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The effect of an enhanced infection-control policy on the incidence of *Clostridium difficile* infection and methicillin-resistant *Staphyloccocus aureus* colonization in acute elderly medical patients

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Abstract

Background: *Clostridium difficile* (CD) infection and methicillin-resistant *Staphylococcus aureus* (MRSA) colonization are increasingly common in elderly patients, are associated with cephalosporin or prolonged aminopenicillin courses and can be transmitted by direct contact. Management is by side-room isolation. Ward closure may be required to control outbreaks.
Methods: following prolonged bed closures due to CD and MRSA in an acute age-related geriatric service, an enhanced infection control policy was introduced—emphasis on handwashing, cephalosporin restriction, 7-day time limits on antibiotics and feedback of infection rates. The effect of this policy was evaluated by investigating 2467 consecutive admissions in the 9 months before and after its introduction.
Results: CD infection fell from 36/1075 admissions (3.35 per 100) to 27/1392 (1.94 per 100; $P<0.05$). MRSA incidence fell from 3.95 per 100 to 1.94 ($P< 0.01$) whilst that in the rest of the hospital continued to fluctuate. Cephalosporin use fell (and aminopenicillin and trimethoprim use rose) by a factor of three. Unoccupied bed days fell from 1164 (12.6%) to 513 (5.1%) over the winter, an increase in bed availability of 4.95 a day.
Conclusions: introduction of the policy was associated with significant reductions in CD infection and unoccupied bed-days and helped maintain a lower incidence of MRSA. It is not clear which elements of the policy most influenced outcome. A multi-centre study is needed to determine whether our findings are generally applicable.

Keywords: *acute medical patients*, Clostridium difficile, *infection-control policy*, *methicillin-resistant* Staphyloccocus aureus

Introduction

Clostridium difficile (CD) infection [1] and methicillin-resistant *Staphylococcus aureus* (MRSA) colonization [2, 3] are common in elderly patients. The incidence of both in hospitals in the UK is rising [1, 4, 5] and epidemics necessitating ward closure to control them are common [2, 4, 6–8]. Both organisms can be transmitted by direct contact [6, 7, 9, 10]. CD infection is associated with more than 7 days of broad-spectrum penicillin use [4] and both organisms are associated with, in particular, cephalosporin therapy [6, 7, 11–15], use of which has been reinforced by the recent British Thoracic Society recommendations for treatment of severe pneumonia [16].

Side-room isolation, barrier nursing and thorough

handwashing are the mainstay of management of CD [4] and MRSA [8], and the recent Department of Health/Public Health Laboratory Service (DoH/PHLS) working party report on prevention and management of CD infection strongly recommends an antibiotic policy. The evidence cited in favour of this [7, 17-21] is limited and the working party has called for collaborative studies between infection-control doctors and clinicians to investigate further the control of CD infection. Antibiotic policies to contain the spread of MRSA, often in conjunction with feedback of infection rates and thorough handwashing in some [3, 13-15, 22, 23] but not all [24] studies. No study has examined the effect of these measures in preventing CD infection and containing MRSA in elderly (over 75) acute medical emergency admissions.

In the winter of 1994/5, the basal endemic rate of CD infection combined with an outbreak of MRSA at the Royal Free Hospital to cause prolonged bed closures in the acute age-related Geriatric Service. Once control of the MRSA epidemic had been gained, it was decided to enhance the existing infection-control policies [8] in line with DoH/PHLS recommendations [4] by adopting a more stringent antibiotic policy, emphasizing handwashing between patient contacts [4, 25, 26] and feedback of CD and MRSA rates. The effect of this policy was evaluated.

Methods

Geriatric service

The Royal Free NHS Trust runs an acute age-related service admitting patients over 75 to one of three acute medical wards for elderly people (one of 18 beds, two of 24 beds). The average length of stay is 11.4 days with about 80% of patients returning home, 10% dying and a further 10% transferred to separate rehabilitation wards off the main teaching hospital site.

Environment

Each ward contains four-bedded bays plus single-bedded side rooms, of which 10 are distributed across the three wards. Each bay and each side room has handwashing facilities with elbow operated taps and 4% chlorhexidine handscrub dispensers and separate toilet facilities.

Infection-control measures

In the winter of 1994/5, cases of CD infection and an outbreak of MRSA, peaking in January-March 1995, resulted in temporary closure of two of the three acute geriatric wards, as side-room isolation and cohort nursing failed to control spread of infection. The MRSA outbreak affected many of the acute wards of the hospital, despite adherence to national guidelines for management of MRSA [8]. As approximately 50% of patients were over 65, it was agreed that the 18 bedded acute geriatric ward act as an MRSA isolation unit for non-surgical patients over 65 years of age from March-June 1995. When this ward reverted to normal usage, the geriatric service introduced an enhanced infection-control policy, consisting of handwashing, feedback of infection rates and a 'low-cephalosporin' antibiotic policy. The policy was not adopted elsewhere in the hospital.

1. Handwashing between examining patients was emphasized. If patient contact was prolonged, hands were washed with 4% chlorhexidine scrub [26]. After less prolonged contact, alcoholic 0.5% chlorhexidine handrub was used, a dispenser of which was present in each bay and side room and was carried on the medical notes trolleys during doctors' rounds. Nurses of all grades were encouraged to remind doctors of all grades to wash their hands. This policy was lead by the consultant geriatricians on each ward.
2. Feedback: as elsewhere in the hospital, each new MRSA or CD case was discussed with the relevant medical and nursing teams at the time of identification. In addition, quarterly CD infection rates and the monthly incidence of new cases of MRSA colonization or infection were provided by the infection-control team. A consultant geriatrician fed these back to medical staff every 4-6 weeks at a regular departmental teaching session. Nurses were kept informed of these rates by circulars.
3. 'Low-cephalosporin' antibiotic policy. A policy that aimed to limit the length of antibiotic courses to no more than 7 days (5 days in urinary tract infection) and to restrict use of cephalosporins was agreed by the consultant geriatricians and consultants in medical microbiology. The British Thoracic Society recommends ampicillin or amoxycillin as first-line treatment for uncomplicated pneumonia [16] and cephalosporins for severe pneumonia. Cephalosporins were therefore largely replaced by ampicillin or amoxycillin for chest infections, by trimethoprim for urinary tract infections and by gentamicin for serious Gram-negative and intra-abdominal sepsis (in conjunction with other antibiotics as appropriate). Exceptions and their clinical indications were clearly described in the policy. This was distributed to all junior medical staff, including locums, on joining the department (a copy is available on application to the authors). Cephalosporins were removed from ward stock by the pharmacy department who recorded all antibiotic usage, for feedback to medical and nursing staff. The policy was reinforced by the three consultant geriatricians on their twice weekly rounds and on their daily visits to see new admissions, discharges and sick patients.

Definition of CD infection and MRSA infection/colonization

Patients with at least one episode of diarrhoea and stool positive for *Clostridium difficile* toxin A were defined as having CD infection [4, 7]. New cases of MRSA (whether infection or colonization) were defined by a positive culture of swabs taken on clinical grounds or in accordance with national guidelines for screening [8].

Laboratory diagnosis

CD toxin A was detected by means of an ELISA (Premier, Meridian Diagnostics, Cincinatti, OH, USA). CD isolates were not typed. MRSA was identified by standard culture techniques. All isolates underwent extended antibiotic sensitivity testing and were submitted to the Staphylococcal Reference Laboratory for phage typing. More than 90% were E-MRSA-16.

Management of CD infection and of MRSA colonization

Patients with CD infection and those with known or newly detected MRSA were isolated in side rooms. Those with CD had antibiotic therapy withdrawn where possible and those who were unresponsive or had serious disease were treated with oral metronidazole (or vancomycin when indicated). Those with MRSA were managed according to national guidelines (8). Patients transferred into the geriatric unit from other wards with MRSA cases and those admitted from nursing homes were admitted to and screened in side rooms. Infected patients were treated with intravenous teicoplanin. Management of patients with MRSA and contact surveillance was the same before and after introduction of the enhanced infection-control policy.

Statistical analysis

Antibiotic usage was expressed in grammes or milligrammes per 100 patients admitted to the acute geriatric wards. The incidence of new cases of CD infection or MRSA was expressed per 100 patients admitted.

Analysis of CD infection rates was confined to admission of unselected acutely ill patients from casualty to acute geriatric wards (October 1994-March 1996) and excludes those admitted to the MRSA isolation unit.

Analysis of MRSA incidence was confined to the periods when all three acute geriatric wards were admitting unselected acutely ill patients from casualty (October 1994-February 1995 and July 1995-March 1996) as the presence of the Isolation Unit (March-June 1995) would have affected spread of MRSA in the other two wards during this time. The incidence of each in the period before introduction of the enhanced infection-control policy was compared with that in the 9 months after (July 1995-March 1996), using χ^2 tests.

Winter bed occupancy (October 1994-February 1995) was compared with that in the same period the following year, to control for seasonal variation.

Results

CD infection rate

A reduction in the CD infection rate appeared almost immediately after introduction of the infection-control policy (Table 1). There was a significant fall in the incidence from 36 out of 1075 admissions (3.35 cases per hundred admissions) in the 9 months before the policy to 27 out of 1392 admissions (1.94 cases per 100 admissions) in the 9 months after ($\chi^2 = 4.84$, $P < 0.05$).

MRSA incidence

The incidence of MRSA fell significantly from 25/633 admissions (3.95 per 100 patients) before the policy to 27/1392 admissions (1.94 cases per 100 patients) in the 9 months after introduction of the policy

Table 1. Incidence of *Clostridium difficile* infection and cephalosporin usage before and after infection-control policy

	Cephalosporin use (g)	*C. difficile* incidence (per 100 patients)	Total no.of patients
Pre-policy			
Oct-Dec 1994	419	3.10	451
Jan-Mar 1995	388	3.16	285
Apr-Jun 1995	354	3.83	339
Post-policy			
Jul-Sep 1995	163	2.36	466
Oct-Dec 1995	182	1.20	500
Jan-Mar 1996	152	2.35	426

Table 2. Incidence of new cases of methicillin-resistant *Staphyloccocus aureus* (MRSA) and cephalosporin usage before and after infection-control policy

	Cephalosporin use (g)	MRSA incidence (per 100 patients)	Total no.of patients
Pre-policy			
Oct-Dec 1994	419	2.00	451
Jan-Feb 1995	392	8.79	182
Pre-policy			
Jul-Sep 1995	163	2.14	446
Oct-Dec 1995	182	2.20	500
Jan-Mar 1996	152	1.41	426

($\chi^2 = 6.73$, $P < 0.01$; Table 2). Much of the initial fall should be attributed to the MRSA isolation unit preventing cross infection, but a lower rate was maintained after the unit re-opened as an acute geriatric ward and the infection-control policy was introduced. In the rest of the hospital, where the enhanced policy was not in use, the MRSA rate continued to fluctuate (Table 3), as it did in the general medical wards, whose population is most likely to resemble that on the acute elderly wards. The winter peak observed in January-March 1995 throughout the hospital, occurred again in January-March 1996, but was avoided in the acute elderly wards.

Antibiotic usage

Tables 4 and 5 shows that cephalosporin usage fell to a nearly a third of its original level almost immediately after introduction of the infection-control policy. Amoxycillin/ampicillin usage and oral trimethoprim usage (i.v. trimethoprim use was negligible) each rose approximately threefold. Gentamicin usage remained stable, as did usage of intra-venous and oral flucloxacillin, benzyl penicillin and penicillin V (results not shown). Erythromycin usage rose a little, possibly due to use in penicillin allergic patients.

Table 5 shows these changes converted into numbers of notional 7-day antibiotic courses and illustrates a change from cephalosporin usage to the aminopenicillin group and trimethoprim. Despite these changes, the crude mortality of acute elderly patients remained the same (11.4% pre-policy, 11.9% post-policy).

Bed occupancy

From October 1994 to February 1995, the number of unoccupied bed days was 1164 (12.6%) i.e. an average of 8.31 empty beds per day, largely as a consequence of ward closure. During the same period the following year, after introduction of the policy, this number fell to 513 (5.1%), equivalent to an average of 3.36 empty beds a day (i.e. a net gain of 4.95 beds a day). Ward closures had been almost completely avoided, except for an outbreak of infection due to small round structured virus.

Table 3. Incidence of new cases of methicillin-resistant *Staphyloccocus aureus* (MRSA) in acute elderly wards, the rest of the hospital and in general medical wards before and after infection-control policy in acute elderly wards

	MRSA incidence (per 100 patients), by ward type		
	Acute elderly	Hospital[a]	General medicine
Pre-policy			
Oct-Dec 1994	2.00 (451[b])	0.46 (15372)	1.04 (1247)
Jan-Feb 1995	8.79 (182)	0.88 (10245)	3.13 (669)
Post-policy			
Jul-Sep 1995	2.14 (466)	0.53 (16893)	2.02 (937)
Oct-Dec 1995	2.20 (500)	0.46 (16891)	1.35 (1260)
Jan-Mar 1996	1.41 (426)	0.72 (17406)	2.95 (1117)

[a]All other specialities except psychiatry, obstetrics, well babies and paediatrics.
[b]No. of patients.

Table 4. Use of cephalosporin and other antibiotics before and after adoption of infection-control policy

	Antibiotic use (g per 100 patients)					
	Pre-policy			Post-policy		
Antibiotic	Oct-Dec 1994	Jan-Mar 1995	Apr-Jun 1995	Jul-Sep 1995	Oct-Dec 1995	Jan-Mar 1996
Cefotaxime (i.v.)	352	300	310	135	172	117
Cephradine (oral)	67	88	44	28	10	35
Pivampicillin (oral)[a]	109	52	147	-	-	-
Ampicillin (i.v.)	6	37	24	82	142	167
Amoxycillin (oral)[a]	-	-	-	171	250	226
Erythromycin (oral)	116	154	144	132	228	164
Gentamicin (i.v.)	0.9	3.2	3.5	2.7	2.4	2.8
Trimethoprim (oral)	13	14	18	36	32	42

[a]Oral pivampicillin was replaced by amoxycillin in July 1995.

Table 5. Notional courses of each antibiotic per 100 patients before and after adoption of infection-control policy

	Course length (per 100 patients)					
	Pre-policy			Post-policy		
Antibiotic	Oct-Dec 1994	Jan-Mar 1995	Apr-Jun 1995	Jul-Sep 1995	Oct-Dec 1995	Jan-Mar 1996
Cephalosporin	22	20	19	8	9	9
Aminopenicllins	17	11	23	22	34	34
Trimethoprim	4	5	6	13	11	15
Gentamicin	1	4	4	3	3	3
Erythromycin	8	11	10	10	16	12

Discussion

Guidelines for infection-control should be based on good evidence and evaluated in clinical practice. The DoH/PHLS Working Party called for further collaborative studies by clinicians and infection-control doctors [4]. This study was designed to investigate the effect of an enhanced infection-control policy on the rates of CD infection and MRSA colonization in acute elderly medical emergency admissions. Introduction of this policy was associated with a significant reduction in the basal endemic rate of CD infection in acute elderly medical emergency admissions and helped maintain a lower incidence of MRSA. The resultant lack of ward closures approximated to an extra five beds a day during the winter months. It is not possible to determine which elements of the policy were most influential: low cephalosporin usage, time limits on antibiotic courses, handwashing or feedback of infection rates.

Cephalosporin reduction has helped contain MRSA in orthopaedic [12] and surgical wards [14, 15] as did other unspecified antibiotic policies [27]. Our findings are consistent with these studies and with those which claim that cephalosporins increase the risk of CD infection [6, 7, 11], especially when the cumulative dose exceeds 10 g [4]. In less acute geriatric patients the relative risk of CD infection was highest for cephalosporins, ampicillin and trimethoprim carrying no extra risk [11]. Our results are consistent with this, as increasing use of ampicillin and trimethoprim did not restore CD to previous levels. We did not find as close a relationship between CD rates and cephalosporin usage as that study reported and two case-controlled studies, largely surgical, have implicated multiple antibiotic use rather than cephalosporins [17, 18]. Prescription of broad spectrum penicillins for longer than seven days increases the risk of CD [4, 28] and although we have no data on the number of courses longer than seven days, it is possible that time limits on antibiotic use may have combined with cephalosporin restriction to reduce CD infection and contain MRSA, by discouraging selection of resistant organisms and other pathogens [29].

Our study perhaps gives the clearest evidence to date that an antibiotic policy as recommended by the DoH/PHLS report [4] may contribute to prevention of CD infection. The evidence quoted in the report is limited to case-control studies [17, 18] of risk factors for CD infection in surgical and dialysis patients and to studies that report an antibiotic policy as one of several measures that control established outbreaks [7, 19–21] in paediatric oncology, renal or general medical patients, without details of the policy or data on changes in antibiotic use. Our study differs in that: (i) the antibiotic policy is explained, allowing replication by other units; (ii) infection rates are adjusted for flows of patients, which allows comparison with future studies; (iii) data on antibiotic use are provided and show that the policy was effective in changing this; (iv) our aim was to reduce the basal endemic rate of CD rather than control an outbreak [7, 18–21]; (v) all patients were elderly (over 75) acute medical emergencies.

The close working relationships between infection-control nurses and ward nurses and between senior medical staff in microbiology and geriatrics probably contributed to the effectiveness of our policy, with one geriatrician taking the clinical lead and co-ordinating feedback to junior staff. Feedback of infection rates is effective in reducing surgical infection rates [22]. In our study this may have combined with consultant emphasis on the antibiotic policy and handwashing. The latter may be especially important in preventing spread of MRSA which, like other *Staphylococcus aureus* [30], is transmitted primarily by direct contact [9, 10, 13]. Our results are consistent with other reports of containment of MRSA by handwashing and basic antisepsis [3, 10] together with, in one study, feedback of MRSA incidence [23].

Although the initial fall in MRSA is most likely due to the MRSA isolation unit, it remained low once the ward reverted to acute geriatric use: this might be due to the enhanced infection-control policy, particularly as the incidence of MRSA was 3.22 per 100 patients in the quarter preceding this study and continued to fluctuate in the rest of the hospital and in general medical wards where the policy was not being implemented. The winter peak first observed in January–March 1995 throughout the hospital was again observed in January–March 1996, but was avoided in the acute elderly wards which, instead, experienced a sustained fall.

Environmental and administrative factors—including adequate handwashing facilities, sufficient side rooms, adequate ward cleaning and avoidance of under-staffing and overcrowding [4, 31], geographical concentration of elderly patients, one consultant per ward, short length of stay and the ability to transfer MRSA patients requiring rehabilitation into side rooms in a rehabilitation hospital—will all have facilitated this policy and may make it less generally applicable in hospitals where these facilities are more limited. Indeed, others have reported failure of side-room isolation, antibiotic policies and handwashing combined, in containing MRSA [24].

Our attempt to control CD infection and contain MRSA was successful in the setting of an acute admitting medical service for elderly people and supported the guidelines for management of these conditions [4, 8, 32]. Given the serious implications of a continued rise in these organisms as the population ages [4], multi-centre studies of infection-control policies from acute geriatric units are required to determine to what extent our findings are generally applicable.

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Key points

- The incidences of *Clostridium difficile* (CD) infection and methicillin-resistant *Staphyloccocus aureus* (MRSA) colonization infection is continuing to rise in elderly patients in hospital.
- An enhanced infection-control policy consisting of handwashing after patient contact, low cephalosporin usage, 7-day time limits on antibiotic courses and feedback of CD and MRSA rates was shown to be effective.
- The incidence of CD infection in elderly patients was significantly reduced and a lower incidence of MRSA was maintained whilst that in the rest of the hospital continued to fluctuate.
- Ward closures were avoided, resulting in an average increase of five available beds a day in the winter.
- Multicentre studies are required to determine to what extent the findings are generally applicable.

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