Patterns of Initial Antibiotic Therapy for Community-Acquired Pneumonia in U.S. Hospitals, 2000 to 2009

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Abstract: *Background:* Although clinical guidelines for management of community-acquired pneumonia (CAP) in non–intensive care unit ("non-ICU") hospitalized patients have changed substantially over the last decade, it is unknown how treatment of this disease has evolved over this period. *Methods:* Using data from >100 U.S. hospitals, we identified all adults (aged ≥18 years) hospitalized for CAP between January 1, 2000, and June 30, 2009 ("study period"). We excluded patients admitted to ICU <24 hours of admission, those not starting antibiotics <24 hours of admission, those not receiving antibiotics for ≥48 hours (if alive), and those with probable healthcare-associated pneumonia. We defined "initial therapy" as all parenteral antibiotics received ≤24 hours of admission, and we examined changes in such therapy over the study period. The statistical significance of changes in initial therapy was ascertained using 2-tailed χ^2 tests. *Results:* We identified 40,392 patients who met all selection criteria. In 2000, the most frequently used initial regimens were levofloxacin (24.0% of all such admissions), ceftriaxone (9.0%), cefotaxime (7.3%), ceftriaxone plus levofloxacin (3.2%) and azithromycin plus cefotaxime (3.0%); in 2009, they were ceftriaxone plus azithromycin (18.5%), levofloxacin (12.7%), ceftriaxone (6.6%), moxifloxacin (4.7%) and ceftriaxone + levofloxacin (3.2%). Use of single-agent regimens declined between 2000 and 2009 (from 48.2%–30.0%); use of vancomycin almost doubled (13.1%–23.3%). All findings were statistically significant ($P < 0.01$). *Conclusions:* Initial antibiotic therapy for non-ICU CAP has changed substantially in the United States over the past decade, in line with evidence of widespread antibiotic resistance, evolving treatment guidelines and, most recently, quality improvement initiatives that tie hospital payments to guideline-based care.

Key Indexing Terms: Antibiotics; Antibacterial agents; Clinical practice patterns; Pneumonia; Community-acquired infections. **[Am J Med Sci 2014;347(5):347–356.]**

Although most patients with community-acquired pneumonia (CAP) are treated successfully in ambulatory care settings, approximately 25% require hospitalization.[1,2] CAP accounts for more than 1 million admissions annually to U.S. hospitals.[3] The vast majority (80%–90%) of patients hospitalized for CAP are treated in non–intensive care unit (non-ICU) settings.[2]

Antibiotic therapy is the cornerstone of treatment for bacterial pneumonia. Because delays in treatment are associated with worse clinical outcomes,[4,5] and causative pathogens are often unknown at clinical presentation,[6] initial antibiotic therapy is usually empiric and presumably informed by recommendations of professional organizations, such as the Infectious Diseases Society of America (IDSA) and the American Thoracic Society.[7–9]

In general, recent guidelines have favored the use of broad-spectrum agents and regimens as initial therapy in CAP.[9] These guidelines also provide specific recommendations concerning empiric therapy where community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) and/or *Pseudomonas* spp are suspected.[9] Compliance with clinical guidelines for CAP has even come to play a role in determining payments that hospitals receive from health insurers; since 2005, Medicare payment levels have been tied to attainment of target levels of a number of "core measures" set forth by The Joint Commission (TJC) (formerly, the Joint Commission on Accreditation of Healthcare Organizations) and the Centers for Medicare and Medicaid Services (CMS), among which is choice of initial antibiotic therapy. The core measure for immunocompetent patients with CAP currently includes a parenteral β-lactam plus a macrolide (intravenous [IV] or oral), monotherapy with an antipneumococcal quinolone (IV or oral), a parenteral β-lactam plus doxycycline (IV or oral) or tigecycline monotherapy; for non-ICU patients with risk factors for *Pseudomonas* spp, they include an IV antipneumococcal/antipseudomonal quinolone (IV or oral), an IV antipneumococcal/antipseudomonal β-lactam plus an IV aminoglycoside plus either an antipneumococcal quinolone (IV or oral) or a macrolide (IV or oral).[10] (A number of exemptions to this core measure exist, including instances of pathogen-directed therapy, diagnostic uncertainty and/or participation in clinical studies.) Approved therapies have changed frequently since they 1st became effective in 2005.

Although the evolution of treatment guidelines and the introduction of financial incentives designed to foster guideline-compliant care might be expected to have resulted in changes in initial antibiotic therapy for CAP, it is unknown to what extent and how the management of this disease has evolved over the last decade. This question is the focus of our study.

METHODS

Data Source

Data for this study were obtained from the Cerner Health Facts Database, which contains comprehensive clinical records from approximately 38 million inpatient admissions, emergency department encounters and outpatient/clinic visits at contributing general, acute care short-term hospitals (more than 100) throughout the United States.

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Submitted July 24, 2012; accepted in revised form March 28, 2013.

Supported by Forest Research Institute.

G. Oster, A. Berger and J. Edelsberg are employed by Policy Analysis, Inc., which received study funding from Forest Laboratories, Inc. D.J. Weber was a paid consultant to Policy Analysis, Inc., on this study. Dr. X. Huang is employed by Forest Research Institute.

Presented in part at the 2010 Annual Meeting of the American College of Clinical Pharmacy ("Use of Single Agents vs Multi-Drug Regimens as Initial Antibiotic Therapy for Community-Acquired Pneumonia [CAP] in U.S. Hospitals, 2000-2009," poster #125) and the 2010 Annual Meeting of the Infectious Diseases Society of America ("Trends in Initial Antibiotic Therapy for Non-ICU Community-Acquired Pneumonia [CAP] in U.S. Hospitals, 2000-2009," Poster #945).

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Information available for each hospital admission includes patient demographics (age, sex and race/ethnicity), hospital characteristics (geographic region, number of beds and teaching status), discharge diagnoses (principal and all secondary) (in ICD-9-CM format), all antibiotic therapy administered, all culture reports and sensitivities, results of other laboratory tests and total in-hospital charges.

All patient-identifying information has been either encrypted or removed from the database; it is therefore fully compliant with the Health Insurance Portability and Accountability Act of 1996 and federal guidance on Public Welfare and the Protection of Human Subjects. Per the Code of Federal Regulations, Institutional Review Board review and approval are not needed for a study of this nature because "subjects cannot be identified, directly or through identifiers linked to the subjects."[11]

Sample Selection

We identified all adult patients aged 18 years or older who were hospitalized with a principal diagnosis of pneumonia (ICD-9-CM diagnosis codes 481, 482.XX, 483.X, 484.3, 484.5, 485, 486 and 487.0) between January 1, 2000, and June 30, 2009 ("study period"). We limited our attention to patients who: (1) began parenteral antibiotic therapy within 24 hours of hospital admission; (2) received parenteral antibiotic therapy for at least 48 hours (if alive) and (3) were not admitted to ICU during the 1st 24 hours in hospital. We excluded patients with: (1) secondary diagnoses of infections of other body sites/organs, except empyema (510.XX), septicemia/bacteremia (003.1, 038.XX) and/or systemic inflammatory response syndrome (995.9X) because these conditions were deemed likely to be present at hospital admission or (2) probable healthcare-associated pneumonia (HCAP), based on evidence of transfer from another healthcare facility (including nursing homes); previous hospitalization, hemodialysis, cancer chemotherapy, IV antibiotics or wound care <30 days before hospital admission or solid organ or bone marrow transplant.

Measures

We characterized the demographic and clinical characteristics of study subjects in terms of age, sex and presence (as secondary discharge diagnoses) of selected comorbidities (Appendix); we also examined selected characteristics of the hospitals to which patients were admitted (eg, number of beds and geographic region).

We defined "initial antibiotic therapy" as all parenteral antibiotics received during the 1st 24 hours after hospital admission; oral antibiotics were not considered in constituting initial antibiotic therapy. Antibiotic treatment received in an emergency department before a patient was admitted to hospital was not considered to be part of initial antibiotic therapy unless it was continued after admission.

Analyses

We examined initial antibiotic therapy principally in terms of regimens (eg, levofloxacin monotherapy, azithromycin plus ceftriaxone). We also examined the use of regimens with activity against MRSA (ie, vancomycin, linezolid, trimethoprim-sulfamethoxazole [TMP-SMX], daptomycin, tigecycline) or *Pseudomonas aeruginosa* (ie, piperacillin-tazobactam, cefepime, ceftazidime, ticarcillin-clavulanate, doripenem, imipenem, meropenem).[12–14] (While daptomycin is not indicated for use in pneumonia, it does have activity against MRSA[14] and therefore was included among such agents.) The statistical significance of changes in antibiotic use over time was ascertained using χ^2 tests. P values were not adjusted for multiple comparisons. All analyses were conducted using PC-SAS v9.1 (SAS, Cary, NC).

RESULTS

We identified 129,289 adult patients who were admitted to hospital with a principal diagnosis of pneumonia between January 1, 2000, and June 30, 2009 (Table 1). Of these patients, 40,392 began antibiotic therapy within 24 hours of hospital admission, were not admitted to ICU during the first 24 hours in hospital, and met all other study inclusion criteria. Demographic and clinical characteristics of patients in each year of the study period are set forth in Table 2. Mean age ranged from 66 to 71 years, and approximately one half of patients were men. Comorbidities were common, including congestive heart failure (ranging from 23% to 29%), chronic obstructive pulmonary disease (21%–27%), type 2 diabetes (15%–24%) and cancer (12%–19%); 2% to 6% annually had at least 1 admission for pneumonia in the preceding year.

In 2000, the 5 most common initial therapies were as follows: levofloxacin (24.0% of all hospitalized adult patients with non-ICU CAP in that year), ceftriaxone (9.0%), cefotaxime (7.3%), ceftriaxone plus levofloxacin (3.2%) and azithromycin plus cefotaxime (3.0%). In 2009, the most common initial therapy was the combination regimen azithromycin plus ceftriaxone (18.5%), followed by the single-agent regimens levofloxacin (12.7%), ceftriaxone (6.6%) and moxifloxacin (4.7%); 3.2% of patients received ceftriaxone plus levofloxacin (Table 3).

The 5 initial regimens most commonly used in 2000 together comprised 46.5% of all initial therapy in non-ICU CAP in that year; by 2009, these 5 regimens represented only 24.2% of all such therapy ($P < 0.01$). The 5 most commonly used initial regimens in 2009 collectively constituted 45.7% of all initial therapy in non-ICU CAP in that year; in 2000, they represented only 36.7% of all such therapy ($P < 0.01$). Between 2000 and 2009, use of azithromycin plus ceftriaxone increased from 0.6% to 18.5% of all non-ICU CAP admissions,

TABLE 1. Sample selection

Admissions criteria	n
Total number of hospital admissions with principal diagnosis of pneumonia[a]	143,263
Aged ≥18 years	129,289
Receipt of parenteral antibiotics within 24 hours of hospital admission	95,637
Receipt of parenteral antibiotics for ≥48 hours[b]	85,715
Exclusion of patients with evidence of	
Transfer from another healthcare facility	6,069
Receipt of hemodialysis during prior 30 days	556
Other infections at hospital admission	30,277
Solid organ/bone marrow transplant	846
Hospitalization ≤30 days before pneumonia admission	3,463
Admission to ICU during the first 24 hours in hospital	17,158
Total in study sample	40,392

[a] Composed of ICD-9-CM diagnosis codes 481, 482.XX, 483.X, 484.3, 484.5, 485, 486 and 487.0.

[b] Or at least 1 dose of such therapy, for those who died within 48 hours of admission.

ICU, intensive care unit.