

An antibiotic policy associated with reduced risk of *Clostridium difficile*-associated diarrhoea

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Abstract

Background: antibiotic-associated diarrhoea caused by *Clostridium difficile* is increasing in hospitals, and older people are at particular risk.

Objective: to establish whether reducing patient exposure to injectable third-generation cephalosporins by substituting alternative antibiotics can produce a cost-effective reduction in the incidence of antibiotic-associated diarrhoea.

Design: we prospectively investigated 2157 patients admitted to the department of elderly medicine in the year before introduction of antibiotic restrictions and 2037 patients admitted in the following year. Patients admitted to other wards, where antibiotic prescribing was unchanged, acted as controls.

Setting: a 900-bed teaching hospital in Cambridge, UK.

Measurements: use and cost of injectable antibiotics prescribed in the department of elderly medicine and the other wards studied; occurrence of *C. difficile*-associated diarrhoea.

Results: in the wards for older people, consumption of injectable cephalosporins fell by 92% (compared with 8% on other wards) and cases of *C. difficile*-associated diarrhoea fell from 98 to 45 (cases in other wards rose from 213 to 253; $P < 0.001$). The £8062 increase in injectable antibiotic costs on the elderly wards were offset by the release of 1087 wasted bed-days attributable to the 53 fewer cases, with potential savings of £212 000.

Conclusions: restricting the consumption of injectable third-generation cephalosporins is a cost-effective method of reducing the incidence of *C. difficile*-associated diarrhoea.

Keywords: antibiotic, *Clostridium difficile*, diarrhoea, nosocomial infection

Introduction

Clostridium difficile-associated diarrhoea is an important and increasing hospital-acquired infection. In 1997 there were 15 360 laboratory reports of this condition in England and Wales, a 32% increase on 1996 [1]. Infection is attributed to alteration in the patient's normal gut flora, usually secondary to antibiotic therapy.

Impallomeni *et al.* reported that the injectable third-generation cephalosporins presented the highest relative risk for antibiotic-associated diarrhoea [2]. As the incidence of *C. difficile*-associated diarrhoea on their geriatric wards was directly related to cefotaxime consumption, they suggested that withdrawal of third-generation cephalosporins could reduce the incidence of the infection. We tested this hypothesis by observing the effect of a policy of restricted use

of these antibiotics in our department of elderly medicine.

Methods

We studied patients admitted to Addenbrooke's Hospital over two 12-month periods (1996 and 1997). We tested all patients with hospital-acquired diarrhoea for *C. difficile* faecal cytotoxin by standard tissue culture neutralization tests.

In 1997, we introduced an antibiotic policy restricting the use of third-generation injectable cephalosporins for patients admitted to the four geriatric wards. Agents in this class used at Addenbrooke's Hospital were ceftriaxone, ceftazidime and cefotaxime, the latter being used most frequently (Table 1). Our policy allowed for the use of a cephalosporin

Table 1. Numbers of admissions, cases of *Clostridium difficile*-associated diarrhoea and antibiotic use by location and study period

Ward type	Year	Admissions	Cases	Injectable antibiotic use (g)		
				All cephalosporins	Cefotaxime	Ciprofloxacin
Elderly care	1996	2157	98	3021	2924	31
	1997	2037	45 ^a	228	210	189
Other	1996	68 174	213	65 380	57 184	1028
	1997	69 463	253	60 034	49 373	1143

^a $P < 0.001$ by χ^2 , compared with cases on elderly care wards in 1996 and on other wards in 1996 and 1997.

(cefotaxime) for the empirical treatment of meningitis only and included guidance on alternative antibiotics for other infections (for example, penicillin with ciprofloxacin for the empirical treatment of severe community-acquired pneumonia).

Patients admitted to the elderly wards in 1996 and patients admitted to other wards in both years, where antibiotic use was not changed, acted as control groups. Only children, mental health patients, obstetric cases and births were excluded from the control group. There were 68 174 patients in the first year and 69 463 in the second. There were no important changes in policy and practices affecting case-mix of admissions and hospital infection control during the study period.

Results

The policy resulted in a 92% reduction in the use of injectable third-generation cephalosporins, with no inconvenience to patients and staff, and was associated with a halving of cases of *C. difficile*-associated diarrhoea. In contrast, there was an increase in cases on wards with no cephalosporin restriction (Table 1). The total injectable antibiotic costs to the elderly unit increased from £22 121 in 1996 to £30 183 in 1997.

We observed no changes in the case-mix of admissions to the wards studied and 38% of control patients were over 60 years of age in both study periods.

Discussion

The increase in injectable antibiotic costs to the department of elderly medicine is largely attributable to increased use of the principal alternative for Gram-negative infections—ciprofloxacin (an agent four times as expensive per treatment day as cefotaxime). This cost may be offset by a reduction in the financial burden of *C. difficile*-associated diarrhoea, recently estimated in our elderly care patients as £4000 per case [3]. The 53 fewer cases than expected in 1997

therefore represent a potential saving of £212 000. The bulk of this expense was related to the 'hotel' costs of extended bed occupancy, and since all beds are usually full such a saving is unlikely to be realised. However, since cases stayed twice as long as controls (means of 39.5 *versus* 19 days, respectively) [3], preventing 53 cases of *C. difficile*-associated diarrhoea could, at least in theory, have released sufficient bed-days for an additional 53 admissions.

The reduction in morbidity and mortality in the 53 patients spared the infection represents a clearer benefit. Ten deaths may have been prevented in patients admitted to the elderly wards in 1997: we found in a case-control study an excess mortality of 20% in elderly-care patients with *C. difficile*-associated diarrhoea [3].

It is difficult to conduct a scientifically rigorous study in this area, as many elements (e.g. changes in case-mix, medical practices and outbreaks of infection with *C. difficile*) are uncontrollable. Although early reports from other centres are encouraging [4, 5], data are incomplete, particularly with regard to details of cephalosporin consumption, admission rates and results for control groups. We therefore encourage other centres to report their findings in detail so that we may gain an overall view of efficiency.

Key points

- Avoiding injectable third-generation cephalosporins can halve the incidence of *Clostridium difficile*-associated diarrhoea in patients in hospital.
- Associated increased antibiotic costs are offset by reduced mortality, morbidity and bed occupancy.

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