The impact of prior antibiotic therapy on the clinical outcomes of hospitalized patients with community-acquired pneumonia (CAP)

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ABSTRACT

Introduction
Infections due to multidrug-resistant (MDR) bacteria are associated with poor clinical outcomes. The use of prior antibiotic therapy has been associated with infections due to MDR bacteria. It is unclear if patients with CAP who were exposed to antibiotics in the prior 30 days have worse clinical outcomes compared with patients who were not exposed.

Objective
The objective of this study was to define if hospitalized patients with CAP who were exposed to antibiotics in the prior 30 days have worse clinical outcomes compared with patients who were not exposed.

Methods
This was a secondary data analysis of the Community-Acquired Pneumonia Organization (CAPO) International Cohort Study database. Patients who received any antibiotic therapy in the prior 30 days were included in the study and were compared to patients who did not receive therapy.

Results
A total of 6919 patients were included, 6555 without prior therapy and 364 with prior therapy. There was no significant difference between the two groups in terms of in-hospital mortality (8.8% without prior therapy, 8.2% with prior therapy, P=0.76) or length of hospital stay (median 7 days for both groups, P=0.57).

Conclusions
This study failed to demonstrate that prior antibiotic use was associated with poor clinical outcomes in hospitalized patients with CAP. The following possibilities may explain our findings: 1) prior antibiotic use may not select for MDR bacteria, 2) our current empiric antibiotic therapy for CAP may be broad-spectrum enough to cover the likely development of MDR bacteria in patients with prior antibiotic therapy.

INTRODUCTION

Community-acquired pneumonia (CAP) is the leading cause of death from infectious diseases in most developed countries.[1-3] Most of the time treatment for CAP occurs in the outpatient setting, leaving hospitalization for more complex patients such as elderly, immunocompromised patients, and patients with multiple comorbidities.[4] Several studies have shown the overuse of antibiotic in the treatment of infections in the community.[5] Data showed that giving antibiotics prior to hospital admission changes the normal flora and increases the chances of opportunistic infections or multidrug resistant pathogens producing worse outcomes.[6]

The association between pre-hospital antibiotic use and outcomes of hospitalized patients with CAP has been investigated, with some studies reporting increased mortality[7], whereas others found no differences.[8] All these studies defined pre hospital antibiotic therapy as the antibiotic received immediately before hospitalization. Little is known about the impact of antibiotic given within 30 days of admission on the clinical outcomes of hospitalized patients with CAP.

OBJECTIVES

The objective of this study was to determine the impact of prior antibiotic therapy given within 30 days of admission in the clinical outcomes of hospitalized patients with CAP.

MATERIALS AND METHODS

Materials and Methods
This was a secondary analysis of patients enrolled in the Community-Acquired Pneumonia Organization (CAPO) international cohort study. Data were collected between 2001 and 2015. In each participating center, non-consecutive medical records of hospitalized patients with the diagnosis of CAP were reviewed. A sample of the data collection form is available at the study website (www.caposite.com). Validation of data quality was performed at the study center before the case was entered in to the CAPO database. Institutional Review Board approval was obtained by each participating center.

Study definitions
- CAP: Diagnosis of CAP required the presence of criterion A, B, and C:
- New pulmonary infiltrate on imaging (CT scan or chest x-ray) at the time of admission to the hospital.
- Signs and Symptoms of CAP (at least one of the following)
- New or increased cough (per the patient)
- Fever >37.8°C (100.0°F) or hypothermia <35.6°C (96.0°F).
- Changes in WBC (leukocytosis >11,000 cells/mm^3, left shift > 10% band forms/microliter, or leukopenia < 4,000 cells/mm^3
- Working diagnosis of CAP at the time of hospital admission with antimicrobial therapy given within 24 hours of admission.

Prior antibiotic use: administration of any antibiotic for any kind of infection within the last 30 days prior to hospital admission due to CAP.

Study Groups
- Group 1: defined as the total of patients without prior antibiotic use within the last 30 days prior to hospital admission.
- Group 2: defined as the total of patients with history of antibiotic use within the last 30 days prior to hospital admission.

Study outcomes
- Length of stay (LOS): defined in days and calculated for each patient as the day of discharge minus the day of admission. Patients hospitalized for more than 14 days were censored at 15 days in an effort to capture LOS data related only to bacterial CAP.
- In-hospital mortality: defined as death by any cause during hospitalization.

Statistical analysis
Baseline categorical explanatory variables were summarized as frequencies and percentages and differences between both groups of patients were analyzed using a chi-square test or Fisher's exact test when appropriate and warranted. Continuous variables were summarized as frequencies and interquartile range and differences between groups were analyzed by Wilcoxn-Mann-Whitney test.

TCS and LOS were analyzed with the Kaplan-Meier method, and log-rank tests were applied to evaluate differences between both groups of patients. P-values ≤ 0.05 were considered statistically significant.

RESULTS

A total of 6919 patients were included, 364 patients receive antibiotic therapy and 6555 without therapy.

RESULTS

Table 1. Patient's characteristics

Variable	Prior Antibiotic Therapy n=364	No Prior Antibiotic Therapy n=6555	P-value
Demographics			
Age , Median (IQR)	65 (30.2)	69 (29)	0.145
Sex, n (%)	236 (65)	3953 (60)	0.088
Nursing home resident, n (%)	26 (7)	329 (5)	0.086
Comorbid Conditions			
Congestive Heart Failure, n (%)	67 (18)	1129 (17)	0.569
COPD, n (%)	108 (30)	1564 (24)	0.012
Diabetes, n (%)	83 (23)	1158 (19)	0.053
HIV, n (%)	27 (7)	419 (7)	0.591
Renal Disease, n (%)	44 (12)	674 (10)	0.289
Liver Disease, n (%)	35 (10)	349 (5)	0.001
Neoplastic Disease, n (%)	42 (12)	638 (10)	0.277
Physical Exam			
Altered mental status on admission, n (%)	44 (12)	862 (14)	0.388
Respiratory Rate, Median (IQR)	22 (10)	22 (10)	0.524
Systolic blood pressure, Median (IQR)	120 (31)	125 (32)	0.12
Temperature (degrees Celsius), Median (IQR)	37.4 (1.7)	37.8 (1.6)	0.023
Heart rate, Median (IQR)	98 (26)	100 (27)	0.233
Lab/Radiography			
pH, Median (IQR)	7.4 (0.1)	7.5 (0.1)	0.542
PaO2, Median (IQR)	62.5 (18.6)	62 (20.3)	0.384
Blood Urea Nitrogen, Median (IQR)	30.4 (30)	31 (32)	0.18
Serum sodium, Median (IQR)	137 (6)	136 (6)	0.955
Serum glucose, Median (IQR)	118 (47.5)	122 (52)	0.239
Hematocrit, Median (IQR)	38 (6.8)	38 (8)	0.601
Pleural effusion, n (%)	77 (21)	1620 (25)	0.133
Severity of Disease			
ICU admission, n (%)	46 (13)	690 (11)	0.221
Pneumonia Severity Index, Median (IQR)	109 (55.2)	98 (49)	<0.001

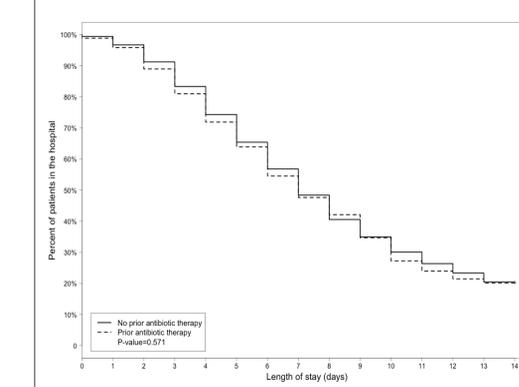Kaplan Meier curve of length of stay by percent of patients in the hospital. No difference.

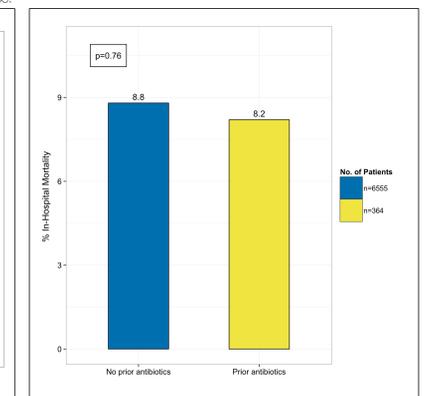Figure1. LOS for both study groups

Figure 2. Mortality rates for both study groups

CONCLUSIONS

This study failed to demonstrate that prior antibiotic use was associated with poor clinical outcomes in hospitalized patients with CAP.
The following possibilities may explain our findings:
1. Prior antibiotic use may not select for MDR bacteria.
2. Our current empiric antibiotic therapy for CAP may be broad-spectrum enough to cover the likely development of MDR bacteria in patients with prior antibiotic therapy.
3. The study may not have enough power to detect small differences in mortality.
- We didn't evaluate the collateral damage of prior use of antibiotic in hospitalized patients with CAP. If an association is found, a better controlled of the antibiotic use in the community may be still needed to improve patients' outcomes.

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