Impact of an intervention to control *Clostridium difficile* infection on hospital- and community-onset disease; an interrupted time series analysis

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Abstract

Strategies to reduce rates of *Clostridium difficile* infection (CDI) generally recommend isolation or cohorting of active cases and the reduced use of cephalosporin and quinolone antibiotics. Data supporting these recommendations come predominantly from the setting of epidemic disease caused by ribotype 027 strains. We introduced an initiative involving a restrictive antibiotic policy and a CDI-cohort ward at an acute, 820-bed teaching hospital where ribotype 027 strains account for only one quarter of all CDI cases. Antibiotic use and monthly CDI cases in the 12 months before and the 15 months after the initiative were compared using an interrupted time series analysis and segmented regression analysis. The initiative resulted in a reduced level of cephalosporin and quinolone use (22.0% and 38.7%, respectively, both $p < 0.001$) and changes in the trends of antibiotic use such that cephalosporin use decreased by an additional 62.1 defined daily doses (DDD) per month ($p < 0.001$) and antipseudomonal penicillin use increased by 20.7 DDD per month ($p = 0.011$). There were no significant changes in doxycycline or carbapenem use. Although the number of CDI cases each month was falling before the intervention, there was a significant increase in the rate of reduction after the intervention from 3% to 8% per month (0.92, 95% CI 0.86–0.99, $p = 0.03$). During the study period, there was no change in the proportion of cases having their onset in the community, nor in the proportion of ribotype 027 cases. CDI cohorting and restriction of cephalosporin and quinolone use are effective in reducing CDI cases in a setting where ribotype 027 is endemic.

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Introduction

Clostridium difficile has emerged as a major nosocomial pathogen. Numerous reports from North America and Europe have described increases in incidence and severity of *C. difficile* infection (CDI) over the last 10 years [1–3]. There were over 290 000 hospitalizations related to CDI in the USA in 2005 and the UK Health protection agency recorded over 40 000 CDI cases in 2008 [4]. CDI severity appears to have increased as new strains, in particular those of restriction endonuclease (REA) type BI/ribotype 027, have emerged [5,6]. Several features have been implicated in the emergence and virulence of BI/027 strains, including the presence of a binary toxin gene, a deletion in the regulatory *tcdC* gene, resistance to quinolone antibiotics and hypersporulation [7].

The most important modifiable risk factors for developing CDI are antibiotic exposure, particularly to cephalosporin and quinolone antibiotics, and contact with patients with CDI or their caregivers and environment [8].

Consequently, recommendations for the control of CDI frequently involve antibiotic policies restricting the use of these antibiotic classes and enhanced efforts to isolate or cohort patients with active CDI [9,10]. In January 2008, we introduced an initiative in our hospital involving a new antibi-

otic policy restricting cephalosporin and quinolone use and the opening of a ward specifically for the cohorting of patients with CDI. In the present study, we report the impact of this on antibiotic use and the frequency of CDI.

Materials and Methods

Setting

Brighton and Sussex University Hospitals NHS Trust (BSUHT) is an 820-bed teaching hospital providing acute secondary care services to 500 000 people in Brighton, Hove and Mid-Sussex and tertiary services (cardiothoracic, oncology and renal) to a population of approximately two million.

Rationale

We launched the initiative in response to recommendations made by the UK Department of Health Healthcare Commission after an inspection of our hospital in October 2007.

Population and case definitions

Table 1 gives details of the population and case definitions throughout the study. All patients testing positive for *C. difficile* toxins A or B were included in the study. The laboratory does not test repeat samples from the same patient within 30 days of a previous positive sample.

Intervention

The initiative introduced had two main components: (i) the opening of an 11-bed cohort ward for patients with CDI and (ii) a new antibiotic policy restricting the use of cephalosporins and quinolones. Although these measures were introduced simultaneously, efforts to improve compliance with good infection control practice and surveillance were ongoing throughout the study period. Throughout the study, alcohol gels were used as the primary agent for hand hygiene with hand-washing advised after contact with CDI cases.

The cohorting ward was specifically for patients with CDI. Patients testing positive for CDI who still had on-going diarrhoea were transferred to the cohort ward on the same day. The ward had its own nursing staff and all patients admitted to the ward were transferred to the care of the infectious diseases team. All staff working on the ward wore scrubs and put on a new apron and gloves between each patient contact. A small minority of CDI patients had health needs, most usually surgical or high-dependency, which prevented transfer to the ward; however, all patients eligible for transfer to the ward were accommodated there.

The new antibiotic policy replaced cephalosporin and quinolone antibiotics with aminopenicillin or antipseudomonal penicillins. Examples of how this was achieved are given in Table 1. The policy was widely publicised in the hospital but no specific measures were put in place to enforce compliance.

Assessment of impact

A retrospective interrupted time series (ITS) analysis looking at antibiotic use and number of CDI cases was conducted, with the pre-intervention phase being January to December 2007 and the post-intervention phase being January 2008 to March 2009. Data were gathered from information routinely recorded by the infection control and pharmacy departments. Bed occupancy data were obtained from the hospital's clinical information unit.

Outcomes

The primary outcomes were: (i) change in use of targeted antibiotics and (ii) the reduction in number of CDI cases. To determine changes in use of untargeted antibiotics we also gathered data on use of aminopenicillins, antipseudomonal

TABLE 1. Population, clinical setting, nature and timing of interventions

Setting: 820–bed acute teaching hospital with a rate of CDI close to the UK average	Dates: 1 January 2007 to 31 March 2009	Population characteristics: all in-patients from whom a diarrhoeal stool tested positive for *Clostridium difficile* toxin >72 h after admission. Total bed days during the study period
Intervention: A package of measures to combat CDI, specifically a cephalosporin- and quinolone-restrictive antibiotic policy and a cohort ward for CDI patients		
	Antibiotic policy	Isolation policy
Phase 1: 12 months (1 January 2007 to 31 December 2007)	Nonrestrictive antibiotic guidelines	All patients with diarrhoea to go into side-rooms, with standard isolation
Phase 2: 15 months (1 January 2008 to 31 March 2009)	Cephalosporin and quinolone restrictive	All eligible patients to go to CDI cohort ward within 24 h of CDI diagnosis until discharge
Nonrestrictive antibiotic guidelines (phase 1): community-acquired pneumonia; cefuroxime + clarithromycin, cellulitis; ceftriaxone, hospital-acquired pneumonia; ciprofloxacin		
Restrictive antibiotic guidelines (phase 2): e.g. community-acquired pneumonia; amoxicillin + clarithromycin, cellulitis; benzylpenicillin and flucloxacillin, hospital-acquired pneumonia; piperacillin-tazobatam.		
Case definition of CDI (both phases): a patient from whom a liquid stool tested positive for *C. difficile* toxin A or B Case definition of hospital-associated CDI (both phases) : onset more than 72 h after admission to hospital or within 72 h after discharge.		
Detail of the cohorting intervention. The cohorting ward was only for CDI patients and had dedicated nursing staff. All patients were looked after by one medical team. All staff wore scrubs and changed gloves and aprons between all patient contacts. All patients eligible for cohorting on the ward were admitted there during the study period.		

CDI, *Clostridium difficile* infection.