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Guideline-concordant antibiotic therapy and clinical outcomes in healthcare-associated pneumonia

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Summary
Background: The 2005 ATS/IDSA guidelines defined healthcare-associated pneumonia (HCAP) as a novel category of pneumonia in patients with significant healthcare exposure in whom the risk of drug resistant bacteria may be higher. In this study, we compare clinical outcomes in patients with HCAP who were treated with guideline-concordant antibiotic regimens with those who were not.
Methods: Medical records of 100 patients meeting HCAP criteria admitted to an academic tertiary care hospital between January 2009 and January 2011 were retrospectively reviewed. Cases were divided into guideline-concordant and guideline-discordant groups based on antibiotic therapy. Demographic, microbiological and clinical outcome data were compared for both groups.
Results: Patients in this cohort had multiple co-morbidities, severe pneumonia (mean PSI score 124.1), and significant mortality (22%). 21 of the 100 cases (21.0%) were culture positive, of which 11 (53.8%) represented drug-resistant pathogens. No statistically significant differences for any of the four clinical outcome measures were detected between the guideline-concordant therapy group and guideline-discordant group. In multivariate regression analysis controlling for possible confounders, similar results were observed, with the exception that length of stay was significantly longer (3.99 days, $p < 0.001$) in the discordant group. Three

Abbreviations: CAP, community-acquired pneumonia; CAP-DRP, community-acquired pneumonia drug-resistant pathogens; GEE, generalized estimate equation; HCAP, healthcare-associated pneumonia; LOS, length of stay; OR, odds ratio; PSI, pneumonia severity index; TST, time to switch therapy; TCS, time to clinical stability.

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or more HCAP criteria (OR 10.89) and wound care (OR 6.32) were characteristics found to be associated with increased risk for drug-resistant pathogens.
Conclusion: In our cohort, the HCAP model identified a population with significant co-morbidities and increased risk for drug-resistant pathogens, severe pneumonia, and increased mortality. However, clinical outcomes were not significantly improved with guideline-concordant antibiotic therapy.

Introduction

In 2005 the American Thoracic Society (ATS) and the Infectious Disease Society of America (IDSA) released updated practice guidelines for hospital-acquired (HAP) and ventilator-associated pneumonia (VAP). In these guidelines, a new category of disease, *healthcare-associated pneumonia* (HCAP), was introduced.[1] This new entity was based upon observations that in community-acquired pneumonia, drug resistant organisms such as *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA) are more frequently implicated in patients with frequent healthcare exposure. This new classification comprises patients hospitalized within the last 90 days, those receiving chemotherapy, wound care or intravenous antibiotics, residents of nursing homes or long-term facilities, and patients undergoing hemodialysis. For these groups, the guidelines recommend a more aggressive empiric antibiotic regimen than that which is used in community-acquired pneumonia (CAP). However, recent studies[2,3] have suggested that when taken in composite, the HCAP criteria have a low predictive value for identifying disease caused by drug resistant pathogens. Furthermore, evidence supporting improved outcomes with the recommended extended-spectrum antibiotic regimen is lacking. Here, we compare clinical characteristics and outcomes in patients who received guideline concordant antibiotics with those who received discordant therapy in a single-center retrospective HCAP cohort.

Methods

This study was approved by the institutional review board of the Mayo Clinic Foundation, IRB number 11-000463. Five hundred and thirty patients admitted to an academic tertiary care hospital between January 2009 and January 2011 whose discharge diagnosis included pneumonia were identified by querying ICD-9 billing code records. All medical records were manually reviewed. One investigator refereed questions regarding how to apply predetermined study definitions. Pneumonia was defined by: 2 or more clinical signs or symptoms (temperature (C°) <36.0 or >38.0; respiratory rate >20 breaths/min; cough; room air O_2 saturation $<90\%$; sputum production; leukopenia $<4000/mm^3$ or leukocytosis $>10{,}000/mm^3$; plus radiographic evidence of infiltrate or cavitation).[3] Using these criteria, 171 cases were excluded because another diagnosis was more likely than pneumonia. An additional 96 cases were excluded because they met criteria for hospital-acquired or post-operative pneumonia.

The HCAP criteria found in the 2005 ATS/IDSA guidelines were then strictly applied to the remaining 263 cases, including: (1) hospitalization for more than 48 h in the last 90 days, (2) residence in a long-term care facility, (3) attendance at an outpatient hemodialysis clinic within 30 days of admission, (4) receipt of infusion therapy at an infusion center within 30 days or (5) receipt of outpatient wound care during the 30 days preceding admission. One hundred and sixty three cases (62.0%) were thereby classified as CAP, while 100 cases (38.0%) met criteria for HCAP. Patients were considered immunosuppressed if any of the following were present: use of systemic corticosteroids equivalent to >15 mg prednisone daily for >5 days; cytotoxic chemotherapy; immunomodulating agents (calcineurin inhibitors, mycophenolate mofetil, cyclophosphamide, methotrexate, TNF inhibitors); presence of hypogammaglobulinemia or other heritable immunodeficiency; active hematologic malignancy; neutropenia (absolute neutrophil count $<1000/mm^3$); or HIV/AIDS with a CD4 count $<200/mm^3$. Microbiological data were included from the following sources: cultures of sputum, bronchoalveolar lavage fluid, and blood if the pathogen was consistent with a respiratory source; urinary antigen tests for *Legionella pneumophila* and *Streptococcus pneumoniae*; respiratory viral panel; and serology in the case of suspected pulmonary coccidioidomycosis. Bacteria were classified as community-acquired pneumonia drug-resistant pathogens (CAP-DRP) if susceptibility testing demonstrated resistance to antibiotics recommended for CAP, i.e. third-generation cephalosporins and macrolides. Examples of CAP-DRP include MRSA, *P. aeruginosa*, Enterobacteriaceae expressing extended-spectrum beta-lactamases, and other resistant non-fermenting gram-negative organisms, such as *Acinetobacter* spp. and *Stenotrophomonas* spp.

The HCAP study group was divided based on antibiotic treatment. The guideline-concordant group was defined as patients whose cumulative antibiotic regimen, initiated within the first eight hours of admission and continued for at least 48 h, met or exceeded coverage recommended by 2005 ATS/IDSA guidelines: Anti-pseudomonal beta-lactam plus *either* a fluoroquinolone *or* an aminoglycoside, plus anti-MRSA coverage if risk factors were present. Risk factors for MRSA in this study included known prior MRSA infection or colonization, positive nasal MRSA swab prior to antibiotic decision making, or recent history of intravenous drug use or incarceration.

Outcomes measured included time to clinical stability (TCS), time to switch therapy (TST), length of stay (LOS) and 30-day mortality. TCS was defined as: temperature <37.2 °C, heart rate <100 beats/min, systolic blood pressure >90 mmHg, respiratory rate <24 breaths/min, and oxygen saturation $>90\%$ on room air or return to preexisting