Using the antibiotic intensity score to evaluate antibiotic use in hospitalized patients with community-acquired pneumonia (CAP) with known versus unknown etiology

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ABSTRACT

Introduction: In CAP patients with an identified pathogen, broad-spectrum antibiotic therapy should narrow to a pathogen-directed therapy. This leads to less antibiotic exposure when compared to patients with CAP of unknown etiology. Less exposure may decrease the risk of toxicity and collateral damage. The antibiotic intensity score combines the number of days of each antibiotic with the antibiotic spectrum to calculate a score that defines antibiotic exposure.
The objective of this study was to use the antibiotic intensity score to define if patients with CAP of known etiology are exposed to fewer antibiotics compared to patients with unknown etiology.
Methods: This was a secondary data analysis of the Community-Acquired Pneumonia Organization (CAPO) International Cohort Study database. The intensity score was calculated as the sum of the number of days of each antibiotic multiplied by the antibiotic spectrum. The spectrum was translated into numeric values from 1 to 9 with increasing spectrum.
Results: A total of 772 patients were included in the study, 401 with an unknown etiology and 371 with a known etiology. The median antibiotic intensity score (IQR) was 60 (54) for those with a known etiology, and 55 (48) for those with an unknown etiology (P=0.33).
Conclusions: This study indicates that there is no difference in antibiotic exposure for patients with CAP when a pathogen is identified or not. Our data suggest that current clinical practice is to manage patients with broad-spectrum antibiotics without performing pathogen-directed therapy once an etiology of CAP has been identified.

INTRODUCTION

Pneumonia management represents an area of concern in current medical society due to its high morbidity and mortality rates. Pneumonia together with influenza remains the 7th leading cause of death in the United States (1). Clinical outcomes of patients with community-acquired pneumonia (CAP) are closely related with appropriate treatment. Initial empiric therapy is chosen according to the likely etiologic organisms, as microbiological diagnosis is not usually completed within the first 48-72 hours. National guidelines recommend broad empiric therapy. Table 1)

Table 1 Most common etiologies of community-acquired Pneumonia(CAP) in regard to the patient type- IDSA/ATS Guidelines for CAP in Adults • CID 2007(1)

Outpatient	• Streptococcus pneumoniae, Mycoplasma Pneumoniae, Haempphilus influenzae, Chlamydophila Pneumoniae, Respiratory viruses
Inpatient non-ICU	• Streptococcus Pneumoniae, Mycoplasma Pneumoniae, Chlamydophila pneumoniae, Haemophilus influenzae, Legionella species, Aspiration, Respiratory viruses
Inpatient ICU	• Streptococcus pneumoniae, Staphylococcus aureus, Legionella species, Gram negative bacilli, Haemophilus influenzae

Once a pathogen is identified, current recommendations state that broad-spectrum antibiotic therapy, should be narrowed to a pathogen-directed therapy; this includes switching antibiotics based on susceptibility report and discontinuing the antibiotics with less or no efficacy (example in Figure 2). This de-escalation is supposed to lead to less antibiotic exposure, which in turn may decrease the risk of toxicity and collateral damage. Previously, our group developed an intensity score with the goal of quantifying the antibiotic exposure (2).
The antibiotic intensity score (AIS) combines the number of days of each antibiotic with the antibiotic spectrum to calculate a score that defines antibiotic exposure. If pathogen-directed therapy is performed, the antibiotic intensity score should be lower for those patients in whom an organism was identified, when compared to those patients with unknown etiology.
The objective of this study was to use the antibiotic intensity score to define if patients with CAP of known etiology are exposed to fewer antibiotics compared to patients with unknown etiology.

Table 2 Example for pathogen directed therapy (Recommended antimicrobial therapy for specific pathogens- IDSA/ATS Guidelines for CAP in Adults • CID 2007)(1)

Streptococcus pneumoniae Penicillin nonresistant MIC<2 mg/mL	Streptococcus pneumoniae Penicillin resistant MIC ≥ 2 mg/mL
• **Preferred antimicrobial(s):** Penicillin G, amoxicillin • **Alternative antimicrobial(s):**Macrolide, cephalosporins (oral [cefpodoxime,cefprozil, cefuroxime, cefdinir, cefditoren]or parenteral [cefuroxime, ceftriaxone,cefotaxime]), clindamycin,doxycyline, respiratory fluoroquinolone*	• **Preferred antimicrobial(s):**Agents chosen on the basis of susceptibility, including cefotaxime, ceftriaxone, fluoroquinolone • **Alternative antimicrobial(s):** Vancomycin, linezolid, high-dose amoxicillin (3 g/day with penicillin MIC≤ 4 mg/mL)

METHODS

Study design
This was a secondary data analysis of the Community-Acquired Pneumonia Organization (CAPO) International Cohort Study database.
In Jefferson County, KY, 9 acute care hospitals were included in a study from 2001-2015. Antibiotic agents were assigned a value 1-9 according to their spectrum of activity, 1 having the narrowest spectrum and 9 having the broadest. The Antibiotic Intensity Score (AIS) was calculated as the sum of: the spectrum value of each administered antibiotic multiplied by the number of days the patient received each antibiotic. Diagnosis of each LRTI subtype was assigned according to the ATS/IDSA criteria (2,3).

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

Antibiotic intensity score
The antibiotic intensity score was calculated as the sum of the number of days of each antibiotic multiplied by the antibiotic spectrum. The spectrum was translated into numeric values from 1 to 9 with increasing spectrum, 1 having the narrowest and 9 having the broadest spectrum (Table 3).

Study groups
Patients were classified in two groups:
Known etiology: if a pathogen was identified in any microbiological test performed upon admission to the hospital
Unknown etiology: no pathogen was identified in any microbiological test

Statistical Analysis
Associations between the categorical predictor and the dependent variable were evaluated using the Mann-Whitney U-Test. All data were analyzed in R v.3.1.1 (R Foundation for Statistical Computing, Vienna, Austria). For the purposes of our research a P-value of ≤ 0.05 was considered statistically significant.

Table 3 Antibiotic intensity score: antibiotic spectrum value

Low score 1-3	Intemediate score 4-6	High score 7-9
• ***1 point:*** Penicillin, Ampicillin, Nafcillin, Azithromycin • ***2 points***: Cefazolin, Cephalexin • ***3 points:*** Metronidazole, Clindamycin, TMP/SMX	• ***4 points:*** Aztreonam, Linezolid • ***5 points:*** Cefotetan, Ciprofloxacin, Gentamycin, Tobramycin • ***6 points:*** Moxifloxacin, Levofloxacin, Amoxicillin/Clavulnate	• ***7 points:*** Cefotaxime, Ceftazidime, Ceftriaxone • ***8 points:*** Ceftaroline, Piperacilline/ tazobactam • ***9 points:*** Meropenem, Imipenem/cilastatin, Tigecycline, Doripenem

RESULTS

- A total of 772 patients were included in the study, 401 with an unknown etiology and 371 with a known etiology.
- The antibiotic score for both study groups is shown in Figure 1. The median antibiotic intensity score (IQR) was 60 (54) for those with a known etiology, and 55 (48) for those with an unknown etiology (P=0.33).

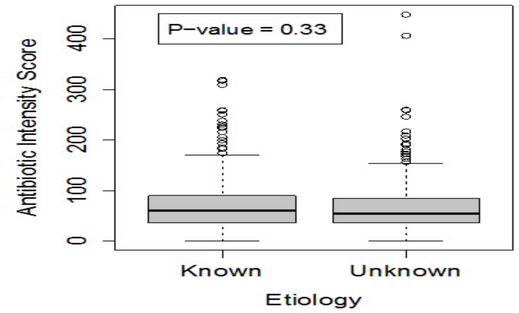

Figure 1 The antibiotic score for both study groups

CONCLUSIONS

- This study indicates that there is not a difference in antibiotic exposure for patients with CAP when a pathogen is or is not identified.
- Our data suggests that current clinical practice is to manage patients with broad-spectrum antibiotics without performing pathogen-directed therapy once an etiology of CAP has been identified. The relevance of this data identifies an important point in our evidence-based practice medicine, regarding the management of pneumonia, which increases the need to implement programs at the national level that will improve the collateral damage and poor outcomes in our patient population.

REFERENCES

1. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults: Lionel A. Mandell, Richard G. Wunderink, Antonio Anzueto, John G. Bartlett, G. Douglas Campbell, Nathan C. Dean, Scott F. Dowell, Thomas M. File, Jr. Daniel M. Musher,Michael S. Niederman, Antonio Torres, and Cynthia G. Whitney
2. Quantifying Antibiotic Collateral Damage: The Antibiotic Intensity Score Daniel R Curran MD, Timothy Wiemken PhD MPH CIC, Robert R Kelley PhD M.S.S, Khan PhD, Paula Peyrani MD, Julio Ramirez MD; Division of Infectious Diseases, University of Louisville, Louisville, KY
3. McCullers, J.A., Insights into the interaction between influenza virus and pneumococcus. Clin Microbiol Rev, 2006. 19(3): p. 571-82.