Impact of a Pharmacist-Driven Azithromycin De-escalation Initiative for Community-Acquired Pneumonia

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INTRODUCTION

- The 2019 IDSA CAP guidelines recommend a respiratory fluoroquinolone or a beta-lactam (i.e. ceftriaxone) plus azithromycin for patients hospitalized with non-severe CAP without risk factors for MRSA or *P. aeruginosa*.[1]
- Discontinuation of azithromycin when atypical bacteria are unlikely represents an antimicrobial stewardship (AS) initiative.[2,3]
  - -Minimize unnecessary azithromycin use
  - -Reduce azithromycin-associated adverse effects
- Atypical bacteria can be detected by polymerase chain reaction (PCR) from respiratory specimens (i.e. *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*) and urinary antigen tests (i.e. *Legionella pneumophila*).[4,5]
- In July 2019, we implemented an AS initiative for a pharmacist to discontinue azithromycin for CAP with a negative PCR and urinary antigen for atypical bacteria.

OBJECTIVES

- To evaluate the impact of this pharmacist-driven azithromycin de-escalation initiative in CAP on azithromycin duration, hospital length of stay (LOS), 30-day all-cause readmission, and in-hospital mortality.

METHODS

- **Study Design**: Single-center, quasi-experimental (pre-intervention: 7/1/18-4/30/19) and (post-intervention: 7/1/19-4/30/20).
- **Study Location**: SUNY Upstate University Hospital is a 472-bed, level 1 trauma, tertiary care, academic medical center in Syracuse, NY.
- **Inclusion criteria**: ≥18 years old, diagnosed with CAP, a negative *Legionella pneumophila* urinary antigen (LPUA), and negative PCR for *M. pneum*oniae and *C. pneumoniae* via the BioFire Respiratory Panel (BFRP).
- **Exclusion criteria**: Immunocompromised, intensive care unit (ICU) admission, prescribed azithromycin for another indication, or prescribed azithromycin monotherapy for CAP.
- **Intervention:** AS pharmacist reviewed patients who received azithromycin-containing CAP regimen to evaluate for discontinuation of azithromycin when atypical bacteria were unlikely.
- **Data Collection**: Demographic data, concurrent infection, anti-pseudomonal beta-lactam, CURB-65 score, Legionella urinary antigen, Legionella culture, hospital length of stay, 30-day all cause readmission, and in-hospital mortality.
- **Statistical Analysis:** Chi-squared or Fisher's exact test and Student's t-test or Mann-Whitney U test were used for categorical and continuous data, respectively, using IBM SPSS Statistics.

RESULTS

Figure 1. Patient Inclusion During Study Period.

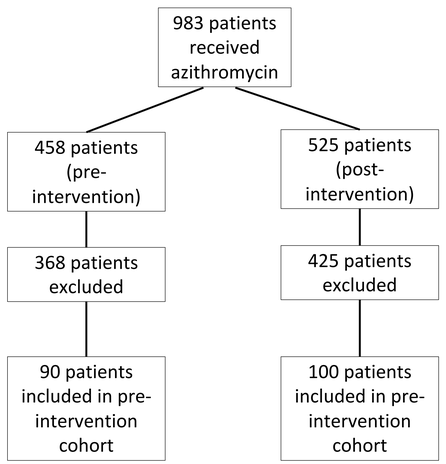

Table 1. Baseline Demographics and Clinical Characteristics.

	Pre-Intervention Cohort (n=90)	Post-Intervention Cohort (n=100)	P-value
Demographics			
Age (years), Median (IQR)	67 (57-78)	67 (55-78)	0.964
Male, n (%)	52 (57.8%)	57 (57.0%)	0.914
Smoking History, n (%)	59 (65.6%)	53 (53.0%)	0.079
Comorbidities			
Chronic Obstructive Pulmonary Disease, n (%)	30 (33.3%)	39 (39.0%)	0.417
Asthma, n (%)	17 (18.9%)	19 (19.0%)	0.984
Diabetes Mellitus, n (%)	24 (27.7%)	26 (26.0%)	0.917
Heart Failure, n (%)	11 (12.2%)	15 (15.0%)	0.578
Clinical Data			
Legionella pneumophila Culture Obtained, n (%)	20 (22.2%)	22 (22.0%)	0.971
Positive Respiratory Panel for Viral Pathogens, n (%)	23 (25.6%)	9 (9.0%)	0.002
Concurrent Infection, n (%)	7 (7.8%)[a]	10 (10.0%)[b]	0.592
Antipseudomonal Beta-Lactam, n (%)	8 (8.9%)[c]	5 (5.0%)[d]	0.289
CURB-65 Score, Median (IQR)	1 (0-2)	1 (0-2)	0.321
Confusion	19 (21.1%)	19 (19.0%)	0.721
Blood Urea Nitrogen >19 mg/dL	39 (43.3%)	31 (31.0%)	0.098
Respiratory Rate ≥30	7 (7.8%)	3 (3.0%)	0.196
Systolic Blood Pressure <90 mmHg or Diastolic Blood Pressure ≤60	12 (13.3%)	10 (10.0%)	0.504
Age ≥65 years	48 (53.3%)	53 (52.0%)	0.895

[a]Concurrent infections included urinary tract infections (5.6%, 5/90), skin and soft tissue infections (1.1%, 1/90), and infective endocarditis (1.1%, 1/90).
[b]Concurrent infections included urinary tract infections (6%, 6/100), skin and soft tissue infections (3%, 3/100), and epididymitis (1%, 1/100).
[c]Piperacillin-tazobactam (8.9%, 8/90).
[d]Cefepime (3%, 3/100) and piperacillin-tazobactam (2%, 2/100).

Table 2. Clinical Outcomes.

	Pre-Intervention Cohort (n=90)	Post-Intervention Cohort (n=100)	P-value
Primary Outcome			
Total Duration of Azithromycin Therapy (Days), Median (IQR)	5 (3-6)	2 (1-2.75)	<0.001
Secondary Outcomes			
Total Length of Hospital Stay (Days), Median (IQR)	5 (3-8.25)	3 (2-5)	<0.001
All-Cause 30-Day Readmission, n (%)	14 (15.6%)	13 (13.0%)	0.614
30-Day Readmission Secondary to Pneumonia, n (%)	4 (4.44%)	2 (2.0%)	0.926
In-Hospital Mortality, n (%)	1 (1.11%)	1 (1.00%)	1.000

DISCUSSION

- To our knowledge, this is the first study to investigate the impact of a pharmacist-driven azithromycin de-escalation initiative in non-ICU, immunocompetent patients hospitalized with CAP.
- Our initiative was associated with a statistically significant reduction in azithromycin duration and hospital LOS without increasing in-hospital mortality or 30-day readmission (all-cause or pneumonia-related).
- Our results support the integration of molecular diagnostics with AS as well as the role of the pharmacist to aid in antibiotic de-escalation in CAP.
- Hopkins and colleagues performed a single-center, retrospective cohort study to evaluate a de-escalation strategy from a beta-lactam-macrolide (n=41) to beta-lactam (n=53) among ICU patients with CAP who had a negative BFRP for atypical bacteria.[6]
  - -No difference in mortality (2.4% vs. 11.3%, p=0.312)
  - -Shorter hospital LOS (6 vs. 7 days, p=0.025)
  - -Shorter azithromycin duration (2 vs. 4, p<0.001)
- Use of LPUA may be a impactful AS tool in combination with BFRP to de-escalate atypical antibiotic coverage in CAP despite IDSA CAP guidelines recommendation to avoid routine use of LPUA.[1]
- Limitations: 1) Results may not be generalizable; 2) Excluded immunocompromised and ICU patients; 3) Did not assess for azithromycin-related adverse effects; 4) Cost-effectiveness analysis was not performed.

CONCLUSIONS

- In non-ICU, immunocompetent patients hospitalized with CAP, a pharmacist-driven azithromycin de-escalation initiative was associated with a significant reduction in azithromycin duration and hospital LOS without increasing 30-day all-cause or pneumonia readmission, or in-hospital mortality.

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Disclosures

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