CONCISE COMMUNICATION

Performance of a Novel Antipseudomonal Antibiotic Consumption Metric Among Academic Medical Centers in the United States

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A metric was developed to identify hospital proportion of carbapenem consumption (PoCC) among antipseudomonal antibiotics. The PoCC varied significantly among academic medical centers by Census Bureau geographic division after adjusting for patient mix. This metric may be useful in identifying disproportionate carbapenem use and potential carbapenem overuse.

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Utilization of antimicrobial use reports is vital for antimicrobial stewardship programs (ASPs) to effectively impact the prescribing of these agents and, ultimately, antimicrobial resistance (AR). Myriad factors may influence a facility's antimicrobial use including case mix, patient comorbid medical illness, specialty unit composition (eg, bone marrow transplant), AR prevalence, and more.[1–5] Previous studies have revealed that geographic location (defined by US Census Bureau regions and 9 divisions) was associated with variation in antimicrobial consumption in the outpatient setting, with the Southern region being associated with increased use. However, little is known regarding specific factors related to this finding.[1,6–8]

The broad-spectrum agents, carbapenems, are often used to empirically cover for the possibility of infection due to *Pseudomonas aeruginosa*, even when more narrow-spectrum agents like cefepime and piperacillin-tazobactam (PT) could be utilized. This practice has been linked to carbapenem resistance in *Pseudomonas* and *Acinetobacter* spp.[9] A single metric that captures relative carbapenem antipseudomonal use could potentially be of high value to ASPs. A novel metric was developed and used to inform the antimicrobial stewardship strategy at Virginia Commonwealth University Health System (VCUHS), which describes the proportion of carbapenem consumption (PoCC) in reference to less broad-spectrum antipseudomonal β-lactams.

The purpose of this study was to characterize broad-spectrum antipseudomonal antimicrobial use across US academic medical centers utilizing PoCC by Census Bureau geographic divisions to determine whether regional variation exists. We also aimed to define regional benchmarks for the PoCC metric as well as institutional predictive factors.

METHODS

Study Design and Participants

A hospital-level cross-sectional study was conducted. Antimicrobial consumption data were extracted from the Vizient clinical data base/resource manager on adult (aged ≥18 years) discharges from 2015. The Vizient Consortium is the largest network of academic medical centers in the United States. All hospitals with complete data on antipseudomonal carbapenem use (ie, meropenem, doripenem, and imipenem-cilistatin), cefepime, and PT were included. Data concerning ceftazidime were not included because this agent was used infrequently; hospital mean use was 6 days of therapy (DOT) per 1,000 patient days (PD) in 2015.

Antibiotic Usage Data and PoCC Measure

Usage data were normalized to DOT per 1,000 PD, and were organized by 9 US Census Bureau Regional divisions (Figure 1).[10] The PoCC metric was calculated using the following formula:

$$\frac{(\text{carbapenem DOT per 1,000 PD})}{(\text{carbapenems} + \text{cefepime} + \text{PT DOT per 1,000 PD})}$$

Hospital Characteristics

Hospital characteristics related to patient mix that may impact antimicrobial consumption were obtained to identify predictors of the PoCC. Case mix index (CMI) was defined as the proportion of admissions per the All-Patient Refined-Diagnosis–Related Group (APR-DRG) Severity of Illness (SOI) subclasses: extreme, major, moderate, and minor. These subclasses were calculated as follows: (cases of APR-DRG classification)/(total cases) × 100. The number of PD among 35 different Vizient clinical service lines (CSLs) per 1,000 PD were collapsed into 4 categories: (1) medicine; (2) surgery; (3) immunosuppressed (which included bone marrow/solid organ transplant), burns, pulmonary/critical care, and oncology service lines; and (4) other. The formula used to calculate the proportions of these subclasses was [(number of CSL classification PD)/(total PD) × 1,000]. Finally, the proportion of admissions aged ≥ 65 years was calculated as follows: (number of cases with patients aged ≥ 65 years)/(total cases).

Analysis

An analysis of variance (ANOVA) test was used to analyze differences in mean PT, cefepime, and carbapenem DOT per

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1,000 PD, and logistic regression in PoCC across Census Bureau divisions. Bivariate logistic regression assessed associations between predictors and the PoCC. An adjusted multivariable analysis [statistically significant predictors ($P \leq .05$) from bivariate analysis] determined if any relationship between PoCC and Census Bureau division remained after accounting for these factors. The significance level was set at $P < .05$; all tests were 2-tailed.

RESULTS

In total, 139 of 149 hospitals were included in the analysis; 10 hospitals were excluded due to incomplete data. The excluded hospitals did not vary significantly from the rest of the cohort in terms of hospital characteristics. Medicine was the most common CSL represented, followed by surgery, other, and immunosuppressed (Table 1). The most common APR-DRG SOI subclass was moderate, followed by major, minor, and extreme. The mean total PD and admissions were 135,359 and 28,802, respectively.

The mean proportion of admissions aged ≥65 years was 40.31%. The mean CMI was 1.56. Across Census Bureau divisions, there were significant differences ($P \leq .05$) in mean DOT per 1,000 PD: carbapenem use, 31 (SD, 24); PT use, 76 (SD, 44); and cefepime use, 60 (SD, 44). There were also significant differences in PoCC by Census Bureau division ($P < .0001$). The hospital PoCC scores were highest in the Pacific region (n = 19) and the West South Central region (n = 8), at 23.1% (SD, 0.13; 95% CI, 0.16–0.29) and 21.1% (SD, 0.06; 95% CI, 0.16–0.26), respectively. The hospital PoCC score was lowest in the Middle Atlantic region (n = 23) at 14.2% (SD, 0.07; 95% CI, 0.11–0.17) (Figure 1).

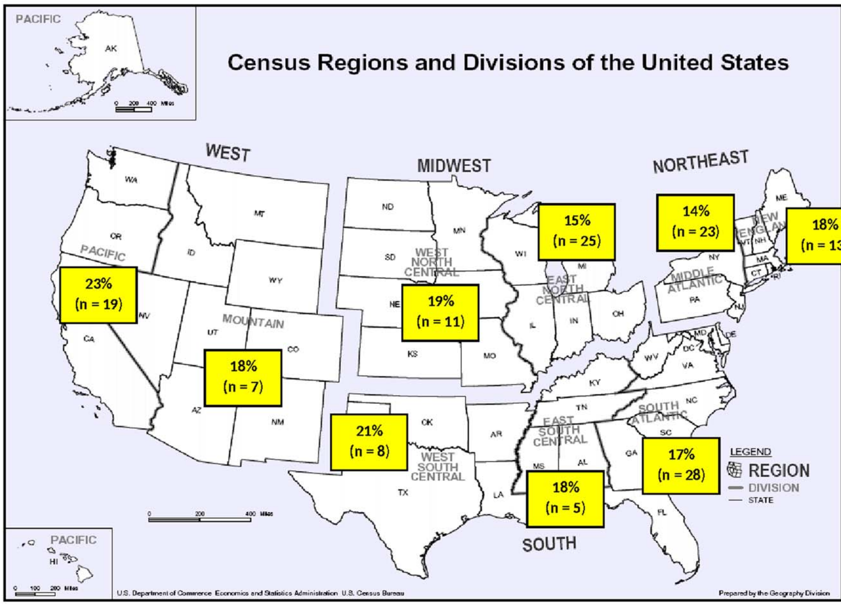
By bivariate analyses, PoCC (outcome) by division (predictor) revealed that 8 divisions had a negative association with the reference (ie, Pacific) (Table 1). Bivariate analyses of PoCC and hospital characteristics revealed statistically significant associations ($P \leq .05$) with all variables except the proportion of the "major" APR-DRG SOI subclass. All significant variables were entered into a multivariable regression model. Adjusted results revealed that some Census Bureau divisions remained significantly associated with PoCC compared to the Pacific region: East North Central; East South Central; Middle Atlantic; and South Atlantic (Table 1). Case mix index had a significant positive association with PoCC, and proportion of patients aged ≥ 65 years had a significant negative association.

TABLE 1. Hospital Characteristics and Bivariate and Multivariable Logistic Regression: Predictors of Proportion of Carbapenem Consumption (PoCC) Metric

Variable	All Hospitals (n = 139), No. (%)[a]	Bivariate Coefficient	Bivariate SE	Bivariate *P* Value	Multivariable Coefficient	Multivariable SE	Multivariable *P* Value
Region[b]							
East North Central	25 (18)	−1.07	0.0400	<.0001	−0.2832	0.0728	.0001
East South Central	5 (4)	−0.6393	0.0601	<.0001	−0.2809	0.1020	.0059
Middle Atlantic	23 (17)	−0.4899	0.0913	<.0001	−0.2529	0.0693	.0003
Mountain	7 (5)	−0.6322	0.0605	<.0001	−0.0740	0.0982	.4509
New England	13 (9)	−0.3465	0.0871	<.0001	0.0061	0.0892	.9459
South Atlantic	28 (20)	−0.4983	0.0807	<.0001	−0.1876	0.0685	.0062
West North Central	25 (18)	−0.5069	0.0551	<.0001	0.0041	0.0799	.9591
West South Central	11 (8)	−0.3747	0.0720	.0070	0.0125	0.0802	.8763
CMI (mean, SD)	1.56 (0.33)	−0.1861	0.0690	<.0001	0.5649	0.1009	<.0001
APR-DRG, SOI subclass mean %							
Extreme	7.6	5.5145	0.4477	<.0001	−0.9793	0.8606	.2551
Major	29.5	0.1709	0.2031	.4000	...[c]	...[c]	...[c]
Moderate	36.6	−1.3442	0.2214	<.0001	−0.3298	0.8283	.3628
Minor	21.7	−1.9253	0.3136	<.0001	−0.2944	0.5590	.5984
CSL PD/10,000 PD, mean (SD)							
Immunosuppressed	10.3 (11.5)	0.0180	0.0010	<.0001	0.0017	0.0034	.6100
Medicine	39.0 (11.1)	−0.0242	0.0016	<.0001	−0.0024	0.0031	.4302
Surgery	29.4 (8.8)	−0.0044	0.0019	.0222	−0.0059	0.0036	.0990
Other	13.8 (8.1)	−0.0154	0.0022	<.0001	−0.0027	0.0040	.4959
Admissions age ≥ 65, mean %	40.3	−0.0176	0.0013	<.0001	−0.0106	0.0019	<.0001

NOTE. SE, standard error; CMI, case mix index; SD, standard deviation; APR-DRG, all-patient refined-diagnosis–related group; SOI, severity of illness; CSL, clinical service line; PD, patient days.
[a]Unless otherwise specified.
[b]Reference, Pacific region, n = 19 (13%).
[c]Excluded from adjusted analysis due to $P > .05$.

Mean Percentage of Carbapenem Consumption (PoCC) by Region



Legend: % = PoCC score

FIGURE 1. Mean Percentage of Carbapenem Consumption (PoCC) by Region.

DISCUSSION

This study is the first to describe a novel antipseudomonal antimicrobial consumption metric and to measure its variability among a large group of US academic medical centers. Across the 9 Census Bureau divisions, there were significant differences in cefepime, PT, and carbapenem usage. We identified geographic differences in proportion of total use that was comprised of carbapenems, as measured by the PoCC. The Pacific, West South Central, West North Central, and South Atlantic divisions had the highest PoCCs. Differences in PoCC remained after adjusting for hospital factors. Case mix index and proportion of admissions aged ≥ 65 years were independent predictors of PoCC in adjusted analysis.

To ascertain whether Census Bureau divisional differences in the PoCC aligned with AR differences, we examined AR data from the CDC Antibiotic Resistance Patient Safety Atlas, which reports healthcare-associated infection (HAI) resistance data. In 2014, the Pacific and West South Central had the second- and third-highest rates of carbapenem-resistant Enterobacteriaceae (CRE), corresponding with our findings of higher PoCC in these regions.[11] Furthermore, the highest rate of *P. aeruginosa* resistant to carbapenems was found in the West South Central division. More data are needed to determine whether a higher PoCC indicates potential carbapenem overuse and whether an ASP target and/or serves as a marker of increased carbapenem resistance.

Interpretation of antimicrobial consumption data is inherently challenging. As part of the National Healthcare Safety Network (NHSN), an Antibiotic Use (AU) Option has been created to collect and report usage data in a standardized way, the Standardized Antimicrobial Administration Ratio (SAAR).[12] The SAAR is an observed-to-predicted ratio and is interpreted similar to the HAI standardized infection ratio (SIR). It provides ASPs with national antimicrobial use benchmarks. The PoCC can serve as a measure that informs ASPs of the relative use of carbapenems in relation to other antipseudomonal β-lactam agents. Among institutions with relatively low PT and cefepime resistance, for example, it can be used as an indicator of potential carbapenem overuse. The NHSN's AU option allows for different antibiotic groupings, such as broad-spectrum agents used for hospital-onset and/or multidrug-resistant infections. This grouping includes the antipseudomonal agents included in the PoCC as well as additional agents that are less frequently used, such as colistimethate, polymyxin B, and amikacin. This grouping allows a broad evaluation of antibiotic utilization toward gram-negative pathogens. The PoCC, in contrast, can provide the relative proportion of carbapenem use to other commonly used antipseudomonal β-lactams.

Our study has several limitations. The hospital sample was limited to academic medical centers and therefore may not be generalizable to community hospitals. Additionally, it was not possible to determine carbapenem or other antipseudomonal agent appropriateness. We also observed a range in the number of hospitals represented per division, from 5 to 28. Data concerning ceftazidime use were not included; however, this agent was used infrequently overall (2015 hospital mean use was 6 DOT per 1,000 PD) and use did not vary significantly by region ($P = .3294$). Antipseudomonal fluoroquinolones were also excluded from the metric because these agents are not usually the primary empiric antipseudomonal agents used at

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our institution. Similarly, aztreonam was excluded because it is primarily used as an alternative agent for penicillin-allergic patients (as opposed to a first-line agent).

In conclusion, there is significant variation in the PoCC metric by US Census Bureau division, independent of patient mix factors. The PoCC metric may provide ASPs with an actionable usage metric by contextualizing the use of anti-pseudomonal carbapenems in reference to other preferred antibiotic options as determined by local gram-negative susceptibility data. The region-specific mean PoCC values identified in this study may serve as a valuable reference for ASPs desiring to apply this metric locally. However, more research is needed to determine the utility of the PoCC metric by ASPs and its potential for the identification of carbapenem overuse.

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