



Clostridium difficile in hip fracture patients: Prevention, treatment and associated mortality

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ABSTRACT

Background: A series of infection control measures were introduced at the University Hospitals of Leicester NHS Trust in 2006–2007 to reduce the incidence of *Clostridium difficile* infection.

Aim: The aim of this study was to assess the impact of these measures on the incidence of *C. difficile* and to record the associated mortality in hip fracture patients.

Patients and methods: A case matched comparison of mortality was conducted between *C. difficile* positive patients and *C. difficile* negative patients admitted with a hip fracture between 1st January 2003 and 30th September 2007. An interrupted time series analysis was performed to assess the effect of various infection control policies on the incidence of *C. difficile* infection.

Results: The interrupted time series analysis showed that the only effective measure was changing antimicrobial prophylaxis to Co-amoxiclav in May 2007. This reduced the incidence of *C. difficile* from 7.1 to 1.5% ($p < 0.001$). Six-month mortality in *C. difficile* positive patients was 71% 1 year before introduction of a diarrhoea treatment policy and 65% 1 year after ($p = 0.5$) indicating treatment was ineffective. A matched cohort comparison over a 57-month period from January 2003 to September 2007 showed that the 6-month mortality was 67% in 170 *C. difficile* positive patients, 27% in 3247 *C. difficile* negative patients and 29% in the 170 *C. difficile* negative matched patients.

Conclusion: This 38% excess mortality indicated that *C. difficile* increased mortality and did not simply colonise the sickest patients. Changing prophylaxis to Co-amoxiclav was the most effective measure. This reduced the incidence of *C. difficile* by 80% and thus reduced mortality by prevention rather than cure.

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Introduction

Clostridium difficile associated diarrhoea (CDAD) is a growing problem worldwide^{9,10,14,15} and is increasingly associated with mortality in hospital patients.^{12,14} In the UK alone, there were more than 55,000 reported cases of *C. difficile* in 2006⁶ and *C. difficile* was mentioned on 6480 death certificates.¹² A study in Quebec found that 23% of patients died within 30 days of contracting *C. difficile* infection.¹⁴ This infection is associated with the use of a variety of antibiotics^{13,21} routinely used in elective and trauma orthopaedic surgery.¹¹

The University Hospitals of Leicester NHS Trust has approximately 4000 trauma admissions in a year. This includes about 700 hip fracture patients, almost all of whom receive antibiotics. Indications for antibiotic use include surgical prophylaxis and treatment of wound and other infections.

In July 2006, a healthcare commission enquiry into a *C. difficile* outbreak in Stoke Mandeville Hospital stated that patient deaths due to *C. difficile* infection could have been avoided.⁷ At this time an increasing number of patients at our hospital were noticed to be suffering from *C. difficile*. As a result of this a *C. difficile* task force overseen by the trust infection control committee was set up in July 2006 and a series of infection control measures were introduced to reduce the rate of *C. difficile* infection and to reduce mortality in patients suffering from *C. difficile* diarrhoea.

The aim of this study was to assess the individual and overall impact of these policies on the incidence of *C. difficile* infection. We also aimed to record the mortality associated with *C. difficile* in order to assess whether patients died “of *C. difficile*” and not just “with *C. difficile*”.

Patients and methods

We performed two separate studies. In the first, we performed a case-matched comparison of mortality between *C. difficile* positive patients and *C. difficile* negative patients and in the second, we assessed the impact of the infection control measures.

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Definitions

“*C. difficile* infection” was defined as positive stool sample for *C. difficile* toxin in a patient with diarrhoea. “*C. difficile* negative” was defined as no diarrhoea or diarrhoea with negative stool sample for *C. difficile* toxin. Fracture neck of femur patients were those admitted with intra-capsular, inter-trochantric and sub-trochantric fractures of the proximal femur.

Infection control measures

The first policy introduced was the five-day antibiotic stop policy in August 2006 wherein antibiotics were to be prescribed for a maximum of 5 days and any further prescription required microbiology department approval. Intravenous administration of certain high-risk antibiotics such as fluoroquinolones¹³ also required microbiology department approval. The next policy was

Antimicrobial Guidelines for the Management of *Clostridium difficile* associated diarrhoea in adults

Background:

These guidelines are for adult patients with suspected or confirmed *Clostridium difficile* associated diarrhoea. Consider *C. difficile* infection in any patient who has diarrhoea following or during antibiotic therapy.

Recommendations:

<p>If possible STOP ANTIBIOTICS and Proton Pump Inhibitors (PPI)</p> <p>Consult Microbiology for advice if antibiotic therapy is still required for treatment of original infection. Consider alternatives to PPI's if acid suppression required.</p>
<p>STOP Laxatives and Prokinetic agents <small>e.g. metoclopramide and erythromycin</small></p> <p>If possible STOP Opioids and Steroids</p>
<p><i>Start treatment with</i> METRONIDAZOLE PO 400mg tds for 10 days <i>even if still awaiting CDT results.</i></p> <p>Complete <u>a full course</u> of treatment if CDT result positive, irrespective of patient's response.</p> <p><i>If the CDT result is negative stop metronidazole and re-test after 72 hours. If a subsequent test is positive give metronidazole treatment for 10 more days.</i></p> <p><i>* If enteral administration is not possible give IV metronidazole 500mg tds until the enteral route is available (to complete a 10 day course)</i></p>
<p>If CDT positive patients are still symptomatic after 10 days treatment of first line therapy</p> <p>VANCOMYCIN PO 125 mg qds for 10 days</p> <p>Complete <u>a full course</u> of treatment, irrespective of patient's response.</p> <p><i>* If enteral administration not possible, discuss with Microbiologist</i></p>
<p>For persistent or relapsing <i>Clostridium difficile</i> associated diarrhoea</p> <p>Refer to Microbiologist</p>

No further stool samples to be sent if the patient has had a positive CDT result
 unless there is a relapse (i.e. symptoms recurring 4 or more weeks after first diagnosis)

In patients with on-going symptoms and CDT negative results
 Repeat stool sample after 72hrs

* The enteral route is more effective for treating *Clostridium difficile* associated diarrhoea.

No dose reductions are required in renal impairment. Refer to Pharmacist / Microbiologist for advice on treatment in patients with liver impairment. For information on contraindications, cautions, drug interactions and adverse effects refer to the British National Formulary www.bnf.org or the Medicines Compendium www.medicines.org.uk

Fig. 1. Antimicrobial policy for the management of *Clostridium difficile* associated diarrhoea in adults.

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