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Brief report

The effect of pharmacy restriction of clindamycin on *Clostridium difficile* infection rates in an orthopedics ward

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A high consumption of clindamycin was noted in an orthopedics ward with high rates of *Clostridium difficile* infection (CDI). We restricted clindamycin for the entire ward. A reduction of 88% in CDI (1.07 to 0.12 × 1,000 patients-days, $P = .056$) and 84% for all-cause diarrhea (2.40 to 0.38 × 1,000 patients-days, $P = .021$) was achieved. Clindamycin was reduced 92.61% without an increase in other antibiotics. We identified high consumption of clindamycin as a risk factor for CDI.

Prior exposure to antimicrobial agents has been identified as a risk factor for *Clostridium difficile* infection (CDI).[1] The most common agents predisposing to CDI have been fluoroquinolones, clindamycin, or broad-spectrum cephalosporins.[2] Restricting exposure to antibiotics associated with increased CDI is an intuitively attractive approach to reduce CDI rates; however, there are few studies that demonstrate the successful implementation of antibiotic prescribing interventions to decrease these rates.[1,3,4] During the months of May and June of 2012, we registered a notable increase in CDI in the orthopedics ward and identified a ward-wide high consumption of clindamycin. The aim of our study was to assess the effect of clindamycin restriction on CDI rates in an orthopedics ward in a university teaching hospital in Mexico.

METHODS

We performed an interventional 23-month study that consisted of 2 periods: a 7-month baseline period (December 2011 through June 2012) and a 16-month intervention period (July 2012 through October 2013). The orthopedics ward unit is a 48-bed area (37 adult beds and 11 pediatric beds) with a mean of 1,200 admissions per year. This orthopedics ward unit primarily hospitalizes patients with fractures because of motor vehicle accidents, gunshot wounds, and multiple trauma.

The intervention period consisted of a pharmacy restriction of clindamycin for the entire orthopedics ward. Only patients with a previous infectious disease consult could receive clindamycin in their antibiotic scheme. Staff members were informed of the restriction and were instructed to use alternative antibiotic schemes during small group and ward academic meetings. Metronidazole was preferred for use in contaminated wounds and empiric anaerobic bacteria coverage. Infectious diseases consultants participated in the treatment of all CDI cases, and, in other cases, the attending physician actively solicited a consult.

During both periods, the same personnel from the infection control unit maintained active surveillance for patients with diarrhea, defined as passage of 3 or more unformed stools in the previous 24 hours, fever, and leukocytosis (>11,000 white blood cells/mm^3). In suspected cases, stool samples were sent for detection of toxin A/B (ImmunoCard Toxins A&B; Meridian Bioscience, Inc, Cincinnati, OH). If these patients were toxin A/B positive, they were categorized as CDI; if they were toxin A/B negative, they were

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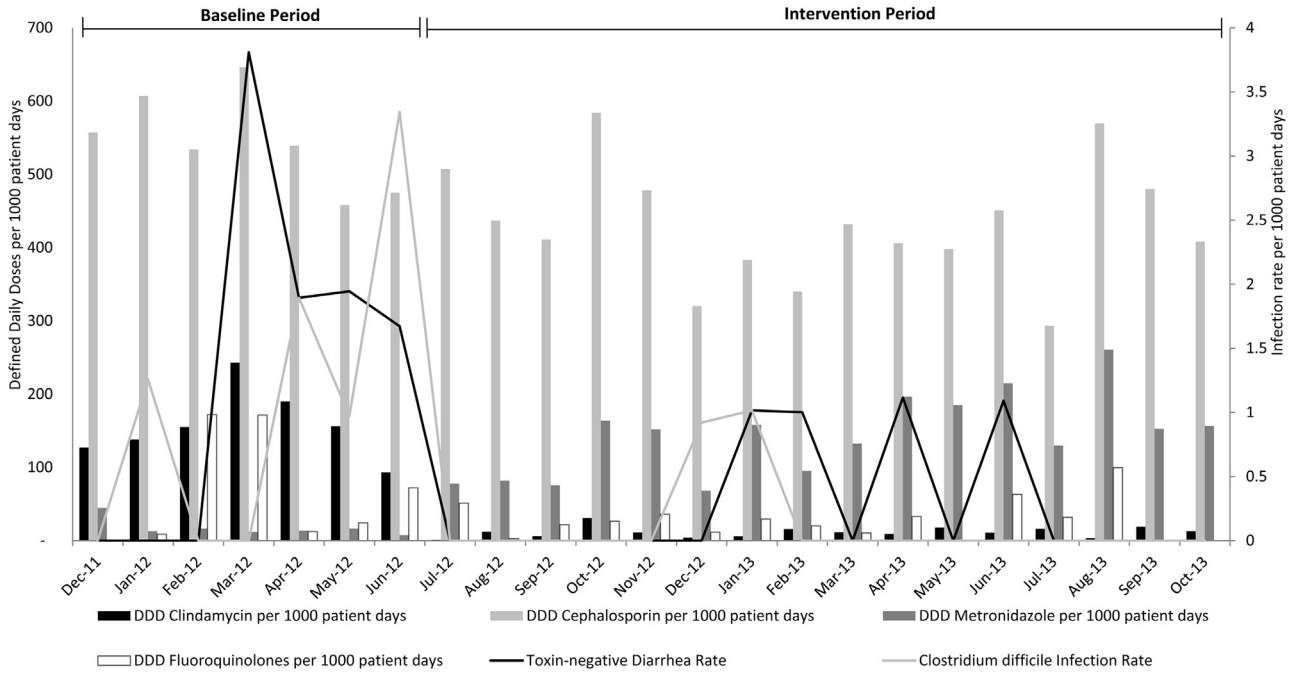

Fig 1. *Clostridium difficile* infection and toxin-negative diarrhea rates and compared to clindamycin, cephalosporins, metronidazole, and fluoroquinolones consumption.

Table 1
Risk factors for CDI of the study population

	Baseline period, n = 684	Intervention period, n = 1,720	*P* value
Mean age, y	35.12	35.08	.93
Total antibiotic DD (per patient)	5,736 (8.38)	9,923 (5.76)	.13
Length of stay (per patient), days	7,026 (10.27)	16,507 (9.59)	.48
Number of surgeries (per patient)	565 (0.826)	1,415 (0.822)	.24

DD, daily dose.
NOTE. Values in parentheses represent means. The number inside the parenthesis refers to the average length of stay per patient, the number outside the parenthesis refers to the total length of stay; this also applies for the other variables.

labeled as toxin-negative diarrhea. All-cause diarrhea was defined as the combined group of patients with CDI and with toxin-negative diarrhea. We excluded patients with recent use of laxatives or with an alternative cause for diarrhea. Prescription information and pharmacy registry for antibiotic consumption were analyzed for both periods. A continuous hospital-wide hand hygiene program was active throughout the study. Contact precautions for CDI cases were not modified, and no other actions were modified during the study.

RESULTS

In this study, 684 patients were included during the baseline and 1,720 during the intervention period. There was no difference in mean length of hospital stay in either group (10.27 vs 9.59 days, respectively; $P = .483$), and there were no differences in age and gender between the 2 study periods. Risk factors for CDI in both groups were similar (Table 1).

The mean infection rate was reduced from 1.07 per 1,000 hospital-days during the baseline period to 0.12 per 1,000 hospital-days during the intervention period, with a decrease of 88.78% ($P = .056$). Furthermore, toxin-negative diarrhea was reduced from a mean of 1.33 to 0.26 ($P = .076$), and all-cause diarrhea was reduced from a mean of 2.40 per 1,000 hospital-days to 0.38 per 1,000 hospital-days, with a decrease of 84% ($P = .021$) (Fig 1).

Defined daily doses (DDD) of clindamycin per 1,000 patient-days declined from a mean 157.43 during the baseline period to 11.63 in the intervention period, with a decrease of 92.61% ($P = .0002$). Use of cephalosporins declined as well, from 545.14 DDD per 1,000 patient-days during the baseline period to 431.1 during the intervention period, with a decrease of 21% ($P = .00681$). Metronidazole usage increased from 17.56 DDD per 1,000 patient-days to 143.72 ($P = .0002$), and fluoroquinolones decreased from 76.77 to 27.31 DDD per 1,000 patient-days with no statistical significance ($P = .2101$).

DISCUSSION

Clindamycin has been known since the seventies to be a risk factor for the development of CDI.[5] After we identified it as an important hazard for our orthopedics ward, the restriction of its use was associated with favorable results. In other studies as well as in ours, a revised antibiotic guideline avoiding broad-spectrum antibiotics can prompt a significant decrease in CDI cases.[6] By establishing an effective antibiotic scheme, clindamycin usage was reduced importantly (157.43 to 11.63 DDD per 1,000 patient-days), an event that did not prompt an increase in cephalosporin and fluoroquinolones use but did cause a consequent increment in metronidazole consumption. Although an alternative antibiotic scheme was discussed with the medical personnel that included cephalosporins, we did not observe an increase in their use. This could represent only a spurious relation. A similar clindamycin restriction in the Hunter Holmes McGuire Veterans Affairs Medical Center, a 703-bed tertiary care hospital, was performed as a control measure during an outbreak of CDI associated to a clindamycin-resistant strain. A sustained decrease in the number of patients with CDI after the restriction was observed (11.7 vs 3.33 cases per month after restriction; $P < .001$). Their use of clindamycin was