DDD/1000 pt days decreased significantly AGI but was still frequently requested by prescribers.
 - Even though IV CP required preauthorization, 14% of patients AGI had received at least 1 dose of IV CP.
- In order to better understand the continued use of AS and IV CP AGI, we evaluated the admitting diagnosis of patients in the AGI group who received these agents:
 - Among patients who received AS
 - 46% (46/101) had a diagnosis of appendicitis
 - 28% (28/101) had a diagnosis of acute cholecystitis/cholangitis
 - Among patients who received intravenous CP
 - 35% (9/26) had a diagnosis of appendicitis
 - 24% (8/26) had a diagnosis of diverticulitis
- According to our guidelines, cefazolin or CX are recommended for appendicitis, cholecystitis/cholangitis or diverticulitis.

Conclusions

- Implementation of guidelines for empiric coverage of cIAI combined with stewardship interventions increased CX utilization.
- Continued high use of AS and CP and low use of cefazolin warrants further education about our institution specific guidelines, including syndrome-specific rationale for empiric therapy.
- Resistance to CX in anaerobic isolates is of concern.^{5,6} Anaerobic susceptibilities will be closely monitored and our guidelines will be reevaluated as needed.
- An early stage post-implementation review of adherence to inpatient guidelines helped our program identify areas to direct further stewardship education to improve the use of appropriate empiric antimicrobial therapy.

References

- Solomkin JS, Mazuski JE, Bradley JB, et al. Diagnosis and Management of Complicated Intra-abdominal Infection in Adults and Children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis* 2010;50:133-64
- http://www.whooc.no/atc_ddd_methodology/who_collaborating_centre/, accessed September 21, 2011
- Polk RE, Fox C, Mahoney A, Letcavage J, MacDougall C. Measurement of adult antibacterial drug use in 130 US hospitals: comparison of defined daily dose and days of therapy. *Clin Infect Dis* 2007;44:664-70.
- MacDonald LC, Coignard B, Dubberke E, et al. Recommendations for surveillance of *Clostridium difficile*-associated disease. *Infect Control Hosp Epidemiol* 2007;28:140-145.
- Hecht DW. Prevalence of antibiotic resistance in anaerobic bacteria: worrisome developments. *Clin Infect Dis* 2004;39:92-97.
- Snydman DR, Cuchural GJ Jr, McDermott L, Gill M. Correlation of various *in vitro* testing methods with clinical outcomes in patients with *Bacteroides fragilis* group infections treated with ceftiofur: a retrospective analysis. *Antimicrob Agents Chemother* 1992;36:540-4.

Results (cont'd)

Table 3: Infection site and microbiological results of culture-positive complicated intra-abdominal infections

	Baseline group n=33	AGI group n=41	p-value
Site of infection, n (%)			
abscess/fluid collection	14 (42)	15 (37)	0.61
abdominal fluid	10 (30)	13 (32)	0.9
bile	1 (3)	6 (15)	0.1
blood	5 (15)	4 (10)	0.48
wound	5 (15)	4 (10)	0.48
Facultative and aerobic Gram-negative, n (%)			
<i>Escherichia coli</i>	16 (49)	24 (59)	0.39
<i>Klebsiella sp.</i>	4 (12)	9 (22)	0.27
<i>Pseudomonas aeruginosa</i>	3 (9)	5 (12)	0.67
<i>Proteus sp.</i>	2 (6)	1 (2)	0.43
<i>Enterobacter sp.</i>	3 (9)	3 (7)	0.78
<i>Morganella sp.</i>	2 (6)	0	0.11
<i>Providencia sp.</i>	0	1 (2)	0.37
<i>Serratia sp.</i>	0	1 (2)	0.37
Anaerobic, n (%)			
<i>Bacteroides fragilis</i>	1 (3)	6 (15)	0.09
<i>B. thetaiotaomicron</i>	1 (3)	1 (2)	0.88
<i>B. ovatus</i>	0	1 (2)	0.37
<i>Prevotella oralis</i>	1 (3)	1 (2)	0.88
<i>Peptostreptococcus magnus</i>	1 (3)	0	0.26
Gram-positive aerobic cocci, n (%)			
<i>Streptococcus sp.</i>	4 (12)	3 (7.3)	0.48
<i>Enterococcus faecalis</i>	6 (18)	1 (2)	0.02
<i>Enterococcus faecium</i>	3 (9)	4 (5)	0.473
<i>Enterococcus sp.</i>	1 (3)	0	0.26
<i>Staphylococcus sp. (all MSSA)</i>	3 (9)	1 (2)	0.25
Polymicrobial infection, n (%)	16 (49)	19 (46)	0.85

Table 4: Susceptibility Data

	Baseline group	AGI group
Nonsusceptible isolates, n (%)		
<i>E. coli</i>		
ampicillin-sulbactam	7/16 (49)	7/24 (29)
ciprofloxacin	4/16 (45)	11/24 (49)
<i>Klebsiella sp.</i>		
ampicillin-sulbactam	1/4 (25)	3/9 (33)
ciprofloxacin	0	3/9 (33)
Anaerobic		
ceftiofur	1/4 (25)	2/9 (22)