

Effect of Pharmacist-Initiated Interventions on Duration of Antibiotic Therapy for Acute Exacerbation of Chronic Obstructive Pulmonary Disease and Community-Acquired Pneumonia

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ABSTRACT

Background: Current guidelines for the treatment of acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and community-acquired pneumonia (CAP) recommend 5 days of antimicrobial therapy. Despite these recommendations, the duration of therapy exceeds 5 days for up to 70% of patients, with most superfluous prescribing occurring upon discharge from hospital. Shortening the duration of antibiotic therapy could decrease adverse events, resistance, and costs.

Objective: To determine whether a pharmacist-initiated modification to the duration of antibiotic therapy prescribed for the treatment of AECOPD or CAP reduced the duration of antibiotic prescriptions.

Methods: In this prospective, single-centre study of adult inpatients receiving antibiotics for the treatment of AECOPD or CAP between October 2020 and March 2021, pharmacists assigned a 5-day duration to antimicrobials prescribed for these indications. For patients discharged before completion of therapy, the antibiotic start date and intended duration were included on the discharge prescription. Study patients were matched 1:1 with historical controls to compare the total duration of antibiotic therapy with and without the intervention.

Results: A total of 100 patients (66 with CAP and 34 with AECOPD) met the inclusion criteria and had their antibiotic treatment duration modified to 5 days. Mean total duration of antibiotic therapy was 5.31 days in the intervention group and 7.11 days in the control group ($p < 0.001$). Outpatient antibiotic prescribing was 0.86 days in the intervention group and 3.2 days in the control group ($p < 0.001$). In both groups, the rates of readmission at 30 and 90 days were 19% and 31%, respectively.

Conclusions: Pharmacist-initiated modification of antimicrobial therapy resulted in shortening of the duration of therapy by almost 2 days. Including information about treatment duration on the discharge prescription reduced outpatient prescribing without affecting readmission rates.

Keywords: community-acquired pneumonia, acute exacerbation of chronic obstructive pulmonary disease, antibiotic duration, antimicrobial stewardship, pharmacist

RÉSUMÉ

Contexte : Les lignes directrices actuelles relatives au traitement de l'exacerbation aiguë de la maladie pulmonaire obstructive chronique (MPOC) et de la pneumonie extra-hospitalière (PEH) recommandent 5 jours de traitement antimicrobien. Malgré ces recommandations, la durée du traitement dépasse 5 jours pour jusqu'à 70 % des patients, et la plupart des prescriptions superflues se produisent au moment du congé de l'hôpital. Le raccourcissement de la durée de l'antibiothérapie pourrait réduire les événements indésirables, la résistance et les coûts.

Objectif : Déterminer si une modification de la durée de l'antibiothérapie prescrite pour le traitement de l'exacerbation aiguë de la MPOC ou de la PEH, initiée par le pharmacien, réduit la durée des prescriptions d'antibiotiques.

Méthodes : Dans cette étude prospective monocentrique portant sur des patients adultes hospitalisés ayant reçu des antibiotiques pour le traitement de l'exacerbation aiguë de la MPOC ou de la PEH entre octobre 2020 et mars 2021, les pharmaciens ont attribué une durée de 5 jours aux antimicrobiens prescrits pour ces indications. Pour les patients quittant l'hôpital avant la fin du traitement, la date de début de l'antibiothérapie et la durée prévue figuraient sur l'ordonnance de décharge. Les patients de l'étude ont été jumelés 1:1 avec des témoins historiques pour comparer la durée totale de l'antibiothérapie avec et sans l'intervention.

Résultats : Au total, 100 patients (66 avec une PEH et 34 avec une exacerbation aiguë de la MPOC) répondaient aux critères d'inclusion et ont vu leur durée de traitement antibiotique modifiée à 5 jours. La durée totale moyenne de l'antibiothérapie était de 5,31 jours dans le groupe d'intervention et de 7,11 jours dans le groupe témoin ($p < 0,001$). La prescription d'antibiotiques en ambulatoire était de 0,86 jour dans le groupe d'intervention et de 3,2 jours dans le groupe témoin ($p < 0,001$). Dans les deux groupes, les taux de réadmission à 30 et 90 jours étaient de 19 % et 31 %, respectivement.

Conclusions : La modification du traitement antimicrobien initiée par le pharmacien a entraîné un raccourcissement de la durée du traitement de près de 2 jours. L'inclusion d'informations sur la durée du traitement sur l'ordonnance de départ a réduit la prescription ambulatoire sans avoir d'incidence sur les taux de réadmission.

Mots-clés : pneumonie extra-hospitalière, exacerbation aiguë de la maladie pulmonaire obstructive chronique, durée de l'antibiothérapie, gestion des antimicrobiens, pharmacien

INTRODUCTION

Antimicrobial resistance is one of the greatest threats to health care. Given that antimicrobial use accelerates the development of resistance, overuse and misuse of these drugs must be decreased to preserve their effectiveness.¹ Lower respiratory tract infection is the most common indication for the use of antimicrobials in Canadian hospitals.¹ Thus, avoiding unnecessarily long durations of antimicrobial therapy for the treatment of respiratory tract infections may have a significant impact on antimicrobial use and resistance.

Courses of antibiotic therapy with duration exceeding that recommended in therapeutic guidelines are most often prescribed for respiratory tract infections.² Antibiotic therapy is recommended for selected patients experiencing acute exacerbation of chronic obstructive pulmonary disease (AECOPD); however, approximately 90% of antibiotic prescriptions for the treatment of AECOPD exceed the current recommended treatment duration of 5 days.³

Historically, community-acquired pneumonia (CAP) was treated with 7- to 14-day courses of antibiotics.⁴ In recent clinical trials, shorter courses of antibiotic therapy were non-inferior to longer courses for the treatment of CAP with respect to clinical success, mortality, and readmission rates.^{5,6} The therapeutic guidelines of the American Thoracic Society and the Infectious Diseases Society of America recommend a 5-day duration of antibiotic therapy for the treatment of CAP, provided the patient has reached clinical stability.⁷ A systematic review and meta-analysis supported this recommendation, showing that short courses (6 days or less) of antibiotic therapy did not increase mortality and resulted in fewer adverse events relative to long courses of treatment (7 days or more).⁸ These adverse events included, but were not limited to, diarrhea, headache, nausea, and rash.⁸ Despite guideline recommendations and literature supporting short-course therapy, a retrospective study of hospitalized patients with pneumonia demonstrated that two-thirds of patients received antibiotic therapy of excess duration, beyond 5 days.² Most of this excess prescribing of antibiotics (93%) occurred at discharge. Each excess day of treatment was associated with a 5% increase in the odds of an antibiotic-associated adverse event occurring after discharge.⁸

The principles of antimicrobial stewardship include using antibiotics only when necessary, selecting the optimal agent at the correct dose, and treating patients for the appropriate duration. The intervention that could most easily reduce antibiotic use and that is considered to be the safest and most attainable is to treat infections for only as long as necessary to achieve optimal cure rates.⁹ Decreased exposure to antibiotics achieved through shorter-course regimens can decrease the selective pressure of resistant strains, leading to lower rates of infection and less colonization with drug-resistant organisms.

Short-course strategies have equivalent clinical outcomes compared with longer courses and are associated with lower rates of infection recurrence, superinfection, antibiotic resistance, and incidence of adverse effects from antibiotic use.⁶ Within our institution, all antimicrobial prescriptions for hospital inpatients are electronically assigned a duration of 7 days; however, this practice is no longer supported for antibiotics prescribed for the treatment of AECOPD or CAP and may result in detrimental consequences. The objective of this study was to determine whether a pharmacist-initiated modification to the duration of antibiotic therapy prescribed for the treatment of AECOPD or CAP reduced total antibiotic prescribing (defined as days of therapy).

METHODS

Study Design

This prospective, single-centre study was designed to include all hospital inpatients at Windsor Regional Hospital – Ouellette Campus (WRH-OC) who received antibiotics for the treatment of AECOPD or CAP between October 15, 2020, and March 31, 2021. Approval for this study was granted by the Windsor Regional Hospital Research Ethics Board. The WRH-OC is a 350-bed community teaching hospital, serving a population of about 400 000 people in Windsor and Essex County. The hospital is responsible for all acute care services and provides the following types of care: complex trauma care, renal dialysis, cardiac care, stroke treatment and neurosurgery, intensive care, and acute mental health care. At the time of this study, the hospital used a paper chart system with paper-based medication orders. Study patients were matched 1:1 with historical controls who had been admitted 1 year before (October 2019 to March 2020). The controls were selected from a historical database and were matched on age, biological sex, and antibiotic indication. The target sample size was 100 patients in the intervention group matched with 100 historical control patients. Data were collected by means of a paper chart review.

Patient Eligibility

Patients were included if they were 18 years of age or older, had been admitted to hospital with a diagnosis of AECOPD or CAP, and had received an antibiotic prescription for treatment of AECOPD or CAP (specifically ceftriaxone, azithromycin, moxifloxacin, cefuroxime, amoxicillin/clavulanic acid, or doxycycline). To be considered for pharmacist-initiated modification of antibiotic duration, patients had to meet clinical stability criteria, defined as temperature 37.8°C or lower for 48 hours and no more than one of the following: systolic blood pressure less than 90 mm Hg, heart rate greater than 100/min, respiratory rate greater

than 24/min, oxygen saturation less than 90% (on room air), or partial pressure of oxygen less than 60 mm Hg.

Patients were excluded if they had any of the following: HIV, neutropenia (defined as absolute neutrophil count less than $1 \times 10^9/L$), treatment in a critical care area, chronic immunosuppression (defined as receipt of immunosuppression for solid organ transplant, receipt of 10 mg/day or more of prednisone or equivalent for longer than 30 days, or receipt of other immunosuppressive agents), need for a chest tube or diagnosis of empyema, infection due to a pathogen that required a longer duration of therapy (*Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Legionella* sp.), residence in a nursing home or acute care hospital within the previous 14 days, a condition complicated by an extrapulmonary infection (e.g., meningitis, endocarditis), or infection secondary to COVID-19.

Study Groups

Before this study was initiated, prescribers were informed of the guideline-recommended changes to the duration of antibiotic therapy prescribed for the treatment of AECOPD or CAP. Prescribers were notified both verbally at their respective departmental meetings and by means of an electronic memo outlining the institution's policy permitting pharmacists to assign a 5-day duration of therapy for patients receiving antibiotics for the treatment of AECOPD or CAP, provided the patients met the study's inclusion criteria. The study was initiated on the day the new policy was implemented.

Hospital inpatients for whom antibiotics were prescribed for the treatment of AECOPD or CAP were identified by the infectious diseases pharmacist (L.N.) from a computer-generated list of all inpatients receiving antibiotic therapy. For patients who met the inclusion criteria, the pharmacist modified the duration of therapy to 5 days through a written order in the patient's paper chart. Once the order was entered into the pharmacy's computer system, the notation "duration of therapy modified to 5 days for AECOPD/CAP" was printed beneath the antibiotic drug name on the respective medication administration record, along with the start date and intended stop date of the medication.

Although all pharmacists were aware of the new policy authorizing pharmacists to modify the duration of antibiotic therapy prescribed for the treatment of AECOPD or CAP, most of the modifications were performed by the infectious diseases pharmacist, given the nature of workflow at WRH-OC. Twenty-four hours before the discontinuation of antibiotic therapy, a notification was placed in the patient chart alerting the prescriber of the impending discontinuation. This gave the prescriber an opportunity to extend antibiotic therapy beyond 5 days, if necessary. If the patient was discharged before the completion of antibiotic therapy, the electronic discharge prescription was

amended to show the start date and intended duration of antibiotic therapy.

The control group consisted of hospital inpatients for whom antibiotics were prescribed for the treatment of AECOPD or CAP between October 2019 and March 2020. These patients were identified using diagnostic codes.

Endpoints

The primary endpoint was duration (in days) of antibiotic prescribing for treatment of AECOPD or CAP, including days of antibiotics received in hospital and after discharge, with pharmacist-initiated modification to the duration of therapy prescribed. In situations where the patient was discharged before the completion of antibiotic therapy, the antibiotic start date and intended stop date were printed on the computer-generated discharge prescription. Ultimately, the prescriber selected the duration of antibiotic therapy on the discharge prescription. The secondary endpoints were the rates of readmission within 30 days and 90 days of discharge.

Data Analysis

The primary outcome, duration of antibiotic prescribing, was analyzed with descriptive statistics, using a *t* test. A nonparametric test was used to confirm the results of the *t* tests. Categorical variables were compared with χ^2 tests. A multivariate linear regression analysis was performed for the primary outcome to account for the following confounders: age, biological sex, indication, and whether a patient was discharged with antibiotics. All effects were considered significant at $p < 0.05$.

RESULTS

Between October 15, 2020, and March 31, 2021, a total of 254 patients were assessed for eligibility; of these, 100 patients met the inclusion criteria (Figure 1). These patients were matched 1:1 with 100 historical control patients from the previous year. Baseline characteristics were balanced between the 2 groups (Table 1). No further data were collected for patients excluded from the study.

Primary Endpoints

The mean total intended duration of antibiotic therapy was 7.11 days in the control group and 5.31 days in the intervention group ($p < 0.001$) (Figure 2). The duration of inpatient antibiotic prescribing was 3.91 days and 4.45 days in the control and intervention groups, respectively ($p = 0.026$). The duration of outpatient antibiotic prescribing was 3.20 days in the control group and 0.86 days in the intervention group ($p < 0.001$). Multivariate analysis confirmed the results for the total duration of antibiotic therapy.

A total of 79 patients in the control group had antibiotics prescribed at discharge, compared with 32 patients in the intervention group ($p < 0.001$). Of patients discharged

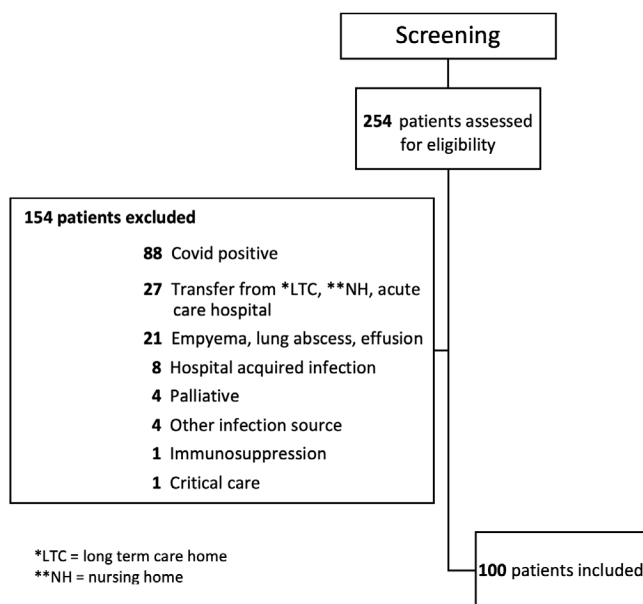


FIGURE 1. Study flow diagram.

with antibiotics, the discharge prescription extended the total duration of antibiotic therapy beyond 5 days for 86% (68/79) of patients in the control group and 31% (10/32) of patients in the intervention group.

Secondary Endpoints

The readmission rate at 30 days after discharge was 19% in both the control and intervention groups. Of readmissions by 30 days, 11 patients in the control group and 6 patients in the intervention group were readmitted because of a respiratory tract infection. The readmission rate at 90 days was 31% in both the control and intervention groups.

DISCUSSION

Among hospital inpatients receiving antibiotic therapy for the treatment of AECOPD or CAP, a pharmacist-initiated modification to duration of therapy significantly reduced total antibiotic prescribing. More specifically, the total duration of antibiotic therapy was reduced by 1.8 days in patients for whom the pharmacist modified the duration of therapy.

According to the workflow at WRH-OC, the infectious diseases pharmacist is responsible for assessing antibiotic therapy for all patients in non-critical care areas. Throughout the period of this study, the infectious diseases pharmacist was responsible for modifying the duration of antibiotic prescriptions for inpatients and outpatients. However, in the future, the goal is for all pharmacists to be capable of adjusting the duration of antibiotic therapy from 7 days to 5 days for patients for whom this change is appropriate.

The prescribed duration of inpatient antibiotic therapy was slightly greater in the intervention group relative to the controls, which may be attributed to longer lengths

TABLE 1. Baseline Characteristics of Study Participants

Characteristic	Study Group; No. (%) of Participants	
	Control (n = 100)	Intervention (n = 100)
Age (years) (mean ± SD)	72.6 ± 14.1	71.9 ± 14.8
Biological sex		
Male	51 (51)	51 (51)
Female	49 (49)	49 (49)
Diagnosis		
Acute exacerbation of COPD	34 (34)	33 (33)
Community-acquired pneumonia	66 (66)	67 (67)

COPD = chronic obstructive pulmonary disease, SD = standard deviation.

of stay for these patients; however, length of stay was not an endpoint in the current study. Multiple factors may have contributed to longer lengths of hospital stay in the intervention group. For example, the timing of this study coincided with the second wave of COVID-19 in Ontario, and many patients had to have a negative result on COVID-19 swab testing within 24 hours of repatriation to another health care facility. The need for this timely COVID-19 swab resulted in some patients remaining in hospital while awaiting test results, despite being medically stable for discharge. Additionally, during the COVID-19 pandemic, the widespread phenomenon of medical avoidance resulted in many patients either avoiding or delaying medical care.¹⁰ During the study timeframe, fear of contracting COVID-19 in hospital may have resulted in only those patients with severe illness presenting to hospital; therefore, the increased length of stay may reflect increased severity of illness.

The most significant impact on antibiotic treatment duration occurred with discharge prescribing. Vaughn and

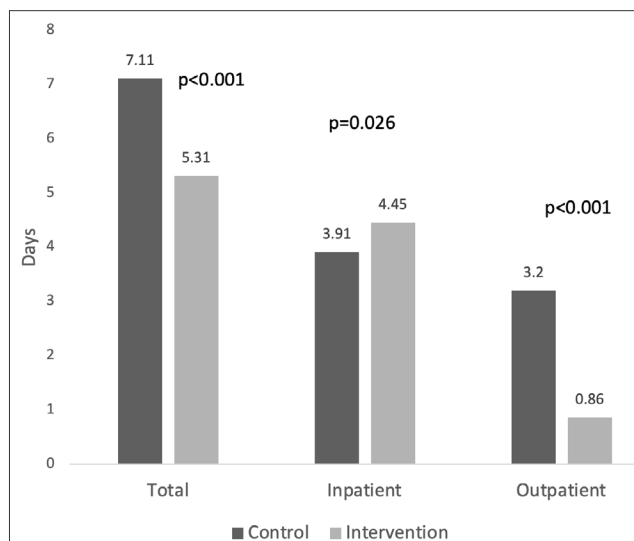


FIGURE 2. Mean duration of antibiotic use.

others⁹ demonstrated that the majority of excess prescribing occurs on discharge, as the clock seems to be restarted at that point, with patients receiving prescriptions for full courses of therapy on discharge. To optimize “discharge stewardship”, we included both the antibiotic start date and the intended duration of therapy on the electronic discharge prescription. Improved documentation at discharge resulted in reduced antibiotic prescribing, with only one-third of patients receiving a discharge prescription for antibiotics, a reduction of 2.34 days of outpatient prescribing relative to the control group. After adjustment for confounders, it was determined that patients discharged without a prescription were more likely to have a shorter total course of antibiotic therapy. The difference between the control and intervention groups, however, was still consistent with our initial results, indicating that the intervention group received fewer days of antibiotic therapy than the control group. In addition, consistent with previous studies, readmission rates were not affected by shorter courses of antibiotic therapy. Patient readmission rates were collected for patients readmitted to either campus of Windsor Regional Hospital or any acute care hospital in Ontario within 30 and 90 days of study enrolment. However, some readmissions might not have been captured, especially if a patient was readmitted to a hospital outside Windsor.

Prescriber education before initiation of this study likely contributed to stakeholder buy-in and successful reduction in the total duration of therapy. Significantly fewer patients in the intervention group were discharged on antibiotics. In contrast to what occurred for the control group, the minimal excess prescribing at discharge rarely extended the total duration of therapy beyond 5 days in the intervention group. Prescribers quickly adjusted to the change in duration of therapy, and, as time passed, the infectious diseases pharmacist made fewer modifications to duration of therapy; more specifically, prescribers were almost 3 times more likely to prescribe a total antibiotic duration of 5 days without pharmacist modification in the intervention group, relative to the control group. Antimicrobial stewardship activities did not differ between the control and intervention periods, other than the implementation of this policy and the prescriber education related to this intervention. It is difficult to determine whether the reduction in antibiotic utilization was affected more by prescriber education or by policy implementation; however, it is likely that both factors contributed.

Our study had several limitations. First, not all patients with AECOPD or CAP were included in this study; rather, only patients admitted from Monday through Friday were included, because these were the days when the infectious diseases pharmacist was available to review patients’ charts. Therefore, the duration of therapy might not have been modified for patients admitted on the weekend and discharged by Monday morning. Second, we did not track outpatient

adherence with antibiotic therapy. Instead, we used the discharge prescription to track outpatient antibiotic prescribing. Our study measured antibiotic prescribing patterns of physicians and the impact that pharmacists can have on these prescribing patterns. Third, we did not control for the severity of illness in either group. This may have led to an imbalance between the groups, which might in turn have affected the total duration of antibiotics in a specific group or the length of the hospital stay. Despite not controlling for the severity of illness, a previous trial demonstrated that even patients with more severe infection did as well with short-course therapy.⁵ Fourth, pharmacists did not confirm the diagnosis of AECOPD or CAP by either physical or radiographic findings in either the intervention or the control group. Rather, the diagnosis was based on documentation by the prescriber for patients in the study group and by diagnostic codes for patients in the control group.

Additionally, lower-than-normal patient volumes within the hospital due to the COVID-19 pandemic and the diagnostic uncertainty for patients presenting with symptoms of respiratory tract infection made it difficult to identify patients eligible for this study. Furthermore, as mentioned previously, COVID-19 may have contributed to longer lengths of hospital stay and greater severity of illness among patients in the intervention group.

CONCLUSION

In this study, pharmacist-initiated modifications adhering to guideline recommendations for AECOPD and CAP reduced the duration of inpatient and outpatient antibiotic prescriptions.

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ON THE FRONT COVER



Kananaskis Country, Alberta

This photograph was taken by Emily Cowley during a fall hiking trip with friends in Kananaskis Country in Alberta. In the small pond, you can see the reflection of Little Arethusia offering incredible views of the Arethusia Cirque filled with larches. Emily captured this image using her Samsung Galaxy S22.

Emily Cowley is a clinical pharmacist in the Cardiovascular Intensive Care Unit at the Mazankowski Alberta Heart Institute in Edmonton, Alberta. In her spare time, Emily enjoys hiking in the Rocky Mountains, travelling, and listening to Taylor Swift.