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Emergency Pharmacist Impact on Health Care-Associated Pneumonia Empiric Therapy

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Abstract

Purpose: Health care-associated pneumonia (HCAP) is a serious infection dependent on proper treatment that often presents in the emergency department (ED) and deviation from treatment guidelines appears to be high. This study was conducted to evaluate the impact of emergency medicine pharmacists (EPhs) on adherence of empiric antibiotic therapy to guideline recommendations. *Methods:* A retrospective chart review of adult patients with HCAP who presented to an academic medical center ED from September 1, 2008 to June 30, 2010 was conducted. The control group included those patients with HCAP who presented to the ED outside of the EPhs' hours (23:00-13:00), and the treatment group consisted of those patients who presented during the EPhs' hours (13:00-23:00). *Results:* The 81 patients presenting inside the EPhs' hours were significantly more likely to receive guideline adherent empiric antibiotics than the 70 patients presenting outside the EPhs' hours (49.38% vs 25.7%, $P = .005$). Also, patients in the treatment group received antibiotics in a shorter amount of time (11.37 vs 15.56 hours, $P = .272$) and at more appropriate doses (85.2% vs 77.1%, $P = .29$) although these outcomes were not statistically significant. *Conclusion:* The presence of the EPh significantly increased the likelihood of at-risk patients receiving empiric antimicrobial therapy consistent with guideline recommendations.

Keywords

health care-associated pneumonia, infection, pharmacist, pneumonia

Introduction

In 2005, health care-associated pneumonia (HCAP) was recognized as its own entity by the publication of the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guidelines.[1] The new emphasis placed on this category has been attributed to a change in the health care system with traditional patient care resources shifting from the inpatient to outpatient setting (eg, dialysis clinics, home infusion services, etc). This shift has increased the risk of patient exposure to multidrug resistant pathogens and organisms that are not usually associated with community-acquired infections.[2]

The emergency department (ED) serves as the gateway to the hospital setting for the majority of patients and emergency medicine (EM) physicians are faced with differentiating patients at risk of community-acquired pneumonia (CAP) from those with more severe HCAP.[3] Similar to CAP, initial antibiotic selection and time to administration of antibiotics for patients diagnosed with HCAP are critical as both may lead to an increase in mortality if inappropriate.[4] Based on these outcomes, it is imperative that the EM health care team identify these patients and start appropriate empiric antibiotics as quickly as possible.

When patients meet HCAP criteria (Table 1), the guidelines suggest that antimicrobial coverage include pharmacologic agents that provide activity against methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug resistant *Pseudomonas aeruginosa*.[1] A previous observational study found that patients with HCAP received guideline adherent empiric antibiotics only about 25% of the time.[5] In addition to opportunities associated with antibiotic selection, ensuring the timeliness of antibiotic administration in the ED can also be an

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Table 1. HCAP Risk Factors.

Recent admission to a health care facility[a]
Residence in long-term care or NH
Dialysis clinic patients
Recent IV antibiotic therapy[b]
Chemotherapy[b]
Home wound care/infusion therapy[b]
Immunosuppressive disease/therapy

Abbreviations: HCAP, health care-associated pneumonia; NH, nursing home; IV, intravenous.
[a] >2 days within past 90 days.
[b] In the last 30 days.

issue. Past literature has revealed that the time to antibiotic administration impacts outcomes, specifically mortality, in patients with pneumonia and other severe infections.[6-8]

The role of emergency medicine pharmacists (EPhs) continues to evolve, and research has proven that EPh play an important role in the ED.[9,10] EPh have the knowledge and skills to evaluate patients for risk factors associated with HCAP and to assist in initiating antimicrobial therapy at potential pathogens in an efficient manner. Additionally, EPh can function as a physician extender and provide increased flexibility to the constraints placed on EM physicians and residents by their workload, allowing for a more thorough evaluation of HCAP risk factors. By having EPh services involved directly in the care of these patients, we anticipated an improvement in guideline adherence and timeliness of therapy.

Methods

Study Design

In order to evaluate the impact of EPh clinical services on HCAP management, a retrospective analysis of patients with HCAP who presented to an academic medical center ED from September 1, 2008 through June 30, 2010 was conducted. This date range was chosen based on the establishment of full-time, consistent EPh coverage of the ED in 2008. Control group data were collected for patients who presented during the hours when the EPh were not present (23:00-13:00) and treatment group data were collected for patients who presented during the hours clinical pharmacy services were present in the ED (ie, 13:00-23:00). The primary objective of the study was to evaluate the effect of the EPh on the identification of patient risk factors for HCAP by evaluating the appropriateness of empiric antibiotic therapy. Risk factors for HCAP were based on those listed in the IDSA's most recent guidelines for the management of HCAP. Secondary objectives were to determine whether the EPh affects appropriateness of antibiotic dosing and the time to administration of appropriate antibiotics. In addition, hospital and intensive care unit (ICU) length of stay (LOS), as well as mortality were compared between groups. Patients were included if they were $\geq$18 years of age and presented to the ED with suspected HCAP. Those patients who presented to the ED but were later transferred to another institution were treated on an intention-to-treat basis and were included in the analysis of appropriate antimicrobial therapy, dosing, and time to appropriate antimicrobials but were excluded in the analysis of other secondary outcomes (eg, LOS and mortality) as this information was not available. Final institutional review board (IRB) approval, number 10-0467-P2H, was obtained on September 1, 2010.

Study Setting and Population

The institution that served as the site for this study is a 473-bed, acute care, academic hospital, and level 1 trauma center. The yearly patient census for the ED exceeds 45 000 patients. Pharmacy coverage in the ED was comprised of a clinical specialist between 13:00 and 23:00. No physical coverage was provided outside those hours, but central pharmacy was responsible for order verification from 23:00 to 13:00. In this study, patients were identified in the designated time period via *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes for pneumonia. Once the patients were identified, it was determined whether they met the criteria for HCAP based on both electronic and paper medical records data from the visit in question. Risk factors that were used to classify the patients as HCAP were taken from the ATS/IDSA guidelines listed previously in Table 1.

Measures

Data collected from the patients' medical records included weight, gender, age, date and time of presentation to the ED, chief complaint upon presentation, antibiotic allergies and the patient's reaction when available, patient's risk factor/factors for HCAP, initial antibiotics administered in the ED, time antibiotics were ordered, time antibiotics were signed off by the nurse on the medication administration record, temperature upon presentation, white blood cell count, cultures performed in the ED, culture results (both preliminary and final) including susceptibility data, changes to antimicrobial therapy by the admitting service, time to appropriate antibiotic therapy if not started in the ED, admitting service, ICU LOS, hospital LOS, and mortality. Patients were excluded if pneumonia was not their primary diagnosis, they did not receive antibiotics in the ED prior to discharge or transfer, they presented with a cystic fibrosis exacerbation, were direct admissions from an outside hospital, had an unknown presentation time, or had inadequate information in their medical records.

Appropriate empiric antimicrobial therapy was assessed by a panel of pharmacists blinded to the presence of the EPh using prespecified criteria, which were based on the ATS/IDSA recommendations. Appropriate dosing was determined by guideline and drug-specific recommendations, and vancomycin was deemed appropriate if dosed between 15 and 25 mg/kg.[11] Time to appropriate antibiotic therapy was defined as the time when the final antibiotic in the regimen was charted as administered as this was the time point that represents comprehensive coverage of potential pathogens. The time to the first antibiotic

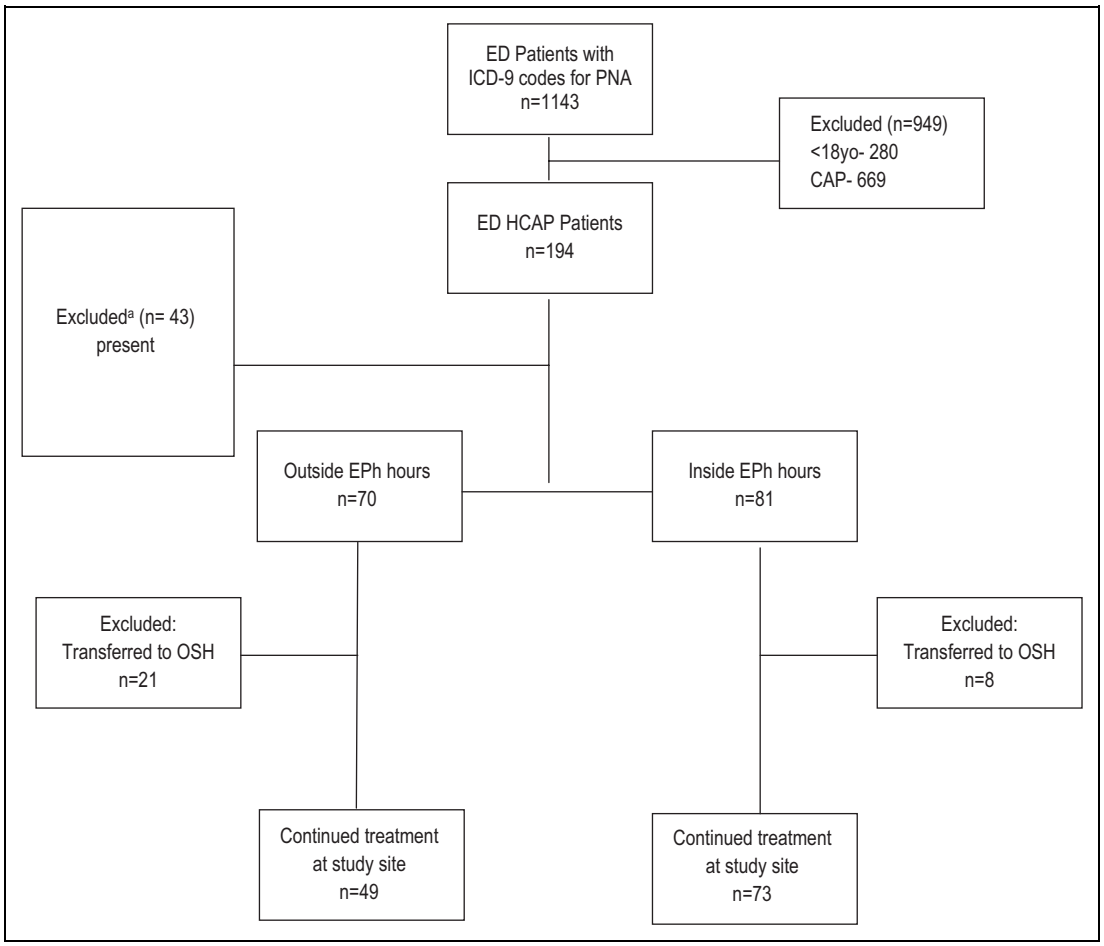

Figure 1. Patient identification. EPhs indicate emergency medicine pharmacists; PNA, pneumonia; CAP, community-acquired pneumonia; HCAP, health care-associated pneumonia; OSH, outside hospital. [a] 10-Not primary diagnosis; 10-inadequate information; 9-no risk factor; 4-no antibiotics in ED; 4-direct OSH admission; 3-cystic fibrosis; 3-transferred prior to treatment.

administered was not assessed as the agent would likely come from an automated dispensing cabinet, and a significant difference in timing would not be expected.

Data Analysis

At a desired alpha of .05 and power of 0.8, in order to detect a $\geq$20% relative difference in selection of appropriate empiric antibiotic therapy, it was determined that a sample size of approximately 200 patients was necessary. Data were compared between groups utilizing chi-square analysis, Fisher's exact test, and Student's *t* test where appropriate. A *P* value of less than .05 was considered to indicate a statistically significant difference.

Results

From September 1, 2008 through June 30, 2010, a total of 194 patients were identified who met criteria for HCAP; of these, 43 patients were excluded during data collection largely due to varying diagnoses or incomplete information (Figure 1). The total population eligible for assessment of appropriate empiric therapy, appropriate dosing, and time to appropriate antibiotics was 151 patients. Following transfer to an outside institution, 122 patients remained to be assessed for secondary outcomes such as LOS and mortality.

Table 2. Baseline Demographics.

	Inside EPh hours, n= 81	Outside EPh hours, n = 70	*P* value
Age, years (SD)	58 (16.5)	63 (16.9)	.077
WBC (mean [SD])	13.7 (8.73)	12.8 (6.8)	.47
Temperature, °F (mean [SD])	95 (15.06)	97 (7.9)	.184
Male, n (%)	60 (74.1)	37 (52.9)	.01
Weight, kg (mean [SD])	75.8 (24.15)	78 (27.1)	.601

Abbreviations: EPhs, emergency medicine pharmacists; SD, standard deviation; WBC, white blood cells.

Baseline demographics between the groups can be seen in Table 2 and HCAP risk factor distribution for the patients is reported in Table 3. No significant differences were seen in baseline characteristics, with the exception of the treatment group having significantly more males (74.1% vs 52.9%, $P = .01$). Recent hospitalization was the most prevalent risk factor

Table 3. HCAP Risk Factor Prevalence.[a]

Risk factor	n (%)
Recent admission to health care facility	73 (48)
Immunosuppressive disease/therapy	70 (46)
Residence in long-term care or nursing home	37 (25)
Dialysis clinic patients	18 (12)
Chemotherapy	12 (8)
Recent IV antibiotic therapy	6 (4)
Home wound care/infusion therapy	1 (0.7)

Abbreviations: HCAP, health care-associated pneumonia; IV, intravenous.
[a] Risk factors were not exclusive so multiple risk factors may have been recorded for some patients, explaining the 217 total risk factors present.

(48%), followed by immunosuppression (46%) and residence in a nursing home or long-term care facility (25%).

As seen in Table 4 and Figure 2, a statistically significant difference was seen in the primary outcome, empiric therapy adherent to guidelines (49.38% vs 25.7%, $P = .005$). Although trends were seen in appropriate dosing (Figure 3) and time to appropriate antimicrobial therapy, there were no statistically significant differences in the secondary outcomes.

Discussion

The purpose of this study was to determine whether the presence of EPh impacted the selection of empiric antibiotic therapy given to patients with HCAP presenting to the ED. It is known from previous studies of HCAP that the inability to provide empiric antimicrobial therapy determined appropriate through culture results increases mortality.[5,12] In 2007, Micek et al published results from a retrospective cohort analysis of 639 patients with culture positive pneumonia. An assessment of 431 patients with HCAP and 208 patients with CAP found that in total, those who received inappropriate empiric antibiotics had increased mortality (32.2% vs 15.7%, $P < .001$). Logistic regression was used to confirm inappropriate empiric antibiotics as an independent risk factor for mortality in this patient population.[12] Venditti et al also conducted a retrospective analysis of CAP, HCAP, and hospital-acquired pneumonia. Of the 90 patients with HCAP included in this analysis, 26.7% were treated with empiric therapy adherent to the guidelines. This study was also able to confirm through regression analysis that inappropriate empiric antibiotics based on culture results were associated with increased mortality (odds ratio [OR] 6.4, confidence interval [CI] 2.3-17.6).[5] Utilization of the HCAP guidelines should decrease the chance of finding empiric therapy inappropriate once cultures are finalized. Similarly to Venditti et al, our control group received guideline adherent empiric antibiotics approximately 25% of the time, thus our treatment group shows the significant impact that EPh can have on this patient population. It is evident that EPh have the ability to recognize the HCAP risk factors and promote the use of guideline adherent antibiotic therapy.

In prior studies, appropriate therapy was determined based on susceptibility results of cultured organisms to the regimen prescribed. Given the study size and timeline, it was not feasible to include only those patients with culture-positive results. Thus, we defined adherent therapy as compliance with ATS/IDSA guideline recommendations to cover *P aeruginosa* with 2 agents and MRSA. Despite one previous HCAP study with culture negative data using the criteria of MRSA and single agent *P aeruginosa* coverage as their appropriate regimen, it was felt that double coverage was more in line with the guideline recommendations and consistent with multiple other HCAP studies analyzing empiric therapy.[1,5,13,14] In addition, it was decided that including culture negative data increased external validity as the majority of patients with HCAP do not have lower respiratory cultures drawn in the ED.[15]

Pneumonia has been shown to be an infection, along with sepsis and meningitis that has a survival benefit with early appropriate antibiotic therapy.[6-8] Meehan et al conducted a multicenter retrospective study of Medicare patients at least 65 years old, reviewing 14 069 patients presenting with pneumonia. They found that those who received antibiotics within 8 hours of presentation had decreased 30-day mortality (OR 0.85; 95% CI 0.75-0.96).[7] Houck et al also performed a retrospective review of 18 209 Medicare patients presenting with CAP and found significantly decreased hospital mortality, 30-day mortality, and decreased LOS.[6] These studies have led the Joint Commission to adopt a requirement of 6 hours from presentation to first antibiotic in patients presenting with CAP.[16] In our study, time to appropriate antimicrobial therapy, as seen in Table 4, favored the treatment group but did not show statistical significance. The inability to show a difference in this category is likely attributed to our small study size and also the availability of antibiotics such as piperacillin/tazobactam, levofloxacin, and vancomycin 1000 mg in automated dispensing cabinets in our ED. Of note, the EPhs are major determinants in what is stocked in these cabinets, thus ensuring the opportunity for an efficient administration process whether the EPh is present or not.

No statistically significant difference was seen in appropriate dosing between the 2 groups, although there was a trend toward more appropriate dosing in the treatment group. One limitation to assessing proper dosing in our facility is our computerized physician order entry in the ED. In the times the EPh was not present to recommend or correct doses, the pharmacists verifying orders in the central pharmacy could facilitate proper dosing if an inappropriate regimen is noticed, thereby somewhat neutralizing this effect. In addition, EM physicians have certain ordersets that assist with proper dosing, have the ability to place an order as "pharmacist to dose," and have also received continued education from EPh regarding dosing of antibiotics.

Pharmacists have the ability to recommend therapy to physicians and physicians may choose to agree or disagree. Although this study is unable to capture attempts to optimize therapy, inherently there will be times when the EPh's recommendation is not taken, therefore, decreasing the percentage of patients with compliant therapy in the treatment group. This hesitancy to accept HCAP and its guidelines for treatment is

Table 4. Primary and Secondary Outcomes.

	Inside EPh hours	Outside EPh hours	*P* value
Adherent empiric therapy, n (%)	40 (49.38%), n = 81	18 (25.7%), n = 70	.005
Appropriate dosing, n (%)	69 (85.2%), n = 81	54 (77.1%), n = 70	.29
Time to appropriate therapy, mean hrs (SD)	11.37 (17.9), n = 59	15.56 (19.37), n = 40	.272
Hospital LOS mean days (SD)	7.86 (6.23), n = 73	8.51 (9.79), n = 49	.958
ICU LOS mean days (SD)	10.2 (7.61), n = 10	10.0 (8.1), n = 8	.656
Mortality, n (%)	6 (7.5%), n = 73	11 (15.7%), n = 49	.176

Abbreviations: EPhs, emergency medicine pharmacists; SD, standard deviation; ICU, intensive care unit; LOS, length of stay.

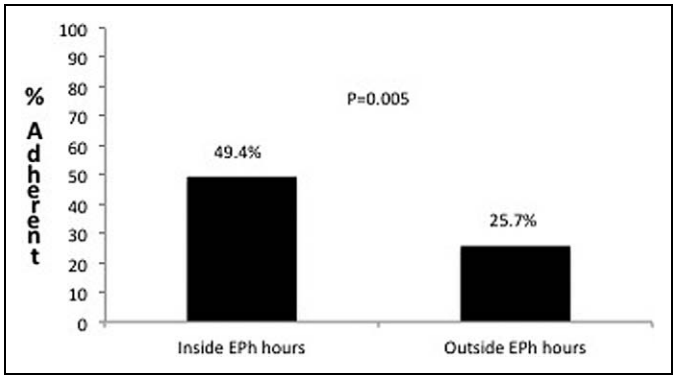

Figure 2. Empiric antibiotic therapy. EPhs indicates emergency medicine pharmacists.

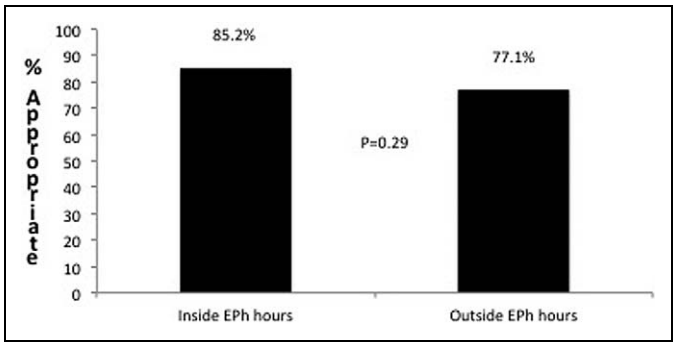

Figure 3. Appropriate dosing. EPhs indicates emergency medicine pharmacists.

currently a topic of discussion. There is a belief that the HCAP population is a heterogeneous group and that each of these risk factors does not warrant treatment with broad-spectrum coverage, but certain risk factors may be more likely to produce specifically just MRSA or just *Pseudomonas* infections.[17-19] Further research is needed to determine whether HCAP can be further delineated into more homogenous groups of risk factors. In contrast to disagreement with the risk factors, Seymann et al performed a survey study suggesting the inability to recognize patient risk factors as the reason for inappropriate treatment of HCAP. A group of internal medicine, emergency medicine, and critical care physicians were given patient scenarios and options for treatment. On average, the surveys showed compliance with HCAP 9% of the time, but the majority of responders claimed they were aware of, agreed with, and practiced concordantly with the guidelines.[4]

Limitations

This study does have some limitations that need to be addressed. First of all, this is a single-center study in an academic medical center ED with a census of over 45 000 patients per year. The practice environment is unique to academic medical centers as patient care is provided by a combination of students, interns, residents, and faculty. Despite this, the guideline adherence in our control group was consistent with the previous adherence rates of a multicenter study that included community hospitals.[5] Second, the topic of HCAP itself is controversial and further studies are being done to assess risk factors, nonetheless current recommendations support its use and proper treatment. Third, we were unable to meet our power set a priori, and although we still showed >20% significant difference in our primary outcome, it is unknown whether other secondary outcomes would show significance given more patients. In our baseline demographics, we saw significantly more males but the HCAP guidelines are not gender specific nor have HCAP studies seen gender independently associated with worse outcomes. Although we did see more males, our HCAP rate (21%) from the 863 adult patients who presented with pneumonia is consistent with a previously recognized range of 17% to 67%.[2] Even though we were unable to capture the number of actual attempts and interventions made, we assume the differences are due to EPh since the EM team is similar and access to central pharmacy services are the same in both groups. Also, the EPh role in the ED is such that based on orders and consultations placed, they must seek out these patients, thus a deficiency to provide therapy compliant with guidelines may not be due to the inability to recognize risk factors, but the lack of knowing a patient with HCAP is present in the ED.

Conclusions

This is the first study to assess the effectiveness of EPh in HCAP empiric treatment. The results of this study show the rates of antimicrobial therapy consistent with guideline recommendations when an EPh is present and not present. As the role of EPh continues to evolve and the multidisciplinary approach becomes increasingly common, this study adds to the growing body of literature supporting the role of EPh in patient-centered

care.[9,10] Further studies in this area should attempt to identify patients who clinically benefit from guideline adherent therapy, culture appropriate therapy, and EPh interventions in both of these areas.

Authors' Note

This research was previously presented at the 26th Annual Great Lakes Residency Conference. Purdue University, West Lafayette, Indiana; April 27-29, 2011.

Declaration of Conflicting Interests

The authors declared no conflicts of interest with respect to the research, authorship, and/or publication of this article.

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