Antimicrobial stewardship interventions in *Clostridium difficile* infections

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Introduction

Clostridium difficile-infections (CDI) are difficult to manage and contribute to significant patient morbidity and mortality. Inappropriate adherence to guideline-driven CDI therapy can lead to poor patient outcomes. Antimicrobial stewardship interventions (ASPI) have been shown to improve patient outcomes and decrease healthcare expenditure. Specific CDI targets for ASPI may include appropriate treatment recommendations, discontinuing unnecessary antibiotics and proton-pump inhibitors (PPI).

We describe the management and outcomes of CDI before and after the implementation of an ASPI that included guidelines, education and prospective audit with feedback.

Methods

Study Design

This was an IRB approved, retrospective quasi-experimental study conducted at the Henry Ford Hospital in Detroit, Michigan, USA. The objectives of this study were to:

i. Assess compliance to institutional CDI guidelines
ii. Compare clinical outcomes of patients receiving ASPI for CDI to those who did not

Study Population

The study population included hospitalized patients with CDI from August 2013 to January 2014 (pre-ASPI) and May 2014 to October 2014 (post-ASPI). Consecutive patients were screened to reach a convenient sample size of 259.

Inclusion Criteria	Exclusion Criteria
• Clinically and microbiologically proven CDI • Positive CDI after admission within inpatient settings or including the following: • Emergency department or outpatient clinic prior to admission	• <18 years old • CDI positive patients transferred from an outside hospital • Patients in outpatient settings who test positive for toxigenic *C. difficile*

Data Collection

Clinical and microbiological data were collected from electronic medical records using a standardized case report form. Data collected included: patient demographics, select comorbid conditions, CDI therapy characteristics (treatment selection, duration of therapy), ASP interventions (appropriate antibiotic use, PPI evaluation, infectious diseases consultation, imaging ordered and evaluated, and proportion of interventions accepted by primary team), and patient disposition/outcomes (patient death, recurrence, colectomy, diverting loop ileostomy, rehospitalization for CDI, and length of hospitalization).

Microbiological data collected included: CDI testing method (toxin A/B or PCR) and date of positive CDI. All laboratory testing was completed by the Henry Ford Health System Clinical Microbiology Core Laboratory according to Clinical and Laboratory Standards Institute (CLSI) standards.

Statistical Analyses

Descriptive statistics were used to characterize the CDI treatment and disease severity. Bivariate analyses were used compare differences in patient outcomes among pre- and post-ASPI. Categorical data were analyzed using Pearson's Chi-square or Fisher's Exact test. Continuous data were analyzed using the Mann-Whitney-U test. All calculations were performed using SPSS version 23.0.

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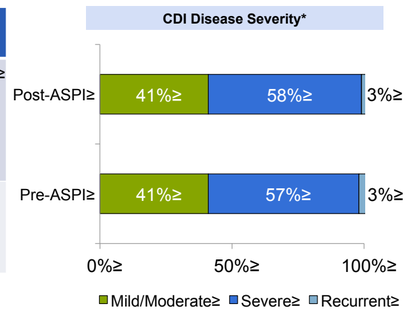
Results

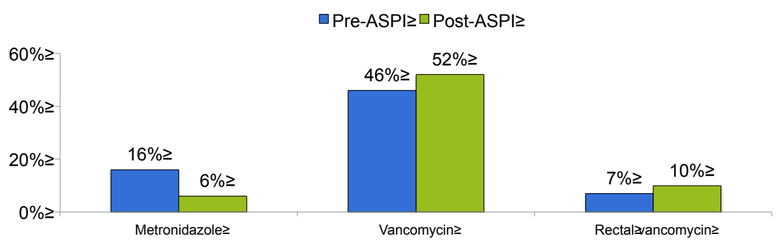
Patient Characteristics

Baseline Characteristics (*n*, % or median, IQR)	Pre-ASPI *n* = 148	Post-ASPI *n* = 111
Age, years	65 (55–75)	63 (53-74)
Male sex	80 (54)	61 (55)
Diabetes	53 (36)	40 (36)
Immunosuppression	33 (22)	21 (19)
Renal disease	24 (16)	14 (13)
Previous broad-spectrum abx	100 (68)	74 (67)
Previous 1-yr CDI history	26 (18)	29 (26)
C diff positive Toxin A/B	78 (53)	50 (45)
C diff positive PCR	70 (47)	61 (55)



Key definitions
Disease Severity was defined as having at least two of the following covariates: age ≥ 65 years, peak white blood cell count ≥ 15,000 cells/mL, peak serum creatinine ≥ 1.5 times the premorbid level, presence of pseudomembranous colitis, ileus, hypotension, shock or megacolon.

Treatment Characteristics*



*Included initial treatment with ANY CDI antibiotic

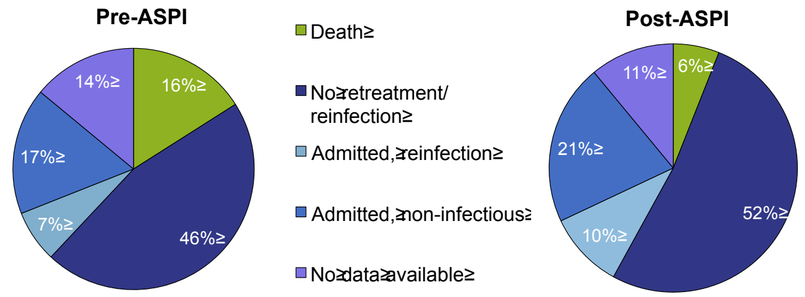
Co-variate (*n*, %)	Pre-ASPI *n* = 148	Post-ASPI *n* = 111	*P*-value
Initial CDI guideline compliance			
Overall	68 (46)	62 (56)	0.11
Mild/Moderate	28 (47)	23 (51)	0.65
Severe	38 (45)	38 (59)	0.08
Recurrent	3 (60)	2 (67)	1.0
Fecal transplant	10 (7)	13 (12)	0.17
Re-current CDI, ≥12 weeks	16 (11)	9 (8)	0.46
Re-hospitalization for CDI, ≥12 weeks	15 (10)	10 (9)	0.76

Intervention Characteristics

- In the post-ASPI group, CDI treatment recommendations were made in 73 (66%) patients

Post-ASPI Recommendations	Interventions (*n*, %)	Accepted interventions
Initiate CDI therapy	9 (8)	78%
Change initial CDI therapy selection	20 (18)	60%
Optimize CDI therapy dose	9 (8)	78%
De-escalate unnecessary antimicrobials	20 (18)	75%
Discontinue/change unnecessary PPI	38 (34)	66%
Discontinue promotility agent	12 (11)	92%
Modify CDI duration of treatment	3 (3)	100%
ID consult	2 (2)	100%
Total:	**111**	**74%**

30-day Outcomes*



*There were no statistical differences between groups

Summary

- CDI-related interventions were attempted and accepted in the majority of patients in the post-implementation group.
- The most common ASPI was discontinuation of unnecessary proton-pump inhibitors
- Appropriate selection of initial CDI therapy or CDI-outcomes were no different between pre- and post-ASPI groups