CONCISE COMMUNICATION

Does Antimicrobial Resistance Cluster in Individual Hospitals?

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Factors that affect the resistance rates for an organism-drug combination in a given hospital also might influence resistance rates for other organism-drug combinations. We examined correlations between resistance prevalence in non-intensive care inpatient areas of 41 hospitals participating in phase 3 (1998–1999) of Project ICARE (Intensive Care Antimicrobial Resistance Epidemiology). We focused on statistically significant (P < .05) Pearson correlation coefficients for methicillin-resistant Staphylococcus aureus, coagulase-negative staphylococci, vancomycin-resistant enterococci, and resistance to third-generation cephalosporins, imipenem, and fluoroquinolones in Escherichia coli, Klebsiella pneumoniae, Enterobacter species, and Pseudomonas aeruginosa. Resistance prevalence rates in individual hospitals were not strongly correlated among gram-positive organisms, and few correlations were seen between rates in gram-positive and gram-negative organisms. More frequent significant associations were found among resistance rates for gram-negative organisms. Resistance to third-generation cephalosporins in K. pneumoniae was significantly correlated with the majority of other sentinel antimicrobial-resistant organisms. High prevalence of this organism may serve as a marker for more generalized resistance problems in hospital inpatient areas.

The increasing prevalence of antimicrobial-resistant organisms is a major public health problem and is of particular concern for hospitals and other health care settings [1]. Patterns of resistance in health care facilities are not uniform; even institutions in the same city may have quite different observed patterns of resistance for a given organism [2]. However, whether hospitals with a high prevalence of resistance to one drug in a specific organism also may have a high prevalence of resistance to other hospital-associated pathogens is unclear. For example, if a hospital experiences a relatively high prevalence of methicillin-resistant strains of Staphylococcus aureus (MRSA), would it be more likely to have a relatively high prevalence of vancomycin-resistant enterococci (VRE) or other resistant hospital-associated organisms?

Several pathways and associated factors are involved in the appearance and spread of antimicrobial resistance [3]. For example, the dissemination of glycopeptide (e.g., vancomycin) resistance among enterococci is based, in part, on the spread of clones that carry resistance determinants [4]. Similarly, the spread of MRSA in the hospital setting often is associated with clonal dissemination [5, 6]. However, independent predictors of acquisition of VRE in the intensive care unit (ICU) include the use of vancomycin and third-generation cephalosporins, colonization pressure, and increased use of drugs effective against anaerobic microorganisms [7, 8].

If hospital resistance patterns were similar for different organism-drug combinations, this might suggest that the same associated factors were influencing this relationship and were present in the institution where resistance patterns were similar. Likewise, variability in hospital resistance patterns by organism-drug combination would imply that different factors affect resistance rates for these organism-drug combinations. Thus, we hypothesized that a significant positive correlation among resistance rates for different organism-drug combinations in a given hospital would suggest that similar factors influence rates of occurrence.

This study used data from Project ICARE (Intensive Care Antimicrobial Resistance Epidemiology) to examine correlations between resistance prevalence rates for selected organism-drug
combinations in non-ICU inpatient areas (INPs) of 41 US hospitals. These 41 hospitals were those participating in phase 3 (1998–1999) of Project ICARE, a joint project of the Division of Healthcare Quality Promotion (Centers for Disease Control and Prevention [CDC]) and the Rollins School of Public Health (Emory University) [1, 9]. Such data have been shown previously to reflect prevalence rates among pathogens associated with hospital-acquired infections [10].

Methods

Surveillance data. Project ICARE involves a subset of hospital participating in the CDC’s National Nosocomial Infections Surveillance (NNIS) system. Hospitals that participate in the ICU surveillance component of the NNIS system were invited to participate in phase 3 (April 1998–July 1999) of Project ICARE. The surveillance methodology and definitions of the NNIS system [11, 12] and Project ICARE have been described elsewhere [1, 7, 9, 10, 13]. Participating hospitals reported monthly susceptibility results of isolates recovered from clinical specimens from hospitalized patients. Duplicate isolates were excluded. These were defined as isolates of the same organism with the same antimicrobial susceptibility pattern that were recovered from the same patient, regardless of the site of isolation, during the same calendar month. Surveillance cultures also were excluded.

Prevalence rates. Resistance prevalence rates were determined for each INP by pooling the data over the study period. We focused on MRSA and methicillin-resistant coagulase-negative staphylococci (MRCNS); VRE; third-generation cephalosporin resistance (i.e., strains of those organisms resistant to any of the drugs cefotaxime, ceftiraxone, or cefazidime, depending on which were tested in a given institution) in Escherichia coli (CF3R-EC), Klebsiella pneumoniae (CF3R-KP), Enterobacter species (CF3R-ENB), and Pseudomonas aeruginosa (CF3R-PA); imipenem resistance in P. aeruginosa (IMR-PA); and fluoroquinolone resistance (i.e., strains resistant to ciprofloxacin, ofloxacin, or levofloxacin, depending on testing performed in a given institution) in E. coli (FQR-EC) and P. aeruginosa (FQR-PA).

Statistical analysis. The data from INPs were aggregated for each month and were pooled within the study period (1998–1999) by organism-drug combination. If ≤10 isolates of a study organism were tested for susceptibility in INPs of a specific hospital during the study period, then the data provided by that particular hospital were excluded from this analysis. Resistance prevalence rates for each organism-drug combination were determined for each hospital as follows: total number of resistant isolates reported during the period (1998–1999)/total number of isolates tested during the period. Correlations between resistance rates for selected organism-drug combinations were assessed by calculating Pearson correlation coefficients and corresponding P values. Comparisons for which P < .05 were considered to be significantly correlated. Because this is an exploratory analysis, P values were not adjusted for multiple testing.

Results

During phase 3 of Project ICARE (1998–1999), 41 hospitals reported monthly susceptibility test results for sentinel organisms in INPs. Of these, 39 (95%) were general hospitals, 2 (5%) were Veterans Affairs hospitals, and 15 (37%) were affiliated with a medical school. The mean number of beds at participating hospitals was 440 beds (median, 356 beds; range, 147–1022 beds).

Results of the correlation analysis (Pearson correlation coefficients and corresponding P values) are presented in table 1. Of the 3 examined correlations among resistance rates of gram-positive organisms, none was statistically significant. Of the 21 examined correlations between rates of gram-positive and gram-negative organisms, 3 were statistically significant (VRE and CF3R-KP; MRSA and FQR-PA; and MRCNS and CF3R-PA). Of the 21 examined correlations among resistance rates of gram-negative bacilli, 9 were statistically significant. The prevalence rate of CF3R-KP was significantly positively correlated with the rates of the majority of other antimicrobial-resistant organisms that were studied (table 2).

Discussion

In this study population, the correlation of resistant prevalence rates in individual hospitals was neither strong nor frequent among the 3 gram-positive cocci studied. At most, a relatively high prevalence of resistance to 1 drug in these gram-positive organisms correlated with relatively high prevalence of resistance for a single other microorganism in the same hospital. The im-
Table 2. Significant correlations of study organisms, by group.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Gram-positive coci</th>
<th>Gram-negative bacilli</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive cocci</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA</td>
<td>0</td>
<td>1 (FQR-PA)</td>
</tr>
<tr>
<td>MRCNS</td>
<td>0</td>
<td>1 (CF3R-PA)</td>
</tr>
<tr>
<td>VRE</td>
<td>0</td>
<td>1 (CF3R-KP)</td>
</tr>
<tr>
<td>Gram-negative bacilli</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CF3R-KP</td>
<td>1 (VRE)</td>
<td>4 (CF3R-ENB, CF3R-PA, FQR-EC, IMR-PA)</td>
</tr>
<tr>
<td>CF3R-ENB</td>
<td>0</td>
<td>2 (CF3R-KP, CF3R-PA)</td>
</tr>
<tr>
<td>CF3R-PA</td>
<td>1 (MRCNS)</td>
<td>3 (CF3R-KP, CF3R-ENB, IMR-PA)</td>
</tr>
<tr>
<td>CF3R-EC</td>
<td>0</td>
<td>1 (FQR-EC)</td>
</tr>
<tr>
<td>FQR-EC</td>
<td>0</td>
<td>3 (CF3R-KP, CF3R-EC, FQR-PA)</td>
</tr>
<tr>
<td>FQR-PA</td>
<td>1 (MRSA)</td>
<td>2 (FQR-EC, IMR-PA)</td>
</tr>
<tr>
<td>IMR-PA</td>
<td>0</td>
<td>3 (CF3R-KP, CF3R-PA, FQR-PA)</td>
</tr>
</tbody>
</table>

NOTE. Significant correlations for each organism in the pair are shown, so there are 24 listings for the 12 organism-drug combinations found to be significant in table 1. Data are no. (type) of significant correlations with other study organisms. CF3R, third-generation cephalosporin resistant; EC, *Escherichia coli*; ENB, *Enterobacter* species; FQR, fluoroquinolone resistant; IMR, imipenem resistant; KP, *Klebsiella pneumoniae*; MRCNS, methicillin-resistant coagulase-negative staphylococci; MRSA, methicillin-resistant *Staphylococcus aureus*; PA, *Pseudomonas aeruginosa*; VRE, vancomycin-resistant enterococci.

The lack of high prevalence of resistance for several organism-drug combinations in the same hospital emphasizes that control programs for antimicrobial resistance cannot be thought of in terms of “one size fits all.” This is similar to the approach taken in dealing with cancer: one speaks of control and prevention of cancer as a general entity, but guidelines for doing this are individualized by type of cancer and vary for each type. Similarly, guidelines for prevention and control of antimicrobial resistance must target individual drug-organism combinations, for which different associated risks and predictors appear to exist. A recent paper emphasizes the common risk factors involved in nosocomial colonization and infection with *S. aureus* and enterococci [15]. Our data suggest that more than these features in common are involved in determining association of resistant organisms in different health care institutions. Finding these differential risks may provide an opportunity for control and prevention.

Acknowledgments

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References

8. Puziak LA, Mayfield J, Leet T, Kollef M, Mundy LM. Acquisition of individual patient would provide insight on other variables that may be confounding or interacting with the findings reported here for hospitals as a whole [14]. Unfortunately, the size of our dataset did not allow for analysis by ICUs; therefore, the associations among resistant organisms in this stratum cannot be assessed. Description of the individual factors in the institution that influence the presence of resistance would be useful in developing programs to deal with resistance at the hospital and health system level [13].

More frequent statistically significant associations were found among resistance rates for gram-negative organisms. The rate of CF3R-KP was positively correlated with the rates of the majority of other sentinel antimicrobial-resistant organisms (VRE, CF3R-ENB, FQR-EC, CF3R-PA, and IMR-PA) and was the most frequently correlated variable in the analysis (5 of 9 possible correlations; table 2). This suggests that factors leading to the presence of gram-negative strains in hospitals are shared. In addition, it seems that the high prevalence of CF3R-KP may serve as a marker for more-generalized resistance problems in INPs. Factors that affect the rate of CF3R-KP also might influence rates for other antimicrobial-resistant microorganisms in a given hospital setting.

This ecologic study involved the assessment of resistance prevalence rates in the population of selected bacterial isolates within our participating hospitals. Project ICARE hospitals are drawn from those participating in the NNIS system, and their characteristics vary somewhat from the characteristics of all US hospitals [11, 12]. Thus, these data cannot be taken as representative of all hospitals in the United States. In addition, further studies that evaluate this question on the level of the...


