Clostridium difficile-associated diarrhoea in primary joint arthroplasty in Aneurin Bevan University Health Board South

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ABSTRACT

INTRODUCTION The choice of perioperative antibiotics to reduce the prevalence of infection after joint arthroplasty should be considered carefully to minimise the risk of nosocomial infections. Dramatic increases in the incidence and severity of health-care-associated *Clostridium difficile* infection with *Clostridium difficile*-associated diarrhoea (CDAD) have occurred since 2000.

METHODS A retrospective audit of patients who underwent total hip and total knee replacement between 1 January 2005 and 31 December 2007 was undertaken in Aneurin Bevan University Health Board South (ABHBS). Stool samples from patients who had diarrhoea <12 months of surgery were recorded. Positive samples for CDAD <1 month of surgery were identified. After the change in practice in June 2010, a re-audit linked joint-replacement patients between 1 July 2010 and 26 June 2013 with infection control-records for CDAD-positive cases.

RESULTS In the first audit cycle, 1900 joint procedures were carried out in 1845 patients. There were 4 cases of CDAD <1 month of surgery (0.22%). In the re-audit period, 2591 joint procedures were undertaken in 2400 patients: no cases of CDAD <1 month of surgery were recorded. Fisher's exact test gave a two-tailed $p=0.036$.

CONCLUSIONS The significant reduction in CDAD cases after the change in perioperative antibiotic regimen for primary joint arthroplasty mirrored a 66% reduction in overall CDAD cases in the ABUHBS between 2008 and 2012. This reduction was accompanied by financial savings in antibiotics and nursing hours.

KEYWORDS

Arthroplasty – *Clostridium difficile* – Antibiotic prophylaxis

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The choice of perioperative antibiotics to reduce the prevalence of infection after joint arthroplasty should be considered carefully to minimise the risk of nosocomial infections. Dramatic increases in the incidence and severity of health-care-associated *Clostridium difficile* infection (CDI) with *Clostridium difficile*-associated diarrhoea (CDAD) have occurred since 2000, particularly in patients aged >65 years.¹

Antibiotic use (including those given perioperatively) is the most widely recognised and modifiable risk factor for CDAD.² The incidence of CDAD in primary joint arthroplasty has been found to be higher in patients who receive antibiotics after surgery,^{3,4} and such patients have more comorbidities⁵ and spend longer in hospital,⁵ than those who do not receive antibiotics after surgery. In primary elective joint arthroplasty, the prevalence of CDAD has been reported to be as high as 2.2%, with a mortality of 0.35%, and it can increase the mean duration of hospital stay by 33 days for affected patients.⁶

Reduction in the prevalence of CDAD in the National Health Service (NHS) was part of a national drive in the late-2000s by the Department of Health (DoH) to tackle healthcare-associated infections (HCAIs). The DoH produced guidelines advising NHS organisations on how to reduce the prevalence of CDIs. The DoH advised that, to manage CDIs, all hospital trusts/health boards should have Infection Control Teams (or equivalent) to monitor CDI/CDAD and implement guidelines for prescribing antibiotics. Recommendations in those guidelines for surgery included avoiding use of second- or third-generation cephalosporins (especially in the elderly) and that, for prophylaxis, one dose of antibiotic should be administered as close to the surgical procedure as possible.⁷

The Infection Control Department (ICD) in the Aneurin Bevan University Health Board South (ABUHBS) began collecting data on CDI/CDAD in January 2007. They recommended that the Department of Trauma and Orthopaedics

should change the perioperative antibiotic regimen for elective orthopaedic surgery in June 2010. The original regimen for surgical prophylaxis in joint-replacement surgery before this date was three doses of cefuroxime (1.5g), one at induction and two doses 6h and 12h after surgery. Paul Roberts, in consultation with the Microbiology Department in the ABUHBS, established a new perioperative regimen of teicoplanin (400mg) plus gentamicin (120mg) at induction only. This new regimen was based on analyses of local bacterial strains and sensitivities, as well as the literature relating to peri-prosthetic infection. Gentamicin appears less likely to predispose to CDI.⁷ Teicoplanin has been found in two randomised control trials to be as effective as cephalosporins in preventing postoperative infection in arthroplasty.^{8,9}

An audit cycle was undertaken to determine if this change in the perioperative antibiotic regimen for primary joint arthroplasty could reduce the prevalence of postoperative CDAD.

Methods

A retrospective audit of patients who underwent primary hip arthroplasty or primary knee arthroplasty between 1 January 2005 to 31 December 2007 and 1 July 2010 to 26 June 2013 was undertaken in our department (ABUHBS) comprising two hospital sites: Saint Woolos Hospital and Royal Gwent Hospital in Newport, Wales. The population of patients who underwent primary total hip arthroplasty or primary total and partial knee arthroplasty was identified through a theatre-management system (ORMIS; CSC Healthcare Group, Banbury, UK) using appropriate procedure codes.

In the first audit, all arthroplasty patients from the three-year time period who had a *Clostridium difficile*-positive stool sample as a result of diarrhoea <1 month of surgery were identified from microbiology records. The re-audit cycle was an equivalent time period taken from 1 month after the change in prescription of prophylactic antibiotics

Table 1 Arthroplasty patients with/without *Clostridium difficile*-associated diarrhoea (CDAD) according to perioperative antibiotic regimen

Perioperative antibiotic regimen	Arthroplasty patients without CDAD	Arthroplasty patients with CDAD
Cefuroxime 1.5g, 3 doses	1,841	4
Gentamicin 120mg plus teicoplanin 400mg	2,400	0

in ABUHBS. During this period, when comparing the list of arthroplasty patients with ICD records of positive cases, no arthroplasty patients were identified as testing positive for *Clostridium difficile*.

Data were analysed using Fisher's exact test in SPSS v20 (IBM, Armonk, NY, USA). The null hypothesis was that there would be no difference between the prevalence of CDAD before and after the change in prescribing practice.

Results

In the first audit period, 1900 joint replacements were carried out in 1845 patients. Fifty-nine patients had diarrhoea <1 month of arthroplasty, of which 4 cases tested positive for *Clostridium difficile* (0.22%). In the re-audit period, 2591 joint replacements were undertaken in 2400 patients, and no cases of CDAD <1 month of surgery were documented (Table 1).

Fisher's exact test gave a two-tailed $p=0.0356$, thereby showing a significant association between the two outcomes. Demographic information of patients who developed CDAD in the first audit period is shown in Table 2. All patients did not receive the standard perioperative antibiotic regimen. In Table 2, patient number 2 received five

Table 2 Details of the four patients who suffered *Clostridium difficile*-associated diarrhoea (CDAD)

Patient number and details	Antibiotic therapy	CDAD episode details
(1) 65-year-old female, THR 21/10/2005	Cefuroxime 1.5g on induction followed by 3 × 750mg doses	Diarrhoea sample 27/10/2005 positive for CD treated with one course of metronidazole
(2) 74-year-old male, TKR 12/09/2006	Cefuroxime 1.5g on induction followed by 3 × 750mg doses	Five doses of gentamicin 12–19/09/2006 for catheterization; single episode of loose stool 19/09/2006 positive for CD
(3) 77-year-old female, TKR 06/10/2006	Cefuroxime 1.5g on induction followed by 2 × 750mg doses	Loose stool sample 11/10/2006 positive for CD treated with one course of metronidazole
(4) 64-year-old female, THR 17/08/2007	Cefuroxime 1.5g on induction followed by 2 × 750mg doses	Diarrhoea 20/08/2007 sample positive for CD treated with vancomycin because of CD 24/09/2005 necessitating hospital admission and antibiotic therapy

THR, total hip replacement; TKR, total knee replacement; CD, *Clostridium difficile*

Figure 1 Total number of cases per year of *Clostridium difficile*-associated diarrhoea in Aneurin Bevan University Health Board South

doses of low-dose gentamicin before the development of diarrhoea, and patient number 4 suffered CDAD 2 years before arthroplasty.

Discussion

Reduction in the number of patients with CDAD after the change in perioperative antibiotic regimen for primary hip arthroplasty and primary knee arthroplasty mirrored a 66% reduction in overall cases of CDAD in the ABUHBS between 2008 and 2012 (Fig 1). This finding is in accordance with a 49% reduction in the prevalence of CDI in NHS hospitals in England between January 2010 and June 2013.¹⁰ A study investigating changes in perioperative antibiotic regimens during similar time periods (2006 to 2011) found no cases of CDAD in either group.¹¹ An original prevalence of CDAD in the ABUHBS of 0.22% was comparable with other studies of CDAD in joint arthroplasty. A study between January 2001 and May 2006, as well as a study between January 2006 and December 2010, gave a prevalence of 0.16%.^{5,12}

Use of a single, high dose of gentamicin (4.5mg/kg body weight) as antibiotic prophylaxis in joint arthroplasty has been associated with an increased prevalence of postoperative acute kidney injury.^{11,13,14} Consequently, this regimen was not considered to be an appropriate option. Combination of low-dose (3mg/kg) gentamicin plus teicoplanin (400mg) at induction only is a safe and reasonable choice based on national recommendations,⁷ microbiological evidence,⁹ and use by other orthopaedic departments.¹⁵

There are additional benefits to single-dose regimens. Using the prices given in the British National Formulary, the ABUHBS made a saving of £6,115 in antibiotics in the re-audit period (not including the cost of consumable equipment). This sum did not include the nursing hours saved in administration of single-dose regimens (which should not be underestimated) nor the additional risk of HCAs from the persistent use of intravenous cannulae required for postoperative antibiotic administration.

Our retrospective audit cycle showed that, between the two limited periods during which practice was changed in perioperative antibiotic regimens, a reduction in the prevalence of CDAD was observed. Statistical analyses supported the notion that this finding was unlikely to be due to chance. Nevertheless, this audit was limited to CDAD and did not consider all nosocomial/surgical-site infections, which are multifactorial in cause and could be considered clinically more relevant than a single infection that has a declining and low prevalence. With respect to perioperative antibiotics and CDAD, Jenkins *et al*⁴ undertook a power calculation that showed 43,198 patients would be required in each arm for a randomised control trial, a number that would necessitate national, multicenter involvement.

Conclusions

Our audit showed that, after changing practice in a perioperative antibiotic regimen for primary hip arthroplasty and primary knee arthroplasty in accordance with NHS guidelines developed to combat CDAD,⁷ a reduction in the prevalence of CDAD from 0.22% to 0% was observed, and this reduction was significant. This finding is important because changes in clinical practice are taking place continuously as a result of local, regional, and national drives to improve patient care. Such changes can be accepted into practice and may not be evaluated routinely. For example, 3 years elapsed between audit periods, and the original audit was carried out well before national changes were implemented. We would encourage other researchers to look critically at established aspects of their practice. Success in surgery is now more likely to be due to attention to the small, routine aspects of our work (eg Surgical Safety Checklist (World Health Organization) or Enhanced Recovery After Surgery (Enhanced Recovery After Surgery Society) protocols) than major changes in surgical methods or new devices.

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