Correspondence

Clostridium difficile–Associated Diarrhea Outbreaks: The Name of the Game Is Isolation and Cleaning

Sir—We read with interest the article by Pépin et al. [1], which reports that use of quinolones is a major risk factor for illness during an outbreak of Clostridium difficile–associated diarrhea (CDAD). These results confirm previous observations that quinolones and other antibiotics, such as third-generation cephalosporins, macrolides, broad-spectrum β-lactams, and aminoglycosides, are important risk factors for CDAD [2, 3]. However, in addition to instating and/or following policies regarding antibiotic use, other infection-control procedures—including environmental hygiene, washing hands with soap and water, and isolating patients who have CDAD—are critical to the prevention of the spread of this disease [4, 5]. This outbreak has also been affecting our institution and has even forced medical units to be closed for varying lengths of time [6]. Interestingly, our institution does not have any respiratory quinolones on formulary and only uses ciprofloxacin. The fact that most patients are naive to treatment with respiratory quinolones leads us to believe that other factors have played a role in this outbreak.

Another observation that the incidence of CDAD markedly decreased during the first half of 2005 in institutions in Quebec initially affected by the outbreak [7]. This phenomenon does not appear to be related to changing patterns of specific antimicrobial agent use; rather, the decrease follows implementation of specific modification of infection-control and cleaning procedures driven by governmental incentives. Indeed, CDAD is affecting institutions regardless of which antibiotic use is used. There are also no data demonstrating that the use of one agent over another has had an impact on the incidence of CDAD during the current outbreak. In our institution, the decreased incidence of CDAD does not correlate with use of any specific antibiotic, because there has been little change in the types of antibiotics prescribed to patients with CDAD during the past years, even though the incidence has gone from >40 cases per 1000 admissions to <12 cases per 1000 admissions. The identification of antibiotics most likely to contribute to C. difficile infection is an important piece of the puzzle. The data presented by Pépin et al. [1] demonstrate that antibiotic use is associated with development of CDAD, and that the judicious use of antibiotics only when indicated is probably appropriate. However, selecting specific antibiotics for use as a means of decreasing the risk of CDAD has yet to be properly demonstrated. In our hospital, the name of the game is still isolation of patients and cleaning.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Mathieu Beaulieu,† Daniel J. G. Thirion,† Daniel J. G. Thirion,† and Gilbert Pichette
†Faculty of Pharmacy, Université de Montréal, and Departments of †Microbiology and †Pharmacy, Hôpital du Sacré-Cœur de Montréal, Quebec, Canada

References


Poor Infection Control, Not Fluoroquinolones, Likely to Be Primary Cause of Clostridium difficile–Associated Diarrhea Outbreaks in Quebec

Sir—I read with interest the paper by Pépin et al. [1], which analyzes the risk factors for Clostridium difficile–associated diarrhoea (CDAD) on the basis of recent outbreak in Quebec. The authors concluded that fluoroquinolones are the predominant risk factor for CDAD. However, retrospective studies are difficult to design, analyze, and interpret, and inappropriate conclusions can easily be drawn.

Pépin et al. [1] ignored various important global aspects in their analysis. First, fluoroquinolones are widely used throughout Canada; yet, the outbreak is affecting only Quebec. The overall rate of consumption of antibiotics nationwide by persons seen outpatient health care set-
ings, which accounts for ~80% of the antibiotics prescribed in the outpatient setting, has decreased from 829 prescriptions per 1000 population in 1998 to 709 prescriptions per 1000 population in 2004 (Intercontinental Medical Statistics Canada, unpublished data). Quebec has the lowest absolute consumption rate of antibiotics of any Canadian province: 774 prescriptions per 1000 population in 1998 and 641 prescriptions per 1000 population in 2004. During the same period, the consumption rate of fluoroquinolones has increased nationally from 61 to 95 prescriptions per 1000 population and in Quebec from 60 to 106 prescriptions per 1000 population, which was not significant. The similarity in rates of total antibiotic and fluoroquinolone use in Quebec and other provinces does not support a link at a macro level between fluoroquinolone use and CDAD. If there was a link, why have other Canadian provinces not experienced the outbreak? In addition, ciprofloxacin, which constitutes the bulk of fluoroquinolones consumed and was associated with CDAD in the article by Pépin et al. [1], has been available in Canada since 1988, yet there were no problems with increased incidence of CDAD from 1988 to 2002.

Second, before the outbreak of CDAD, Quebec was behind other Canadian provinces in instituting proper infection-control practices, and had fewer infection-control personnel. Following the outbreak of CDAD, in June 2004, the provincial government of Quebec introduced stringent infection-control measures and increased monetary investment in this area [2]. Infection control plays a key role in controlling CDAD outbreaks. This was evidenced in Calgary, Canada, which had a much smaller outbreak of the same strain of C. difficile [3]. In the Calgary hospital, as in my own, there is a large bone marrow transplant program, but CDAD was extremely rare in this population, despite the use of large amounts of antibiotics [3]. These patients have private rooms, and the hospital has a better nurse-patient ratio. Infection-control measures implemented in the affected areas of Quebec included increased hand washing, disinfection of rooms with a spore-killing bleach, isolation of infected patients, rigorous appraisal of the use of antibiotics, and investment in hospital renovations. Surveillance of CDAD by the Quebec Health Ministry from August 2004 to March 2005 shows that the new, stringent infection-control measures have resulted in a decreasing incidence of CDAD [4]. During the same time period, patterns of antibiotic use had not changed in the province, which suggests that poor infection control coupled with older facilities—rather than antibiotic use—was the main risk factor in the CDAD outbreak.

Third, the CDAD outbreak occurred mainly around Montreal and the eastern townships [4]. It was not a problem throughout the province, despite the fact that the pattern of antibiotic use was the same across Quebec. In a study that compares 4 institutions from 2001 to 2004 (2 in the area affected by the outbreak and 2 in the area not affected), no link was found between the type and amount of antibiotics being used and the incidence of CDAD [5]. In 2004, the institution hit hardest by the outbreak (an incidence of 33 CDAD cases per 1000 admissions) had a total consumption rate of 81.2 defined daily doses of fluoroquinolone per 1000 hospital-days, compared with 141.1 defined daily doses per 1000 hospital-days reported by the institution with the lowest incidence of CDAD (5.5 per 1000 admissions).

Fourth, there is some debate that suggests that antibiotics with greater activity against anaerobes may increase the risk for CDAD by altering the normal bowel flora [6, 7]. However, moxifloxacin, which has significant anaerobic activity [8], was associated with a relatively low risk of CDAD in the analysis of Pépin et al. [1]. Ciprofloxacin and levofloxacin, which have limited activity against anaerobes, were associated with much higher risks of CDAD in the analysis by Pépin et al. [1], but in another study, the reintroduction of levofloxacin decreased the rate of CDAD [7]. All this contradictory information suggests that the impact of fluoroquinolone use on the incidence of CDAD is poorly understood. Drawing conclusions from local studies that look at a specific relationship when multiple factors may impact results is a difficult task.

Fifth, it appears that Pépin et al. [1] are looking for an antibiotic culprit responsible for the CDAD outbreak, and they are downplaying the importance of traditional infection-control measures. In a previous publication, the some of the authors and their colleagues incriminated use of macrolides as a risk factor for CDAD [9]. However, macrolides are very rarely used in monotherapy for hospitalized patients; rather, they are usually used in combination with cephalosporins. Therefore, it would be very difficult to attribute any increased risk of CDAD to use of macrolides alone, because cephalosporins have been more-strongly associated with C. difficile infection. It is relevant to ask whether the authors’ hospital banned macrolide–β-lactam combination therapy following their previous findings [9] and switched to treatment with fluoroquinolones during the course of the CDAD outbreak. Did they alter their infection-control practices during the outbreak? And what happened to their patients in the oncology unit? In their study, fluoroquinolones were prescribed in 23% of all CDAD episodes, which is 3% more often—a 15% increase—compared with the frequency at which all of the antibiotics of all of the classes with no significant risk factors put together are prescribed (narrow-spectrum penicillins, aminoglycosides, intravenous vancomycin, trimethoprim-sulfamethoxazole, and amoxicillin–clavulenate). In an area where C. difficile is endemic, any antibiotic prescribed in large quantity will always become a risk factor.

Finally, in the discussion, Pépin et al. [1] suggest that, for patients hospitalized with community-acquired pneumonia, the risk of CDAD associated with using evidence-based, recommended antibiotic
Acknowledgments

Potential conflicts of interest. K.W.: no conflicts.

Karl Weiss
Faculty of Medicine, University of Montreal and McGill University, Montreal, Quebec, Canada

References


2. Eggertson L. Quebec puts up 20 million dollars for *C. difficile* fight. CMAJ 2005;172:622.


Reply to Weiss and to Beaulieu et al.

SIR—Beaulieu et al. [1] and Weiss [2] assert that the key elements of control of *Clostridium difficile*-associated diarrhea (CDAD) are isolation of patients and cleaning, rather than antibiotic stewardship, but they provide few data supporting their view. Few people would oppose better infection control in any hospital for the same reason that few people oppose sunny weather: it is obviously a good idea. However, the relevant questions for clinicians who are confronted with this emerging strain of *C. difficile* and want to reduce its devastating morbidity and mortality rates are as follows: can we rely on the business-as-usual recipe of strengthening infection control measures, and if not, what else should we do?

Although we agree with Weiss [2] that infection-control procedures in Quebec hospitals were suboptimal prior to this epidemic, the experience of many hospitals, including ours, was that the improvement of infection-control measures during August–September 2003 had, unfortunately, no impact whatsoever on the incidence of CDAD, which became truly catastrophic during the winter of 2003–2004 [3]. This disappointing impact of traditional infection-control measures against *C. difficile*, known for years, is thought to be a consequence of the prolonged survival of its spores in the hospital environment and on the hands of hospital personnel. In 1995, the Society for Healthcare Epidemiology of America stated that “the most successful control measure directed at reduction of symptomatic disease has been antimicrobial restriction” [4, p. 459].

Beaulieu et al. [1] and Weiss [2] rather imprudently—and coincidentally—claim that there was a marked reduction in the incidence of CDAD in hospitals of Quebec in early 2005 as a result of stricter isolation of patients with the infection. The exact opposite is revealed in publicly available data from the Quebec provincial surveillance system for CDAD [5]: during late 2004 and early 2005, the incidence rates...

CORRESPONDENCE • CID 2006:42 (1 March) • 727