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Antibiotic resistance in long-term care facilities

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SUMMARY

Long-term-care facilities (LTCFs) comprise a heterogeneous group of institutions that provide a wide variety of services to diverse groups of patients, most of whom are elderly. Infections are common in LTCFs and these are complicated by antimicrobial-resistant pathogens. The residents in LTCFs have a high frequency of colonization with antimicrobial-resistant organisms, including methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, penicillin-resistant pneumococci, extended spectrum β-lactamase-producing gram-negative organisms, and fluoroquinolone-resistant gram-negative organisms. Although several control programs have been published, up to now there still is a long way to go in this area of health care. This review will briefly touch upon the clinical relevance of antimicrobial resistance in LTCFs.

KEY WORDS: Antibiotic resistance, Bacterial infections, Long-term care facilities

INTRODUCTION

The populations of developed countries are becoming increasingly elderly. Aging is associated with an increased frequency of chronic diseases and declining functional status necessitating institutional care for at least some time for a substantial proportion of the elderly. Infections are common among residents in long-term care facilities (LTCFs), with a frequency comparable to rates observed in acute care facilities. Infection rates vary from 1.8 to 7.1 per 1,000 resident days (Nicolle *et al.*, 1996). Respiratory tract infections, urinary tract infections, and skin and soft tissue infections are the most common (Nicolle, 2000). The reported incidence of nursing home-acquired pneumonia ranges from 0.3 to 2.5 episodes per 1000 days of resident care (Muder, 1998; Medina-Walpole and Katz, 1998; Mylotte, 2002). At 5 nursing homes in Toronto, Ontario, Canada, from 1993 through 1996, the incidence of home-acquired pneumonia was 0.7 episodes per 1000 days of resident care (Loeb *et al.*, 1999). Other prospective studies on the epidemiology of infections in residents of LTCFs report an incidence of symptomatic urinary infection that varies from 0.1 to 2.4 cases per 1000 resident-days; while most patients are asymptomatic, the prevalence rates of bacteriuria are 25% to 50% (Nicolle, 1997; Nicolle, 2000). Skin and soft tissue infections include decubitus ulcers, infected vascular or diabetic foot ulcers, erysipelas, and other types of cellulitis. The residents of LTCFs have a high frequency of colonization with antimicrobial-resistant organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), penicillin-resistant pneumococci (PRP), extended spectrum β-lactamase–producing gram-negative organisms (ESBL), and fluoroquinolone-resistant gram-negative organisms (FQ-R). This review will briefly touch upon clinical relevance of antimicrobial resistance in LTCFs.

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METHICILLIN-RESISTANT STAPHYLOCOCCI

MRSA was first described in 1961, and since then it has become a worldwide problem (Jevons, 1961; Diekema *et al.*, 2004; Tansel *et al.*, 2003;

Corrente *et al.,* 2005) The presence of MRSA in nursing homes was first reported in 1970 by O'Toole (O'Toole *et al*., 1970). MRSA is a frequent colonizer of debilitated patients. On this point, Bradley observed that the rate of colonization with MRSA was >25% (Bradley *et al.*, 1991). The same author showed that in two of the most common sites of colonization, nares and wounds, colonization rates range from 8% to 53%, and from 30% to 82%, respectively (Bradley *et al.*, 1999). Lee reported a 1-year prospective surveillance study of *S. aureus* colonization and infection. Nasal and stool or rectal screening cultures were done on admission, and all patients underwent screening on at least a quarterly basis for 1 year. Overall, 35% of patients were colonized at least once with *S. aureus*, (72% MS, 25% MR, and 3% mixed phenotypes) (Lee *et al*., 1997).
Mendelson evaluated the rate of colonization by *S. aureus*, especially MRSA, in 270 elderly residents of a large LTCF. The authors showed that 63 (23.3%) were carriers of *S. aureus* and 17 of those (27%) had MRSA (Mendelson *et al*., 2003). It is estimated that residents of LTCFs who are colonized with MRSA have a 4-6 fold increase in infection rate. In a study by Muder, 25% of MRSA carriers had an episode of staphylococcal infection, versus only 4% of methicillin-susceptible staphylococci carriers (Muder *et al*., 1991).
In a retrospective cohort study, Capitano showed that the median infection management cost of an MRSA infection was six times greater than that of a MSSA infection (P <.001), whereas the median associated nursing care cost was two times greater (P= .001). The median overall infection cost associated with MRSA was 1.95 times greater than that associated with MSSA (P<.001). Nursing care cost constituted the major portion of the overall infection cost for both groups (MSSA 51%, MRSA 48%) (Capitano *et al*., 2003). Risk factors for MRSA colonization include: residence in a medical ward or medical intensive care unit or prolonged hospitalization (13 weeks), advanced age, and history of invasive procedures (Asensio *et al*., 1996). In a case control study conducted in a community nursing home, Thomas reported that nasogastric intubation and antibiotic therapy in the previous 6 months were the most important factors associated with MRSA colonization (Thomas *et al*., 1989). In a study by O'Sullivan, the risk factors significantly associated with MRSA colonization were male sex, age >80 years, residence in the nursing home for more than six months, hospitalization during the previous 6 months, peripheral vascular disease, pressure sores, steroid therapy, poor general skin condition, antibiotic therapy during the previous three months and a mental test score of ≤14. Multivariate analysis identified male sex and pressure sores as independent variables (O'Sullivan *et al*., 2000). Other risk factors are pressure ulcers, feeding tubes, urinary catheters, and urinary incontinence (Terpenning, *et al*., 1994).

VANCOMYCIN-RESISTANT ENTEROCOCCI

First described in 1987 in Europe vancomicin resistant enterococci have recently emerged as important nosocomial pathogens and in the last 10 years have become among the most feared pathogens in US hospitals. Studies dealing with the emergence of VRE in the United States revealed that most patients with VRE were in ICUs (Clark *et al*., 1993). Colonization with VRE has been reported from community settings in the United States, including, to a limited extent, LTCFs (Coque *et al.*, 1996; Bonten *et al*., 1998). Bonilla showed that prevalence of VRE colonization among patients in the LTCF at the Ann Arbor Department of Veterans Affairs Medical Center exceeded the prevalence in the intensive care unit and general medical wards (Bonilla *et al.*, 1997). Brennan described the epidemiology of VRE colonization in a 400-bed LTCF for veterans. The author observed that twenty-four of 36 patients were colonized with VRE that persisted for 67 days and were associated with antibiotic administration (Brennan *et al*., 1998).
In a prospective cohort study, Elizaga showed that 45% (45 of 100 patients) were colonized with VRE. The following risk factors were identified by univariate analysis: hospitalization in the prior 60 days; an admission diagnosis of infection; inability to ambulate; presence of a feeding tube, urinary catheter, or decubitus ulcer; and documented or probable antibiotic use in the previous 60 days (particularly the use of vancomycin and third generation cephalosporins). Stepwise logistic regression analysis identified the presence of a decubitus ulcer on hospital admission

and documented or probable antibiotic use in the 60 days before admission as significant risk factors for colonization with VRE at the time of admission (Elizaga *et al.*, 2002).

PENICILLIN-RESISTANT PNEUMOCOCCI

Penicillin resistance is common in *Streptococcus pneumoniae*, many strains being resistant to other antibiotics as well. PRP is a problem all over the world, both in the community and hospital setting. In 2002, the EARSS project reported five countries with a prevalence of PRP of greater than or equal to 30%. Overall, in 2002 the EARSS project reported 11% of *S. pneumoniae* strains as non-susceptible to penicillin and 17% as non-susceptible to erythromycin (http://www.earss.rivm.nl). Two events have occurred since 2000 that may have reduced the selective pressures driving antimicrobial resistance: the more appropriate use of antimicrobials and the pneumococcal conjugate vaccine (Klugman, 2004). The earlier study reports by Millar and Denton were among the first to describe penicillin-resistant pneumococcal infection in elderly institutionalized and debilitated patients (Millar *et al.* 1994; Denton *et al.*, 1993). Nuorti reported a significant outbreak of penicillin-resistant pneumococci in an LTCF in rural Oklahoma. The author observed that 13% of the residents developed a pneumonia and that the mortality rate was 23%. Resistant isolates were recovered from 64% of residents with pneumonia and from 23% of noninfected residents (Nuorti *et al.*, 1998).

EXTENDED SPECTRUM β-LACTAMASE GRAM-NEGATIVE PATHOGENS

The first reports of ESBLs in gram-negative bacilli came from Europe and were quickly followed by reports in the United States. This type of antimicrobial resistance is now recognized worldwide. The prevalence of ESBLs in LTCFs is becoming alarming. The first reported outbreak of bacteria resistant to ceftazidime in the United States occurred in 1990 among patients in a chronic care facility in Massachusetts (Rice *et al.*, 1990). In a study of ceftazidime-resistant *E. coli* and *K. pneumoniae* in Chicago, 31 of 35 patients from 8 nursing facilities harboured an ESBL-producing enteric pathogen.
Weiner reported that prior exposure to ciprofloxacin or trimethoprim-sulfamethoxazole was an independent predictor of colonization with *Escherichia coli* resistant to ceftazidime among nursing home residents. Molecular analysis of isolates showed that a particular resistance-conferring plasmid appeared frequently, thus supporting the growing concern that long-term facilities may act as a reservoir for antimicrobial drug–resistant organisms (Weiner *et al.*, 1999).
Several studies have evaluated the risk factors for colonization or infection with ESBL-producing organisms in the hospitalized patient. Reported risk factors include presence of intravascular catheters, emergency intraabdominal surgery, gastrostomy or jejunostomy tube, gastrointestinal colonization, length of hospital or intensive care unit stay, prior antibiotics (including third-generation cephalosporins), severity of illness, presence of an urinary catheter, and ventilator assistance (Schiappa *et al.*, 1996).
In a case-control study, Sandoval showed that exposure to any cephalosporin (adjusted OR 4.0, 95% CI 1.2 to 13.6) and log percentage of residents using gastrostomy tubes within the nursing home (adjusted OR 3.9, 95% CI 1.3 to 12.0) were associated with having a clinical isolate resistant to third-generation cephalosporins (Sandoval *et al.*, 2004). Nursing home residents would appear to have several additional risk factors for infection with ESBL-producing organisms. It has been well documented that handwashing rates are low among nursing home personnel (Denman *et al.*, 1992).
Urinary catheterization and decubitus ulcers are frequent, and have been associated with colonization of non-ESBL-producing, antibiotic-resistant gram-negative bacilli (Smith *et al.*, 2000; Muder *et al.*, 1997).

FLUOROQUINOLONE-RESISTANT GRAM-NEGATIVE PATHOGENS

Resistance to FQs has been increasing over time in LTCFs. In a correlational longitudinal survey study, Viray showed that *E. coli* FQ-resistance rates was high but variable (for five sites: 5%, 14%, 19%, 23%, 41%), and were generally

Table 1 - *Possible control measures foe preventing spread of antimicrobial-resistant pathogens in LTCFs.*

Surveillance
Review microbiology data
Maintain line listing of cases
Prevalence surveys of residents, staff, or new admissions
Identify readmission cases
Precautions
Handwashing
Antimicrobial soaps
Environmental decontamination
Private room for C/I residents
Barrier precautions for C/I residents
Strict isolation for C/I residents
Isolation of new admissions
Special placement C/I residents
Cohort C/I residents
Cohort C personnel
Establish isolation ward
Reduction of reservoir
Exclusion of C/I residents from facility
Rapid discharge of C/I residents
Decolonization therapy of residents, personnel, or new admissions

Abbreviation: C/I = colonized/infected

increasing over time (Viray *et al*., 2005). In a case-control study, Cohen showed that FQ-resistant *E. coli* urinary tract infection was more common with prior FQ use (OR 21.8, 95% CI, 3.7-127.1) (Cohen *et al*., 2006). Maslow conducted a cross-sectional study to determine the prevalence of, and risk factors for, colonization with FQ-resistant *Escherichia coli* in residents in a LTCF. FQ-resistant *E. coli* were identified from rectal swabs for 25 (51%) of 49 participants at study entry. On multivariable analyses, prior FQ use was the only independent risk factor for FQ-resistant *E. coli* carriage and was consistent for FQ exposures in the previous 3, 6, 9, or 12 months. Pulsed-field gel electrophoresis of FQ-resistant *E. coli* identified clonal spread of one strain among 16 residents (Maslow *et al*., 2005).

PREVENTING ANTIBIOTIC RESISTANCE

In the LTCF setting, antimicrobial use is an important issue relevant to antimicrobial resistance. Previous studies have found relatively high rates of antimicrobial use and substantial inappropriate use of antimicrobial agents in LTCF residents. In addition to increasing the risk of colonization or infection with antimicrobial-resistant organisms, inappropriate antimicrobial use adds costs to resident care and may place the patient at increased risk for medication-related adverse events (Mylotte, 1999).

Recommendations for improving antimicrobial use have included development of a formulary and continuing review of antimicrobial use and prevalence of antimicrobial resistance in cultures obtained from patients with suspected infection. In the last two decades, an increasing number of long-term care facilities have developed infection control programs with surveillance and control activities (Smith, 1999). A major contribution to this development was the publication of guidelines by the Association for Professionals in Infection Control and Epidemiology (APIC) - Society for Healthcare Epidemiologists of America (SHEA) in 1997 (Smith et Rusnak, 1997) (Table 1).

CONCLUSIONS

Infections with antimicrobial-resistant bacteria in LTCFs are an important public health concern, can result in serious illnesses and death in LTCF residents. It is our opinion that the future strategies for antimicrobial use in LTCF setting should be based on more appropriate therapy. In addition to controlled comparative trials to identify appropriate antimicrobial drug use, patients who do not require treatment need to be identified. Finally, the feasibility of minimising antibiotic resistance requires further study.

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