of influenza A 2009 H1N1 by rapid testing that noted moderate sensitivity,[2-3] despite confirmation of adequate quality-control checks prior to testing specimens obtained from the nasopharynx, nose, and throat. Although predictive values will vary with the prevalence of circulating influenza virus among populations at risk, the moderate NPVs of 66%–77% suggest there were a substantial number of false-negative test results and, thus, a need for continued improvement in rapid diagnostic tests for novel influenza A 2009 H1N1.

ACKNOWLEDGMENTS

Financial support. This study was supported by a grant from National Center for Genetic Engineering and Biotechnology, National Science and Technology Development (BT-B-01-MG-13-5019) to A.A.

Potential conflicts of interest. L.M.M. is a consultant for WWEpidemiology at GlaxoSmithKline

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Infect Control Hosp Epidemiol 2010; 31(6):663-664

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Correlation between Rates of Carbapenem Consumption and the Prevalence of Carbapenem-Resistant *Pseudomonas aeruginosa* in a Tertiary Care Hospital in Brazil: A 4-Year Study

To the Editor—Antimicrobial resistance is a major concern in hospitals throughout the world. Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) is a leading cause of hospital-acquired infection worldwide and has contributed to increased morbidity and mortality among hospitalized patients.[1]

Various previous studies found that use of these drugs was a risk factor for CRPA infection.[2,3] However, more recent, well-designed studies have not found that use of carbapenem drugs was a potential risk factor for CRPA infection.[1,10]

Data on antibiotic use and bacterial resistance are important for helping to understand the relationship between the use of these drugs and the emergence of resistance. Thus, hospital-wide surveillance studies aiming to evaluate the correlation between these 2 variables have been undertaken worldwide in recent years.[4-9] In fact, the studies have found discrepant results with regard to this relationship. The aim of our study was to assess the correlation between hospital-wide carbapenem consumption and the incidence of CRPA strains in our institution.

This ecological study was undertaken at our university-affiliated 750-bed hospital in São Paulo, Brazil. No novel carbapenem resistance mechanism or outbreak was detected during the study period. Use of carbapenem antibiotics, in defined daily doses (DDDs) per 1,000 patient-days, and the number of CRPA isolates per 1,000 patient-days was recorded on an annual basis from January 1, 2005, through December 31, 2009. All cultures positive for CRPA were recorded. The susceptibility of *P. aeruginosa* isolates was determined by the disk diffusion method. One isolate per patient was included in the analysis. The incidence density of these carbapenem-resistant isolates was calculated on the basis of the number of resistant isolates per 1,000 patient-days. The Pearson correlation coefficient was calculated to identify any relationship between antimicrobial use and the incidence of CRPA.

The mean number of hospital patient-days was 167,382 during the study period. Consumption of carbapenem drugs increased during the 4-year period: the mean and median were 74.07 and 68.34 DDDs per 1,000 patient-days, respectively (range, 67.84–92.81 DDDs per 1,000 patient-days). The mean incidence density of CRPA isolation was 1.40 isolates per 1,000 patient-days (range, 1.13–1.78 isolates per 1,000 patient-days) during the study period (Figure). The Pearson correlation coefficient between carbapenem consumption and the incidence density of CRPA isolation was -0.53 ($P = .46$).

Despite of a slight reduction in 2006 (to 66.81 DDDs per 1,000 patient-days), our study demonstrated increased use of carbapenem antibiotics during the study period. In comparison, we noticed a progressive reduction in the incidence density of CRPA isolation.

In recent years, we have seen controversial results with regard to consumption of carbapenem antibiotics and carbapenem resistance among gram-negative pathogens in surveillance studies. Despite the positive correlation found in some studies,[5,8] various recent studies have demonstrated a negative relationship between increased carbapenem consumption and

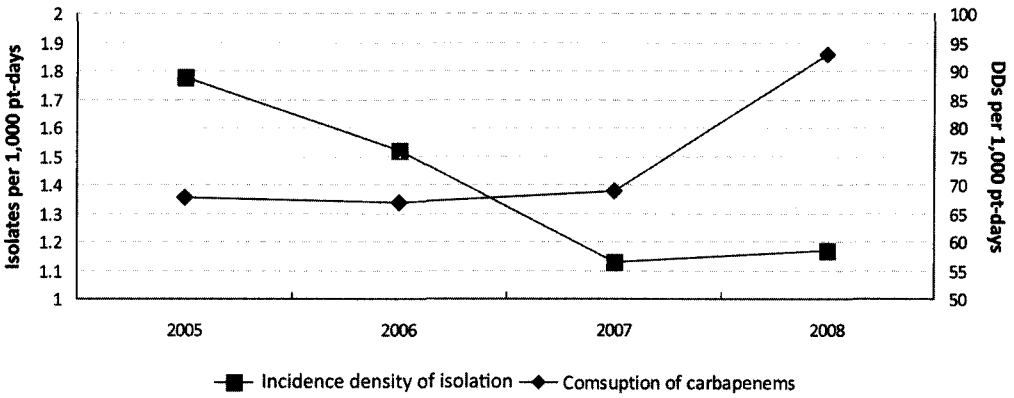

FIGURE. Comparison of the incidence density of carbapenem-resistant *Pseudomonas aeruginosa* (*left scale*) and consumption of carbapenem antibiotics (*right scale*) during the period 2005–2008. DDD, defined daily doses.

a trend toward increased resistance among gram-negative rods.[4,6,8,9]

One can argue that hospital-wide, ecological studies are not the ideal study design for this assumption. Nonetheless, recent well-designed case-control or cohort studies have demonstrated a lack of association between these variables as well.[1,10] Paramythiotou et al[1] recently did not find that use of carbapenem antibiotics was a risk factor for emergence of imipenem-resistant *P. aeruginosa.* The only independent risk factor found was prior fluoroquinolone use. Lautenbach et al[10] demonstrated similar findings. Use of fluoroquinolones was previously related to carbapenem resistance among gram-negative rods in surveillance studies.[4,5,9] These results suggest that curtailing the use of other antibiotic classes (particularly fluoroquinolones) may be more important than reducing carbapenem use in attempts to curb further emergence of carbapenem resistance.

Our study has limitations. We described observations from a single institution, and larger, multicenter studies are needed to confirm these findings. In addition, 4 years might be a relatively short period of observation. Otherwise, to our knowledge, this is the first study specifically investigating *P. aeruginosa* isolates. In summary, our findings reinforce the results of other previous hospital-wide surveillance studies that demonstrated a lack of correlation between increased carbapenem consumption and emergence of carbapenem resistance among *P. aeruginosa* isolates.

ACKNOWLEDGMENTS

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

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Infect Control Hosp Epidemiol 2010; 31(6):664-666

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Antibiotic Stewardship: The "Real World" When Resources Are Limited

To the Editor—Infections caused by multidrug-resistant bacteria continue to challenge physicians in daily practice.[1] In this context, controlling antibiotic use and bacterial resistance through antibiotic stewardship programs are of major importance to all professionals involved in infectious diseases.[1]

Although it has been well established that an appropriate antibiotic stewardship program must include optimum selection, dose, and duration of treatment and control of antibiotic use,[2] other additional factors in the implementation of infection control policies may contribute to reduce amplification and dissemination of bacterial resistance in the hospital (eg, hand hygiene and isolation precautions).[3] On the basis of these data, the antibiotic stewardship program team should include professionals from different specialities (eg, infectious diseases physicians, clinical microbiologists, information system specialists, and clinical pharmacists) and the commitment of the hospital administrative director.[4] However, in developing countries, this infrastructure is uncommon in most hospitals, and the antibiotic stewardship programs are based on individual efforts of infectious diseases physicians who are willing to develop these programs as part of their activities as attending physicians.

The Infectious Diseases Society of America–Society for Healthcare Epidemiology of America guidelines identify 2 core proactive evidence-based strategies and several supplemental strategies for promoting antimicrobial stewardship.[4] The first proactive strategy is a formulary restriction and/or a requirement for preapproval for administration of specific drugs, and the second is a prospective audit with intervention and feedback to the prescriber. Restriction of antimicrobial use may be obtained either by limited access to available antimicrobials through restriction of the hospital formulary or implementation of a requirement for preapproval and a justification for prescribing drugs on the restricted list. Both methods have been shown to be effective in reducing the use and costs of restricted antimicrobials.[5] However, the major disadvantage of this strategy is that prescribers can have a perceived loss of autonomy when making clinical decisions, which may cause conflict and be controversial among the different specialties and the infectious diseases physician[6]; in addition, physicians perceive the preapproval system as stressful and time consuming.[7]

I have coauthored 2 studies[8,9] of prospective audits, with intervention and feedback to the prescriber, that focused on shifting the leadership of antibiotic use to an infectious diseases physician consultant. In both studies, we reduced use of vancomycin and third-generation cephalosporins significantly.

The logistics of auditing should be adapted to local needs and resources, because, as with formulary restriction, this strategy is time consuming. The supplemental strategies used in antibiotic stewardship programs include education of prescribers, implementation of guidelines, use of antimicrobial order forms, de-escalation, combination therapy, dose optimization, and intravenous-to-oral route switch, therapeutic substitution, cycling, mixing, and use of computer decision support.

In general, several of these strategies are implemented in the daily practice simultaneously with some of the 2 core strategies. The most important point is that all of these strategies require the evaluation of the patient at "bedside" (ie, before the approval or refusal of use of an antibiotic in a formulary-restriction strategy). This issue has been identified as a barrier to antibiotic stewardship programs because of the time and effort required and the lack of economic compensation. These could be the reasons why the authorization of an antibiotic and the feedback to the prescriber by telephone or through informal ("curbside") consultations are very common in developing countries.[10]

To avoid these difficulties, it is essential to select the core strategy (ie, formulary restriction or prospective audit of prescription) and the forms to implement it on the basis of the institution's resources (eg, control of all the antibiotic prescriptions versus control only of the prescription of "restricted" antibiotics; hospital-wide control versus control only in the intensive care unit, and control every day versus control 3 times per week). The characteristics of the antibiotic stewardship program would have to be selected such that the infectious diseases physician has the time necessary to evaluate patients and to discuss treatment with the attending physicians. With these considerations taken into account, in the Table, I discuss the "real world" of antibiotic stewardship program implementation in 2 different hospitals that selected the strategy of prospective audit of the prescription plus feedback to the prescriber.

In both hospitals, the duration of an infectious diseases consultation (which included review of the clinical chart, examination of patients, and feedback to the attending physician during the writing of the clinical chart) was 20–25 minutes. As you can see in the Table, if institution A, which has 2 infectious diseases physicians who are available for 8 hours per day, decided to audit all antibiotic prescriptions, it would be technically impossible. However, these hospitals implemented an antibiotic stewardship program to audit only the hospital-wide prescriptions of restricted ("key") antibi-