Infection Control & Hospital Epidemiology (2020), **41**, 216–218
doi:10.1017/ice.2019.346

Concise Communication

Efficacy of a stewardship intervention focused on reducing unnecessary use of non–*Clostridioides difficile* antibiotics in patients with *Clostridioides difficile* infection

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Abstract

In a tertiary-care hospital and affiliated long-term care facility, a stewardship intervention focused on patients with *Clostridioides difficile* infection (CDI) was associated with a significant reduction in unnecessary non-CDI antibiotic therapy. However, there was no significant reduction in total non-CDI therapy or in the frequency of CDI recurrence.

(Received 27 September 2019; accepted 16 November 2019; electronically published 17 December 2019)

Clostridioides difficile infection (CDI) is a consequence of antimicrobial therapy that offers challenges and opportunities for antimicrobial stewardship programs.[1–4] Stewardship interventions have been effective in improving CDI management, including reducing delays in treatment initiation and increasing adherence to practice guidelines for management of CDI.[5,6] Opportunities also exist for antimicrobial stewardship programs to address inappropriate non-CDI antibiotic use in CDI patients.[1–4,7] Practice guidelines for CDI recommend that therapy with the inciting antibiotic be discontinued as soon as possible.[8] However, recent studies suggest that patients with current or recent CDI often receive non-CDI antibiotics.[1–3] Such therapy is a major risk factor for recurrence and is often prescribed unnecessarily.[7] In the current study, we examined the impact of a stewardship intervention focused on improving CDI treatment and reducing non-CDI antibiotic use during CDI treatment.

Methods

Clostridioides difficile stewardship intervention

A stewardship intervention focused on CDI patients was implemented in a 700-bed academic hospital and affiliated long-term care facility (LTCF). The goal of the intervention was to ensure concordance of CDI treatment with practice guidelines and reduce inappropriate non-CDI antibiotic use during CDI therapy. Beginning in May 2014, the antimicrobial stewardship team reviewed encounters for all CDI patients (inpatients, outpatients, and LTCF residents). Appropriateness of CDI treatment and non-CDI antibiotic therapy was reviewed within 2 days of the CDI diagnosis. Feedback was provided if CDI treatment was not concordant with guidelines and/or if non-CDI antibiotic treatment was considered inappropriate or unnecessary. If non-CDI treatment was considered necessary, feedback was also provided to ensure that the duration of treatment was appropriate and to avoid agents associated with a high risk for CDI (eg, fluoroquinolones, clindamycin, and cephalosporins).[8] Both before and after the intervention, audit and feedback was provided for routine stewardship activities such as management of bacteremia and avoidance of treatment of asymptomatic bacteriuria.

Evaluation of the impact of the stewardship intervention

We conducted a retrospective evaluation to assess the impact of the stewardship intervention. The study was approved by the hospital's institutional review board. Medical record review was conducted for random samples of ~100 patients with initial episodes or first recurrences of CDI during the 1-year periods before and after the intervention. Random samples were generated using Random.org software. Research staff performed the initial medical record review and presented the information to an infectious diseases specialist (C.J.D.) for determinations regarding necessity and appropriateness of therapy. The infectious diseases specialist was blinded to whether the case occurred before or after the intervention (ie, dates of treatment were not shown).

We assessed CDI treatment for concordance with CDI practice guidelines with regard to treatment choice, dose, and duration.[8] Non-CDI therapy regimens were determined to be necessary or unnecessary based on published guidelines or standard principles

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Cite this article: Hecker MT, *et al.* (2020). Efficacy of a stewardship intervention focused on reducing unnecessary use of non–*Clostridioides difficile* antibiotics in patients with *Clostridioides difficile* infection. *Infection Control & Hospital Epidemiology*, 41: 216–218, https://doi.org/10.1017/ice.2019.346

Table 1. Comparison of the Appropriateness of *Clostridioides difficile* Infection (CDI) Treatment and of Non-CDI Antibiotic Use in the Preintervention Versus Intervention Periods

Process Measure	Preintervention (N = 103)[a]	Intervention (N = 105)[a]	*P* Value
Appropriateness of CDI treatment[b]			
Appropriate medication	82 (80)	94 (90)	.07
Metronidazole for severe CDI	10/18 (56)	3/17 (18)	.04
Appropriate treatment duration	70 (68)	86 (82)	.03
Appropriate dose	78 (76)	84 (80)	.21
Days unnecessary CDI treatment, mean (SD)	1.4 (3.7)	0.4 (1.7)	.02
Non-CDI antibiotic therapy during CDI treatment			
Received non-CDI antibiotic treatment	38 (37)	44 (42)	.48
Days non-CDI treatment, mean (SD)	5 (8)	6 (4)	.13
Entire regimen unnecessary	15 (15)	5 (5)	.09
Part of regimen unnecessary	4 (4)	3 (3)	.7
Part or all of regimen unnecessary	19 (18)	8 (8)	.02
Days unnecessary non-CDI antibiotics, mean (SD)	1.0 (2.6)	0.4 (1.5)	<.001
Non-CDI antibiotic therapy within 2 months after CDI therapy			
Received non-CDI antibiotic treatment	18 (17)	28 (27)	.13
Days non-CDI treatment, mean (SD)	16 (17)	10 (11)	.14
Entire regimen unnecessary	6 (6)	6 (6)	1.00
Part of regimen unnecessary	2 (2)	0 (0)	.24
Part or all of regimen unnecessary	12 (12)	8 (8)	.34
Days unnecessary non-CDI antibiotic, mean (SD)	0.9 (4.6)	0.2 (0.8)	<.001
Recurrence of CDI	11 (11)	13 (12)	.83

Note. Nonsevere, white blood cell count <15,000 cells/mL and serum creatinine <1.5 mg/dL; severe, white blood cell count >15,000 cells/mL or serum creatinine >1.5 mg/dL; fulminant, hypotension or shock, ileus, megacolon.
[a]Data are no. (%) unless otherwise specified.
[b]Appropriate based on recommendations from CDI management guidelines.

of infectious diseases as described previously.[9] If a non-CDI regimen was deemed necessary, additional assessments were made regarding whether part of the regimen was unnecessary.[9] Information was obtained regarding demographics, admitting service, indication for antibiotics, laboratory data, adverse effects associated with CDI treatment, and unexpected adverse effects in patients whose non-CDI antibiotics were discontinued.

Data analysis

The primary objectives were to determine whether the intervention was associated with a reduction in unnecessary non-CDI antibiotic use during and within 2 months after CDI treatment and a decrease in CDI recurrences. With 100 patients per group, we calculated >80% power to detect a 50% reduction in unnecessary non-CDI antibiotic treatment from an anticipated 40% to 20% and >70% power to detect a 50% reduction in recurrence from 30% to 15%. Bivariate analyses were used to compare patient characteristics and CDI and non-CDI treatment in the preintervention and intervention periods. Continuous data were analyzed using the Student unpaired *t* test. Categorical data were analyzed using the Pearson χ^2 test or the Fisher exact test. All analyses were performed using R software 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

As shown in Supplementary Table 1 (online), we detected no significant differences in the characteristics of the CDI patients reviewed during the preintervention and intervention periods. Table 1 provides a comparison of the appropriateness of CDI treatment and of non-CDI antibiotic use in the preintervention period versus the intervention period. Compared with the preintervention period, during the intervention, CDI patients were significantly less likely to receive metronidazole for severe CDI and more likely to receive an appropriate treatment duration.

Non-CDI antibiotic therapy was common during and after CDI treatment with no significant difference in the percentage of patients receiving treatment in the preintervention and intervention periods. The intervention was associated with a significant reduction in the percentage of CDI patients in whom part or all of a non-CDI antibiotic treatment regimen was unnecessary during CDI treatment (18% vs 8%; $P = .02$) but not after CDI treatment (12% vs 8%; $P = .34$). A significant reduction in the mean number of unnecessary days of non-CDI therapy occurred both during (1.0 vs 0.4 days; $P < .001$) and after (0.9 vs 0.2; $P < .001$) CDI treatment. However, there was no difference in the frequency of recurrence before versus after the intervention was detected (11% vs 12%).

Table 2 shows the number of antibiotic regimens that were entirely unnecessary and the associated days of unnecessary

https://doi.org/10.1017/ice.2019.346 Published online by Cambridge University Press

Table 2. Syndromes for Which Unnecessary Antimicrobial Regimens Were Prescribed During the Preintervention and Intervention Periods[a]

Syndrome	Preintervention[b]	Intervention[b]
During CDI treatment		
Asymptomatic bacteriuria	5 (30)	2 (7)
Gastrointestinal	2 (12)	2 (6)
Respiratory	4 (19)	0
Skin and soft tissue	4 (16)	1 (1)
Total	15 (77)	5 (14)
Within 2 mo after CDI therapy		
Asymptomatic bacteriuria	3 (10)	2 (7)
Gastrointestinal	0	3 (10)
Respiratory	2 (19)	0
Skin and soft tissue	1 (1)	1 (1)
Total	6 (30)	6 (18)

Note. CDI, *Clostridioides difficile* infection.
[a]Regimens included are those that were deemed entirely unnecessary.
[b]Data are number of unnecessary regimens (number of days of unnecessary treatment).

treatment prescribed during and within 2 months after CDI treatment, stratified by infectious diseases syndrome. Asymptomatic bacteriuria was the most common syndrome for which unnecessary antibiotic regimens were prescribed. No adverse effects were attributable to withholding antibiotic therapy or shortening the duration of therapy in the postintervention period.

Discussion

As has been demonstrated in previous studies,[5,6] we found that a stewardship intervention focused on CDI patients resulted in a significant improvement in appropriateness of CDI treatment. Our findings expand upon prior studies by demonstrating that such interventions can also reduce unnecessary non-CDI antibiotic treatment in CDI patients. The intervention was associated with significant reductions in the proportion of patients receiving any unnecessary non-CDI antibiotic therapy during, but not in the 2 months after, CDI treatment, and in the mean number of unnecessary days of non-CDI therapy during and after CDI treatment. However, the intervention did not result in reductions in total non-CDI antibiotic treatment or in the frequency of recurrence. Our findings demonstrate the feasibility of stewardship interventions in CDI patients and suggest that such interventions have the potential to improve outcomes.

Our study has several limitations. First, the number of patients was small and the study was underpowered to detect a reduction in recurrence. However, there was no evidence of a trend toward reduced recurrences during the intervention. Second, although unnecessary non-CDI antibiotic treatment was reduced, total non-CDI antibiotic use did not decrease significantly. Notably, approximately half of the antibiotic days of therapy were deemed necessary. Third, the intervention was quasi-experimental and was conducted in a facility with a well-established antimicrobial stewardship program including ongoing efforts to reduce treatment of asymptomatic bacteriuria and minimize overuse of fluoroquinolones.[10] Fourth, the primary intervention occurred at the time of CDI diagnosis with less feedback after completion of CDI treatment, particularly in outpatients. Finally, bivariate analyses were conducted without correction for multiple comparisons.

In conclusion, our study demonstrates that interventions focused on CDI patients can be effective in reducing unnecessary non-CDI therapy. Additional studies are needed to determine whether such interventions are effective in improving outcomes such as CDI recurrence, mortality, and costs.

Acknowledgments. We thank the administration and clinical staff at MetroHealth Medical Center for their support of the Antimicrobial Stewardship Program.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2019.346

Financial support. This work was supported by a grant from Merck Pharmaceuticals to CJD and by the Department of Veterans' Affairs.

Conflicts of interest. C.J.D. has received research grants from Pfizer, GOJO, Clorox, PDI, Boehringer Laboratories, and Avery Dennison. All other authors report no conflicts of interest relevant to this article.

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