Archives of Gerontology and Geriatrics 56 (2013) 227–230

Contents lists available at SciVerse ScienceDirect

Archives of Gerontology and Geriatrics

journal homepage: www.elsevier.com/locate/archger

Increased multi-drug resistance among the elderly on admission to the hospital—A 12-year surveillance study

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ARTICLE INFO

Article history:
Received 30 March 2012
Received in revised form 7 May 2012
Accepted 10 May 2012
Available online 6 June 2012

Keywords:
Community-acquired infections
Antimicrobial resistance
Elderly
MDRGN

ABSTRACT

Resistance to antimicrobials continues to increase worldwide. Data suggest that older patients are among the main reservoirs of multidrug-resistant organisms (MDROs) in the hospital. We hypothesized that older patients (≥65 years of age) are more likely to harbor MDRO at hospital admission. We compared rates of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE) and multidrug-resistant gram-negative bacteria (MDRGN) recovered from clinical cultures within the first 48 h of admission to an adult acute care hospital between the elderly (≥65 years old) and young per 1000 age-stratified admissions over a 12-year study period. Trends in antimicrobial resistance, sites of recovery and species for MDRGN were also characterized. An average of 7534 positive bacterial cultures were collected per year. The admission prevalence per 1000 age-stratified admissions was consistently higher among the elderly for all three MDRO under investigation. Among the elderly, the admission prevalence increased significantly for VRE (0.89 in 1998 to 3.62 in 2009 per 1000 admissions; $p < 0.001$) and MDRGN (1.41 in 1998 to 11.33 in 2009 per 1000 admissions; $p < 0.001$). Percentage resistant for all three MDRO increased as well. These data suggest that elderly patients are contributing substantially to the influx of MDRO into the hospital setting.

1. Introduction

MDROs, including MRSA, VRE and MDRGN continue to be a major public health threat worldwide both in the community and hospital setting. Elderly patients residing in long-term care settings are at high risk of harboring MDRO (Lautenbach et al., 2009; O'Fallon, Pop-Vicas, & D'Agata, 2009; Pop-Vicas, Mitchell, Kandel, Schreiber, & D'Agata, 2008; Tacconelli, Pop-Vicas, & D'Agata, 2006; Viray et al., 2005; Weber et al., 2009). Contributing factors to these high rates include cross-transmission within long-term care settings and substantial antimicrobial exposure (D'Agata & Mitchell, 2008; O'Fallon, Kandell, Schreiber, & D'Agata, 2010; O'Fallon, Schreiber, Kandel, & D'Agata, 2009). Infections caused by MDRO are associated with 2–5 times higher mortality rates compared to infections caused by antimicrobial-susceptible bacteria (Melzer & Petersen, 2007; Schwaber & Carmeli, 2007). One of the main reasons for these high mortality rates is the delay in effective antimicrobial therapy among newly admitted patients to the hospital (Schwaber & Carmeli, 2007). It is therefore important to characterize the patient population at highest risk of harboring MDRO at hospital admission in order to optimize antimicrobial therapy. We hypothesize that elderly people are the subgroup of patients at highest risk of harboring MDRO at hospital admission. Validating this hypothesis is important, as it would suggest that elderly patients presenting to the hospital with an infection should be treated initially with broad-spectrum antimicrobials, which target MDROs. Furthermore, proving this hypothesis correct would emphasize the need to evaluate infection control efforts aimed at preventing MDRO spread, which target the elderly patient at hospital admission. A 12-year study was therefore conducted to compare rates and trends of MDRO among the elderly and young at hospital admission.

2. Methods

The study was conducted at a 620-bed tertiary care healthcare facility in Boston, MA with an average of 39,000 adult patients admitted per year. Microbiological data from the hospital's computerized database were reviewed. The Clinical Committee of Investigation of the Beth Israel Deaconess Medical Center approved this study.

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http://dx.doi.org/10.1016/j.archger.2012.05.006

The analysis was restricted to *S. aureus*, *Enterococcus* spp. and gram-negative bacteria recovered from clinical and surveillance cultures from 1998 to 2009. The nine most common gram-negative species were evaluated: *Escherichia coli*, *Klebsiella* spp., *Enterobacter* spp., *Morganella* spp., *Proteus* spp., *Pseudomonas aeruginosa*, *Citrobacter* spp., and *Acinetobacter* spp. Only isolates recovered within 48 h from the date of hospital admission were included. In addition, the analysis was restricted to only the first isolate of the same species per year recovered from an individual patient. MDROs included MRSA, VRE and MDRGN.

MDRGN were defined as gram-negative bacteria that were resistant or intermediately susceptible to three or more of the following antimicrobials or antimicrobial classes: (1) extended-spectrum penicillins (ampicillin–sulbactam or piperacillin–tazobactam); (2) carbapenems (imipenem or meropenem); (3) third- or fourth-generation cephalosporins; (4) fluoroquinolones (ciprofloxacin or levofloxacin); and (5) aminoglycosides (gentamicin, tobramycin, or amikacin). Identification and susceptibility testing was routinely performed by the microbiology laboratory in accordance with the Clinical and Laboratory Standards Institute guidelines (Clinical and Laboratory Standards Institute (CLSI), 2011) by using the automated Vitek I system (bio Merieux Vitek, Durham, NC).

Cultures were categorized by site of recovery, which included wound, blood, urine, respiratory, surveillance and other sites (i.e., peritoneal fluid or cerebrospinal fluid culture).

The metric used to quantify MDRO exposure burden estimates was admission prevalence as per the recommendations of the Centers for Disease Control and Prevention Healthcare Infection Control Prevention Committee and the Society of Healthcare Epidemiology of America (SHEA/HICPAC) (Cohen et al., 2008). This metric allows healthcare settings to quantify the extent of MDRO influx into the healthcare setting. Thus, only the first MDRO isolates recovered from any clinical culture within 48 h of admission to the hospital were included. Age groups were divided into <65 years of age for the young and ≥65 years of age for the elderly. Prevalence was calculated for each age group and was stratified for admissions in each age group to exclude that changes in the age structure of admissions would confound time trends (Cohen et al., 2008). Antimicrobial resistance percentages were calculated for methicillin resistance among *S. aureus*, vancomycin resistance among *enterococci* and multidrug-resistance among gram-negative bacteria and were compared between younger (<65 years of age) and older adults (≥65 years of age).

2.1. Statistical analysis

Trends in the annual prevalence of MDRO were analyzed using the Cochran–Armitage trend test. Comparison in trends between young and elderly was analyzed using linear regression analysis with an interaction effect in the model to allow for the effect of age group to vary with the year. Linear regression was used to determine if increases in MDRGN prevalence were related to a specific MDRGN species. A significance level of $p < 0.05$ was used for all statistical tests. Statistical analysis was performed with STATA, version 10.1 (STATA Corporation, College Station, TX).

No funding was received for this research.

3. Results

During the 12-year study period, there was an average of 39,197 admissions per year (range 36,733–42,262) with an average of 7534 (range 5541–8726) positive bacterial clinical and active surveillance cultures collected per year. Age groups were divided into <65 years of age for the young and ≥65 years of age for the elderly. In the young, the mean age was 47 years (range 0–64). In the elderly group, the mean age was 79 years (range 65–118).

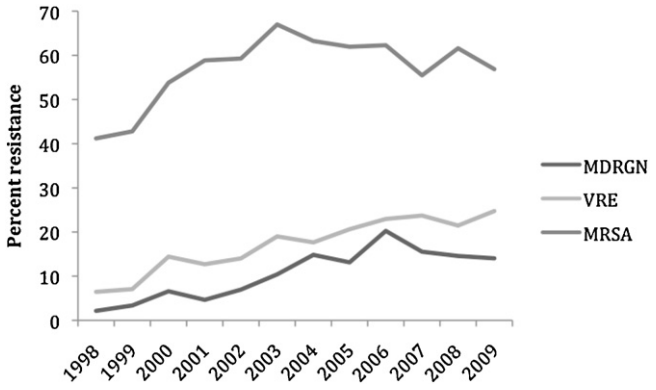

Fig. 1. Percentage of antimicrobial resistance for MRSA, VRE and MDRGN among isolates recovered within 48 h of hospital admission among older patients. The percentage of resistant pathogens increased for all MDRO throughout the study period.

3.1. Antimicrobial resistance among older patients

During the study period, 4637 *S. aureus* isolates were recovered from cultures, of which 2636 (56.8%) were resistant to methicillin. The percent of isolates resistant to methicillin increased from 41% in 1998 to 57% in 2009 ($p < 0.001$) (Fig. 1). Sites of MRSA recovery were as follows (% of isolates): wound (42%), sputum (23%), screening cultures (14%), urine (11%), blood (9%) and other (1%). A total of 2681 *enterococcal* isolates were recovered of which 471 (17.6%) were resistant to vancomycin. In 1998, 6% of *enterococcal* isolates were resistant to vancomycin and by 2009, this percentage increased to 25% ($p < 0.001$) (Fig. 1). Sites of VRE recovery were as follows (% of isolates): urine (49%), wound (33%), blood (13%), screening cultures (4%) and other (1%). There were no changes in the percent of screening cultures performed over the study period for MRSA and VRE ($p < 0.05$).

A total of 10,192 gram-negative isolates were recovered from clinical cultures of which 1060 (10.4%) were multidrug-resistant. In 1998, only 2% of isolates were multidrug-resistant compared to 14% in 2009 ($p < 0.001$) (Fig. 1). Sites of recovery were as follows (% of isolates): urine (61%), sputum (16%), wound (15%), blood (5%) and other (3%).

In 1998, only 2.2% of isolates were multidrug-resistant compared to 14% in 2009 ($p < 0.001$). In 2009, among all MDRGN isolates, 44.4%. 22.9%, 8.5% and 5.2% were represented by *E. coli*, *Klebsiella* spp., *Proteus mirabilis*, *Acinetobacter baumannii*, respectively. Among all species, MDR-*E. coli* and MDR-*Acinetobacter* spp. increased significantly over the study period ($p < 0.05$) (Fig. 2).

3.2. Comparison of trends in MDRO over time between young and older patients

Among the young, the admission prevalence per 1000 age-stratified admissions increased over the study period for MRSA, VRE and MDRGN. For MRSA, the admission prevalence in 1998 was 0.7/1000 admissions and increased to 8.6/1000 admissions in 2009 ($p < 0.01$). For VRE, the admission prevalence in 1998 was 0.15/1000 admissions and increased to 1.51/1000 admissions in 2009 ($p < 0.01$). For MDRGN, the admission prevalence increased from 0.22/1000 admissions in 1998 to 3.1/1000 admissions in 2009 ($p < 0.01$) (Fig. 3).

Among the older patients, there was a statistically significant increase in the admission prevalence for VRE and MDRGN over the study period ($p < 0.01$). The admission prevalence increased from