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Reminding doctors which antibiotics to prescribe cuts *C. difficile* infection rates

A study published today in the *Journal of Antimicrobial Chemotherapy*¹ provides the best available evidence that cases of *Clostridium difficile* infection (CDI)---one of the most common and increasing types of hospital-acquired infection---can be reduced in hospital wards if doctors prescribe narrow-spectrum antibiotics rather than broad-spectrum agents.

Researchers at the Royal Free Hospital in London, which now has the lowest CDI rates of any teaching hospital in the UK, investigated the best way to encourage doctors to make the switch from broad spectrum to narrow spectrum agents. They found that use of a pocket-sized laminated card telling doctors which antibiotics to prescribe combined with feedback on antibiotics use and CDI rates led to a significant drop in prescriptions of broad-spectrum agents, and an accompanying fall in CD infections.

The research team, from the Academic Department of Geriatrics, in the Medical School, suggest that both the study and the intervention could be successfully replicated in other hospitals in an attempt to reverse the rapid increase in CDI in the NHS.

This finding is especially important because CDI rates are rising rapidly in the UK and a new more virulent strain has recently been identified² A 2005 study by the Healthcare Commission³ found that 38% of NHS Trusts did not restrict broad-spectrum antibiotic use, despite the known association between these compounds and CDI.

BACKGROUND

Drugs such as cephalosporins---so-called broad-spectrum agents because of their action against many types of bacteria---damage normal intestinal flora in addition to killing disease-causing microbes. This damage gives CD the opportunity to spread in the guts of patients recently treated with antibiotics. Infected patients can develop diarrhoea, colitis, and other conditions associated with intestinal inflammation. Rarely, CD infection can be fatal.

By contrast, drugs that target only specific types of bug cause less damage to normal gut bacteria and therefore reduce the likelihood that CD will take hold.

In their audit study, Dr Sheldon Stone, of the Academic Department of Geriatrics, Royal Free and University College Medical School, London, and colleagues investigated whether use of feedback to individual doctors about their prescribing habits can improve adherence to a narrow-spectrum antibiotic prescribing policy, thereby reducing CD cases.

“National guidelines recommend narrow-spectrum antibiotic policies and suggest a variety of methods to ensure these are implemented, but feedback is not mentioned in national guidelines as a way of addressing prescribing behaviour,” says Dr Stone.

The team, working at the Royal Free Hospital in London, studied prescribing and CDI rates in three wards for acute care of the elderly where CD was endemic. When the study began, doctors working on the wards had already been told to use less cephalosporin to treat bacterial infections, but this policy had resulted in increased use of another broad-spectrum antibiotic, amoxicillin/clavulanate.

To prevent future CDI rises as a result of the increased use of amoxicillin/clavulanate, a new narrow-spectrum policy was implemented as part of the hospital’s clinical governance programme at the beginning of July 2001. This policy recommended less use of amoxicillin/clavulanate, increased use of benzyl penicillin, trimethoprim, and amoxicillin, and further restricting cephalosporin use.

Dr Stone and colleagues analysed the effectiveness of reinforcing this new policy with a pocket-sized laminated card telling doctors which drugs to use in which circumstances. These instructions were combined with feedback to doctors every 2-3 months on how many courses of each specific drug they had prescribed, and ward rates of CD infection and MRSA.

Doctors’ prescriptions were compared before the policy change (September 1999-June 2001) and afterwards (July 2001-March 2003). A statistically significant drop in use of both cephalosporin and amoxicillin/clavulanate was observed after the narrow-spectrum policy came into effect. Prescriptions for antibiotics not specified by the policy did not change during this time, suggesting that the feedback and laminated card had had the desired targeted effect. There was also a significant fall in rates of CDI associated with the policy change.

“We have shown that introduction of a narrow-spectrum antibiotic policy, reinforced by feedback, was associated with significant changes in targeted antibiotics and a significant reduction in CDI”, explains Dr Stone.

“National figures for CD and associated diseases showed the Royal Free to have the lowest rates of any teaching hospital. This success is largely being attributed to the antibiotic policies described in the paper”, he adds.

The authors think their study could be a useful reference for other centres where cephalosporin use is higher than in the Royal Free. Compared with many other hospitals, cephalosporin use was already low at the beginning of the study and the intervention was still highly successful, indicating that even better results could be achieved in institutions where a greater reduction is desirable.

Dr Stone and colleagues used an interrupted time series design, which includes a single group of study subjects assessed before and after an intervention (in this case a change to antibiotic prescribing policy). This design includes measurement of many different variables both before and after the intervention, including a set of “control outcomes” that are not expected to change during the course of the study, to reduce the potential contribution of confounding factors to any result.

This design means the study provides stronger evidence than previous investigations of similar interventions. “Nearly all previous studies assessing interventions to improve prescribing were poor quality unplanned studies with no control groups or outcomes and inadequate statistical analysis,” explains Dr Stone.

The authors suggest that wider use of this method to study interventions in other hospitals would enhance the pool of good quality evidence on the best ways to change antibiotic prescribing. It would also enable meaningful comparisons between studies and interventions.

The paper is intended to be an example of best practice for reporting such studies. Guidelines laying out minimum requirements for data recording, statistical analysis, and reporting are contained in the consensus statement for infection control studies---labelled the **ORION (Outbreak Reports and Intervention studies Of Nosocomial infection)** statement---are being published simultaneously in *The Lancet Infectious Diseases* this month and also the *Journal of Antimicrobial Chemotherapy*.⁴ This statement, put together with the aim of improving the quality of research in hospital epidemiology to ensure it is robust enough to influence policy and practice, is intended to be an equivalent to the CONSORT standards and checklist for reporting of randomized controlled trials.

Dr Stone says: “The quality of research in infection control must be robust enough to influence policy and practice in the fight against hospital acquired infection. This statement is intended to help produce well designed studies that will aid that fight”

The ORION statement was prepared and revised following widespread consultation with learned societies, editors of journals, and researchers with

knowledge relevant to infection-control. It consists of a 22 item checklist and a summary table.

The statement has been endorsed by several professional special interest groups and societies including the Association of Medical Microbiologists (AMM), British Society for Antimicrobial Chemotherapy (BSAC) and the Infection Control Nurses' Association (ICNA) Research and Development Group.

(ends)

Notes to editors:

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1. S. Fowler, A. Webber, B.S. Cooper, A. Phimister, K. Price, Y. Carter, C.C. Kibbler, A.J.H. Simpson, S.P. Stone. Successful use of feedback to improve antibiotic prescribing and reduce Clostridium difficile Infection (CDI): A controlled Interrupted Time Series (ITS). *Journal of Antimicrobial Chemotherapy* 2007. doi:10.1093/jac/dkm014

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2. Source: Health Protection Agency. Outbreak of Clostridium difficile infection in a hospital in southeast England. *CDR Weekly* 2005; 15: 2-3.

3. Source: Healthcare Commission. Management, prevention and surveillance of Clostridium difficile, 21 Dec 2005. www.healthcarecommission.org.uk.

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4. S. P. Stone, B.S. Cooper, C.C. Kibbler, B.D. Cookson, J.A. Roberts, G.F. Medley, G. Duckworth, R. Lai, S. Ebrahim, E.M. Brown, P.J. Wiffen and P.G. Davey.

The ORION statement: guidelines for transparent reporting of Outbreak Reports and Intervention studies Of Nosocomial infection *Journal of Antimicrobial Chemotherapy* 2007.

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6. The JAC website is <http://jac.oxfordjournals.org/>

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