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Changing prophylactic antibiotic protocol for reducing *Clostridium difficile*–associated diarrhoeal infections

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ABSTRACT

Purpose. To determine whether a change in prophylactic antibiotic protocol for orthopaedic surgeries may reduce the frequency of *Clostridium difficile*–associated diarrhoeal infections.
Methods. Records of 1331 patients who underwent trauma or elective surgeries involving implantation of metalwork were reviewed. 231 trauma and 394 elective patients who received intravenous cefuroxime–based antibiotic prophylaxis between August 2006 and January 2007 were compared with 216 trauma and 490 elective patients who received a single dose of gentamicin and flucloxacillin or teicoplanin for antibiotic prophylaxis between August 2007 and January 2008. Diarrhoeal faecal specimens of 148 (33%) trauma patients and 106 (12%) elective patients were examined. The outcome variables were the rates of *C difficile* infection and early deep wound infection.
Results. There were 32 cases of *C difficile*–associated diarrhoeal infection and 28 cases of early deep wound infection. The frequency of *C difficile*–associated diarrhoeal infection decreased after use of the new antibiotic protocol (from 4 to 1%, p=0.004), particularly in the trauma patients (from 8 to 3%, p=0.02); in the elective patients the difference was not significant (from 1 to 0.5%, p=0.27). The change of antibiotic protocol did not significantly affect the incidence of deep wound infections in the trauma (p=0.46) or elective (p=0.90) patients. The rate of *C difficile* infection was 8-fold higher in the trauma than elective patients, both before and after the change of protocol.
Conclusion. Changing antibiotic protocol is one way of reducing the incidence of *C difficile*–associated diarrhoeal infections in orthopaedic patients, without increasing the rate of deep wound infections.

Key words: *antibiotic prophylaxis; cefuroxime; Clostridium difficile; enterocolitis, pseudomembranous*

INTRODUCTION

Clostridium difficile is a Gram-positive, anaerobic,

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spore-forming bacillus that can cause pseudomembranous colitis.[1] *C difficile*–associated diarrhoea confers a mortality of up to 25% in frail elderly people.[2] It predominantly affects older, hospitalised patients or younger immunosuppressed patients,[2] following administration of antibiotics, particularly those that achieve high concentrations in the intestinal lumen and are active against bowel flora.[3] Antibiotics with a high potential to induce *C difficile*–associated diarrhoea include aminopenicillins, cephalosporins, and clindamycin.[4–6] Therapy with these agents (especially cephalosporins) reduces normal colonisation resistance within the colon; overgrowth then occurs.[3–7]

In recent decades, among hospitalised patients, antibiotic-associated diarrhoea has been associated with increases in mortality, length of stay, and cost of medical care.[8] The cost of treating one such case was estimated to be £4000.[8]

The incidence and severity of *C difficile*–associated diarrhoea has increased in the UK[8] and US,[9,10] likely owing to hospital-wide use of cephalosporins.[11] It has therefore been suggested that cephalosporins should not be prescribed in elderly care units.[12]

We investigated the rates of postoperative infection in orthopaedic patients, assuming that the new prophylaxis protocols may reduce the frequency of *C difficile* infections but not affect the rate of early deep wound infections in patients undergoing surgery involving metalwork implantation.

MATERIALS AND METHODS

Records of 1331 patients who underwent trauma or elective surgeries involving implantation of metalwork were reviewed (Table). Patients who had revision surgery or those who died within one month from causes not related to *C difficile* infection were excluded.

Patients who sustained a closed proximal femoral fracture and underwent total hip arthroplasty, hemiarthroplasty or internal fixation were classified into the trauma group. Patients who underwent elective total knee or total hip arthroplasty were classified into the elective group.

Between August 2006 and January 2007, 231 trauma and 394 elective patients received intravenous cefuroxime–based antibiotic prophylaxis. This entailed a dose of 1.5 mg at induction, followed by 2 doses (each 750 mg) 8 and 16 hours after the operation.

In May 2007, the antibiotic protocol was changed with a view to minimise the cephalosporin-related *C difficile* infections, despite concerns of a possible increase in the frequency of deep wound infections.

Between August 2007 and January 2008, 216 trauma and 490 elective patients received a single dose of gentamicin (3 mg/kg) and flucloxacillin (1 g) or teicoplanin (600 mg for patients <80 kg or 800 mg for those >80 kg) at induction for antibiotic prophylaxis. Teicoplanin was given to patients from

Table
Comparison of patent outcome in 2 different antibiotic protocols

Variable	Antibiotic protocol before May 2007		Antibiotic protocol after May 2007	
	Trauma group	Elective group	Trauma group	Elective group
Mean (range) age (years)	83 (42–106)	70 (33–91)	82 (31–102)	70 (36–95)
No. (%) of males	55 (24)	141 (36)	68 (31)	190 (39)
No. (%) of females	176 (76)	253 (64)	148 (69)	300 (61)
No. (%) of operations				
Dynamic hip screw fixation	89 (39)	-	83 (38)	-
Hemiarthroplasty	74 (32)	-	73 (34)	-
Long gamma nail fixation	1 (0)	-	6 (3)	-
Short gamma nail fixation	6 (3)	-	9 (4)	-
Garden screw fixation	59 (26)	-	29 (13)	-
A/O screw fixation	0 (0)	-	15 (7)	-
Total hip arthroplasty	2 (1)	-	1 (1)	-
Hip resurfacing or total hip arthroplasty	-	151 (38)	-	189 (39)
Total or unicompartment knee arthroplasty	-	243 (62)	-	301 (61)
No. (%) of *Clostridium difficile*–associated diarrhoeal infections	19 (8)	4 (1)	7 (3)	2 (0)
No. (%) of early deep wound infections	6 (3)	6 (2)	8 (4)	8 (2)

whom methicillin-resistant *Staphylococcus aureus* had been isolated (from their nose or groin) or to those suspected of being allergic to penicillin.

Both protocols allowed 20 minutes between administration of the antibiotics and inflation of the tourniquet.

Diarrhoeal faecal specimens were examined using an enzyme-linked immunosorbent assay for the detection of *C difficile* toxins A and B.[13] The outcome variables were the rates of *C difficile* infection and early deep wound infection (necessitating operative intervention within the first postoperative 3 months[14]).

A 2x2 contiguency table was constructed for the occurrence of *C difficile* as well as for deep wound infections in the trauma and elective patients before and after the prophylactic antibiotic protocol change. Comparisons were made using the Pearson uncorrected test with significance set at $p<0.05$.

RESULTS

148 (33%) of the trauma and 106 (12%) of the elective patients had their diarrhoeal faecal specimens examined. There were 32 cases of *C difficile*–associated diarrhoeal infection and 28 cases of early deep wound infection (Table). The frequency of *C difficile*–associated diarrhoeal infection decreased after use of the new antibiotic protocol (from 4 to 1%, p=0.004), particularly in the trauma patients (from 8 to 3%, p=0.02); in the elective patients the difference was not significant (from 1 to 0.5%, p=0.27). The change of antibiotic protocol did not significantly affect the incidence of deep wound infections in the trauma (p=0.46) or elective (p=0.90) patients. The rate of *C difficile* infection was 8-fold higher in the trauma than elective patients, both before and after the change of protocol.

DISCUSSION

The rate of early deep wound infections in our department was in keeping with those previously reported.[15–17] Specifically, the rate of early deep wound infection in trauma patients was nearly twice that of elective patients, which again was in keeping with other study.[18] The higher incidences of both early deep wound infections and *C difficile*–associated diarrhoea in trauma patients reflects the increased patient age (83 vs 70 years, Table) and hence higher likelihood of associated comorbidities.

Even after the change in antibiotic protocol, the frequency of *C difficile*–associated diarrhoea remained high, especially in trauma patients. More initiatives are warranted, e.g. more prudent antibiotic prescribing, isolation of infected patients, enhanced environmental cleaning, hand hygiene, personal protective equipment, and staff education and training.

In our department, compliance to the antibiotic prophylaxis regimens was over 95%; all infected patients received appropriate antibiotics at the appropriate time. Owing to the increase in workload, the number of elective patients was larger after the protocol change, but the frequency of *C difficile*–associated diarrhoea still went down. This finding is consistent with a study using a single dose of cefuroxime with gentamicin as prophylactic antibiotics for proximal femoral fractures.[19]

Hospitals or countries that enforce low usage of cephalosporins (through education, strict antibiotic policies coupled with prescribing penalties) result in lower rates of infections with multiple-resistant organisms.[20–24]

Change of antibiotic prescribing practices demands a strong microbiology presence, robust antibiotic policies, education and laboratory support, as well as a careful evaluation of infected patients and potential pathogens (whether or not confirmed).[25]

There are considerable cost benefits from reducing the numbers of patients treated for overgrowth secondary to cephalosporin therapy, apart from reducing the morbidity and mortality of patients with *C difficile* infections.[26]

Although cephalosporin antibiotics are useful to eradicate a number of common pathogens (especially in patients allergic to penicillin), they should not be used for routine prophylaxis, as their efficacy needs to be preserved for more rational therapeutic prescribing in specific scenarios.[27–30] Orthopaedic surgeons should consider alternative antibiotic regimens for both elective and trauma surgery, whenever the use of metal implants is contemplated.

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