Journal of Hospital Infection (2009) **72**, 111–118

Available online at www.sciencedirect.com

ScienceDirect

www.elsevierhealth.com/journals/jhin

Clostridium difficile ribotypes 027 and 106: clinical outcomes and risk factors☆

F. Sundram [a,*], A. Guyot [a], I. Carboo [a], S. Green [b], M. Lilaonitkul [a], A. Scourfield [a]

[a] *Department of Microbiology, Royal Surrey County Hospital and PPS Laboratory, Frimley Park Hospital, Surrey, UK*
[b] *Department of Molecular Microbiology, Health Protection Agency, Southampton, UK*

Received 30 March 2008; accepted 20 February 2009
Available online 21 April 2009

KEYWORDS
Ciprofloxacin;
Clostridium difficile-associated diarrhoea;
Ribotyping; Spores

Summary The present study investigates risk factors for onset of *Clostridium difficile*-associated diarrhoea, specific ribotype and environmental spore contamination in a District General Hospital in South East England. *C. difficile* isolates were ribotyped from 97 diarrhoeal cases, following detection of *C. difficile* toxin from faecal specimens by enzyme immunoassay (Health Protection Agency, Southampton). The isolates were tested for various antimicrobial susceptibilities by E-test. Cases were assessed for prior antibiotic use and followed up for clinical outcomes. Controls were matched for age, sex, ward, length of stay and comorbidity to identify any antibiotic risk factors using conditional logistic regression analysis. Environmental sampling on wards was performed with cycloserine–cefoxitin–egg yolk agar. Forty-five percent *C.difficile* isolates ribotyped as 027, 39% as 106 and 10% as 001. All ribotypes were resistant to ciprofloxacin, erythromycin and cefotaxime but remained susceptible to metronidazole and vancomycin. The crude (death within 28 days) and early (death within 72 h) mortalities were 23% and 11% for the 027 strain, whereas for the 106 ribotype they were 11% and 3%, respectively. The case–control study identified ciprofloxacin usage for >7 days as a significant risk factor (adjusted odds ratios of 3.72; 95% CI: 1.38–10.02; $P = 0.019$). Environmental sampling revealed the presence of spores on

☆ The findings were presented at the Federation of Infectious Societies Meeting in Cardiff, November 2007.

* Corresponding author. Address: Royal Surrey County Hospital, Guildford, Surrey GU2 7XX, UK. Tel.: +44 208 445 7201; fax: +44 208 079 6408
E-mail address: fredasundram@btinternet.com

doi:10.1016/j.jhin.2009.02.020

faecally contaminated equipment such as commodes and bedpan shells, which persisted after cleaning. Ciprofloxacin appears to encourage *C.difficile*-associated diarrhoea and should be restricted to short courses. Cleaning agents for clinical equipment must have sporicidal activity to prevent cross-transmission.

Introduction

Since 2001, outbreaks have occurred due to a hypervirulent strain of *C. difficile* which has affected hospitals in Europe and North America. More than 150 polymerase chain reaction (PCR) ribotypes and 24 toxinotypes of *C. difficile* have been identified. The new *C. difficile* strain (PFGE type NAP-1, which is ribotype 027 and toxinotype 3) generates amounts of toxins A and B 16—23 times greater than other pulsed-field gel electrophoresis (PFGE) types, thought to be due to an 18 bp deletion in the negative regulator gene *tcdC*.[1] This strain also possesses a binary toxin, described in 1988, which is encoded by genes *cdtA* and *cdtB* outside the pathogenicity island *PaLoc* but the role of this toxin is unclear.[2]

In the UK until 2003, ribotype 001 was responsible for ~60% of cases of *C. difficile*-associated diarrhoea (CDAD). Molecular surveillance in 2006 demonstrated that 40% of C. *difficile* isolates from 21 hospitals in South East England were ribotype 027, 21% ribotype 106 (toxinotype 0) and only 10% ribotype 001.[3] In acute trusts in South East England the incidence of *C. difficile* ranged between 2 and 6/1000 bed-days in 2006. At the Royal Surrey County Hospital (RSCH), a district general hospital in the South East of England, the incidence of *C. difficile* reached a peak of 3.56 per 1000 bed-days among elderly admissions and prompted the current study.

The primary aim of this study was to identify risk factors for the development of CDAD using a case—control design and to relate the clinical presentation and any complications to the PCR ribotype. Variables studied included antibiotic risk factors, enteral feeding, and gastric acid suppression therapy. A secondary aim was to detect the environmental reservoir by undertaking environmental sampling. Third, isolates from different ribotypes were tested against a panel of eight antibiotics to determine the association between antibiotic selection and susceptibility.

Methods

Data collection and definitions

Hospital-acquired CDAD was assessed in 97 patients from 1 March 2006 until 31 March 2007 at the Royal Surrey County Hospital (RSCH), which is a medium-sized district general hospital with 520 beds. The hospital has 18 wards, each of which has four six-bedded bays and four side-rooms.

The project was approved by the local ethics committee at RSCH.

Hospital-acquired infection was defined as onset of diarrhoea (more than one loose stool per day for at least two days) occurring >48 h after admission. Cases whose stool tested positive for *C. difficile* toxin (CDT) A or B by enzyme immunosorbent assay (Meridian Premier, Meridian Bioscience Inc., Cincinnati, OH, USA) had their stool samples saved. Data were then collected retrospectively and entered on to a standardised clinical questionnaire.

Cases who had tested positive within four weeks of the original result were excluded as new cases. Any positive paediatric samples were also excluded. A total of 159 cases of all 302 hospital-acquired CDAD patients were captured during the 13 month study period. Of those, 62 were not included for the following reasons: 20 failed to grow on culture, nine failed to ribotype, and 33 stools were not stored after toxin test.

Ninety-seven controls were matched to the cases and were selected from hospital inpatients, who did not have diarrhoea at the time of the study and had never tested positive for CDAD before. Each control was matched to a case by sex, age, ward, American Society of Anesthesiologists' (ASA) score and length of stay (LOS). Patients' medical records were examined for the following clinical information: age, gender, LOS, ward location seven days prior to onset of symptoms, ASA score, admission diagnosis and indication for antibiotics, enteral feeding, proton pump inhibitor (PPI) or H2 blocker use and antibiotics