

## ORIGINAL ARTICLE

**Evaluating Duration of Antimicrobial Therapy for Community-Acquired Pneumonia in Clinically Stable Patients**Lucy Hahn<sup>1</sup>, Anita Hegde<sup>2</sup>, Norman Mang<sup>1,2</sup>, Jessica K. Ortwine<sup>1,2</sup>, Wenjing Wei<sup>1,2</sup>, Bonnie Chase Prokesch<sup>2</sup><sup>1</sup>Parkland Health and Hospital System, Dallas, Texas<sup>2</sup>University of Texas Southwestern Medical Center, Dallas, Texas

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**Introduction:** The Infectious Diseases Society of America guidelines for treatment of community-acquired pneumonia (CAP) recommend a minimum five-day course of antibiotics for patients who achieve clinical stability within 48 to 72 hours from initiation of appropriate therapy, though patients are often treated with a prolonged course of antibiotics.

**Methods:** A retrospective chart review was conducted between January 1, 2015 and December 31, 2015 of all patients  $\geq 18$  years of age treated at Parkland Memorial Hospital to assess the percentage of hospitalized patients diagnosed with uncomplicated CAP receiving antimicrobial therapy in excess of the guideline-recommended duration, evaluate subsequent 30-day all-cause readmission rates, and determine if select co-morbidities influenced the length of antimicrobial therapy prescribed.

**Results:** In eligible patients, 91.3% (178/195) received antimicrobial therapy in excess of the guideline recommended duration, with the average being 3.6 additional days. Mean length of stay (LOS) and duration of therapy were 2.3 ( $\pm 1.6$ ) days and 8.3 ( $\pm 2.6$ ) days, respectively. The 30-day all-cause readmission rate was 11.3% (22/195). The mean duration of therapy in the subgroup of patients requiring readmission was 7.8 ( $\pm 2.2$ ) days and was similar to the study average. Duration of therapy was not significantly affected by age, selected comorbidities (Pearson correlation coefficient 0.08,  $p=0.24$ ), or LOS.

**Discussion:** The majority of patients treated for CAP received durations of therapy exceeding national guideline recommendations resulting in a total of 645 excess days of antimicrobials. These results reveal potential opportunities for antimicrobial stewardship and provider education regarding duration of therapy for CAP which may help improve prescribing practices and decrease antimicrobial overuse.

Keywords: Community-Acquired Pneumonia, Antibiotics, Duration

**INTRODUCTION**

In the United States, community-acquired pneumonia (CAP) results in an estimated 2 to 3 million diagnoses each year, 10 million

physician visits, and 600,000 hospitalizations resulting in a total cost of over 20 billion dollars annually.<sup>1</sup> Common causative organisms of CAP include *Streptococcus pneumoniae*, *Haemophilus*

*influenzae*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *Legionella pneumophila*.<sup>1,2</sup> Identifying the etiologic organism helps guide therapeutic decisions, however, the pathogen remains unknown in about 50% of cases.<sup>3</sup> Therefore, optimal empiric therapy relies on a physician's experience and clinical judgment.

The Infectious Diseases Society of America (IDSA) guidelines for treatment of community-acquired pneumonia (CAP) recommend a minimum 5-day course of antibiotics for patients who achieve clinical stability within 48 to 72 hours from initiation of appropriate therapy.<sup>4</sup> A multicenter, cohort study of 686 patients hospitalized with CAP found that most were treated for 7 to 10 days despite median time to clinical stability of 3 days, indicating that a shorter duration of therapy is often not favored by clinicians despite guideline recommendations.<sup>5</sup> Moreover, although many patients receive active antimicrobial therapy while hospitalized, additional courses of antimicrobials are often prescribed upon discharge resulting in excessive antibiotic use. While many patients are given prolonged courses of therapy for CAP, shorter durations of antibiotics in patients eligible for such courses of treatment offer a number of advantages such as minimizing the emergence and selection of resistant organisms, increasing patient compliance, and reducing the risk of medication adverse effects.<sup>6</sup>

The objective of this study was to assess the percentage of hospitalized patients diagnosed with uncomplicated CAP receiving antimicrobial therapy in excess of the guideline-recommended duration, evaluate subsequent thirty-day all-cause readmission rates, and determine if select co-morbidities influenced the length of antimicrobial therapy prescribed.

## METHODS

A retrospective chart review was conducted at Parkland Memorial Hospital, one of the largest public hospital systems in the country with 862 licensed beds serving a large indigent population in Dallas, Texas averaging more than 1 million patient visits annually and acting as the primary teaching hospital for the University of Texas Southwestern Medical Center. The study was conducted between January 1, 2015 and December 31, 2015. Eligible patients were identified by the institution's Office of Research Administration. Criteria for inclusion were age  $\geq 18$  years, principal billing diagnosis of pneumonia or principal billing diagnosis of sepsis and secondary billing diagnosis of pneumonia (identified by International Classification of Diseases, Ninth Revision (ICD-9) codes 481.xx, 482.xx, 483.xx, 485.xx, and 486.xx for pneumonia and 038.xx and 995.xx for sepsis), and treatment with antimicrobials active against the most common etiologies of CAP. Patients were excluded if they were on treatment with antimicrobials inactive against the most common etiologies of CAP, failed prior or initial antimicrobial therapy for CAP (defined as persistent fever greater than 38 degrees Celsius, malaise, cough, expectoration, or dyspnea after at least 72 hours of antimicrobial therapy), admitted to the intensive care unit, diagnosed with healthcare-associated pneumonia, ventilator-associated pneumonia, or hospital-acquired pneumonia, or presented with signs and symptoms inconsistent with pneumonia or had concomitant infection at other sites.

To determine eligibility for short course (5 days of) therapy, patients were assessed for clinical stability on day 5 of admission (or the last day of hospitalization if the patient was discharged prior to day 5). Patients were considered to be clinically stable if afebrile for 48 hours and if without signs of systemic inflammatory response

syndrome or altered mental status.<sup>4,6</sup> Patients with a length of stay (LOS) less than 5 days were assumed to have met criteria for short course therapy. Duration of antimicrobial therapy was determined based on the sum of prescribed inpatient and outpatient days. Readmissions were categorized as pneumonia-related, medication-related, or unrelated. The Naranjo adverse drug reaction probability scale was used to assess nonspecific readmission complaints.<sup>7</sup>

Descriptive statistics were used to assess the duration of antimicrobial therapy and baseline characteristics. Frequencies were used to determine the percentage of patients prescribed durations of therapy beyond guideline recommendations and readmission rates. Pearson's product-moment correlation coefficient was used to determine the association between number of comorbidities and total duration of therapy. This study was approved by the University of Texas Southwestern Institutional Review Board.

## RESULTS

Of the initial 741 patients assessed for eligibility, 195 patients met all inclusion criteria and were considered eligible for short course therapy. Baseline demographics for this cohort were as shown in Table 1. In eligible patients, 91.3% (178/195) received antimicrobial therapy in excess of the guideline recommended duration, with the average being 3.6 additional days. Mean LOS and duration of therapy were 2.3 ( $\pm 1.6$ ) days and 8.3 ( $\pm 2.6$ ) days, respectively. The 30-day all-cause readmission rate was 11.3% (22/195). Of the 11.3% of readmissions, 8.7% (17/195) were unrelated to pneumonia or infection, 2.6% (5/195) were pneumonia-related, and none were due to medication adverse effects. The mean duration of therapy in the subgroup of patients requiring readmission was 7.8

( $\pm 2.2$ ) days and similar to the study average. Duration of therapy was not significantly affected by age, selected comorbidities (Pearson correlation coefficient 0.08,  $p=0.24$ ), or LOS (Table 1). Sputum cultures were obtained in 11.8% (23/195) of patients with a single positive result of *Haemophilus influenzae*. Blood cultures were obtained in 92.8% (181/195) of patients and 7.7% (14/181) were positive; however each of these was determined to be a microbiological contamination event as only one of two blood culture sets were positive and all cultures grew organisms consistent with contamination including coagulase-negative staphylococci species and *Corynebacterium* species. The most commonly utilized antimicrobial therapy was the combination of a beta-lactam and macrolide for inpatients and a respiratory fluoroquinolone for outpatients.

## DISCUSSION

Overall, a majority of patients treated for CAP received durations of therapy exceeding national guideline recommendations resulting in a total of 645 excess days of antimicrobials. Additional antimicrobial therapy was often ordered at time of discharge. This retrospective review demonstrates that clinical practice often differs significantly from best practice guideline recommendations. The excess duration of and increased exposure to various antimicrobials increases costs of care, risk of resistant organism development, and decreases patient compliance and satisfaction.<sup>8</sup> Automatic stop dates and protocols to decrease duration of antibiotic therapy have been successful in the inpatient setting.<sup>9</sup> However, orders prescribed at discharge have been more challenging to prospectively identify and intervene upon in a similar fashion.

**Table 1.** Patient Characteristics (COPD = Chronic Obstructive Pulmonary Disease, HIV = Human Immunodeficiency Virus, LOS = length of stay).

	<b>Total cohort (n=195)</b>	<b>≤ 5 days therapy (n=17)</b>	<b>&gt;5 days therapy (n=178)</b>	<b>P value</b>
<b>Gender</b>				
Male	88 (45.1%)			
Female	107 (54.9%)			
<b>Race</b>				
Hispanic	94 (48.2%)			
African American	60 (30.8%)			
Caucasian	34 (17.4%)			
Asian	4 (2.1%)			
Other	3 (1.5%)			
<b>Age in years (mean)</b>	56.6	53.6 ± 19.4	56.9 ± 16.7	0.44
<b>Selected Comorbidities</b>				
Diabetes Mellitus	48 (24.6%)	4 (23.5%)	44 (24.7%)	1.0
Asthma	27 (13.8%)	4 (23.5%)	23 (12.9%)	0.26
COPD	13 (6.7%)	0	13 (7.3%)	0.61
Immunosuppression*	12 (6.2%)	0	12 (6.7%)	0.60
Malignancy	8 (4.1%)	0	8 (4.5%)	1.0
Cirrhosis	6 (3.1%)	0	6 (4.3%)	1.0
HIV	5 (2.6%)	0	5 (2.8%)	1.0
<b>LOS (mean in days)</b>	2.3 ± 1.6	1.8 ± 1.7	2.4 ± 1.6	0.14

This study has several limitations, including the retrospective nature of this analysis. The total duration of antibiotic therapy was composed of what patients received inpatient combined with what was stated on the discharge summary. Patients may not have filled the prescription or taken the total course of antimicrobial therapy as prescribed. Hospital emergency department visits and readmissions to outside facilities were unknown. In addition, clinical stability could not be assessed in patients with a LOS less than 5 days. However, if patients were stable enough to be discharged it may be reasonable to assume they would have met criteria. The severity of pneumonia was not directly determined by an objective measure. Rather, patients admitted to the intensive care unit were excluded and all assessable

patients met clinical stability criteria required to discontinue therapy by day 5.

Despite the limitations of this study, overuse of antibiotic therapy is a clear problem in healthcare at present and treatment of uncomplicated CAP is an area in which antimicrobial use can easily be modified. These results reveal potential opportunities for antimicrobial stewardship and provider education regarding duration of therapy for CAP which may help improve prescribing practices and decrease antimicrobial overuse.

#### Notes

All authors have seen and approved the manuscript, and contributed significantly to the work.

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