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ORIGINAL ARTICLE

Effect of Pharmacist Audit on Antibiotic Duration for Pneumonia and Urinary Tract Infection

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Abstract

Objective: To assess the effect of clinical pharmacists in daily audits, under the direction of an antimicrobial stewardship program, of antibiotic treatment durations for the common inpatient disease states of community-acquired pneumonia (CAP) and urinary tract infection (UTI).

Patients and Methods: This was a retrospective single-center cohort study that evaluated the difference in the duration of antibiotic therapy for CAP or non–catheter-associated UTI of hospitalized patients who received a daily audit by clinical pharmacists compared with patients who did not receive a daily audit. Retrospective chart review included randomly selected hospitalized patients diagnosed with CAP or UTI during preaudit and postaudit periods.

Results: The preaudit group had 64 patients; and the postaudit group, 51 patients. The therapy duration was 7 days in the preaudit group and 6 days in the postaudit group (P=.55). Fluoroquinolone use was reduced in the postaudit group and was significantly less than in the preaudit group (24 [37.5%] vs 7 [13.7%]; P=.007).

Conclusion: The daily audits of clinical pharmacists may be an effective method to reduce the duration of antibiotic therapy and are effective in the reduction of fluoroquinolone use. Additional studies must be done to further investigate the effects of clinical pharmacist antimicrobial stewardship efforts.

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Antimicrobial resistance is increasing in the United States, and stewardship programs across health systems have made considerable efforts to minimize the inappropriate use of antibiotics.[1] National efforts placed by governing bodies in the United States have contributed to antimicrobial stewardship program (ASP) implementation. In 2014, the Centers for Disease Control and Prevention (CDC)[2] promoted the implementation of ASPs in all acute care hospitals, acknowledging the benefits they provide, such as improvement in patient outcomes and safety, reduced rates of antibiotic resistance, and cost savings. The Joint Commission[3] released a medication management standard that took effect in 2017 and requires ASPs in hospitals. In March 2020, the Centers for Medicare & Medicaid Services[4] began to require hospital ASPs as a condition of participation, further recognizing the importance of ASPs.

Because many institutions have limited resources, implementation of ASP efforts is a challenge and several barriers exist, such as personnel and time. Although few studies have considered clinical pharmacist assessment of antibiotic use, a clinical pharmacist is equipped to affect antibiotic therapy duration and to contribute to ASP efforts for de-escalation of treatment.[5]

Several studies have reported that a decreased duration of antibiotic therapy is noninferior to a longer duration for the treatment of community-acquired pneumonia (CAP) and non–catheter-associated urinary tract infection (UTI). Conclusions from these studies suggest that decreasing the duration of antibiotic therapy for CAP and UTIs is as

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effective as a longer duration while not increasing the adverse events.[6-10]

In its 2016 guidelines, the Infectious Diseases Society of America[1] strongly suggested that pharmacist involvement and ASP team prospective audits are beneficial to optimize antibiotic utilization. In 2019, the CDC[11] released an update to the core elements of ASPs, highlighting the importance of pharmacy expertise in implementing stewardship efforts. The CDC recommended that a pharmacist have a leadership role in an ASP to implement interventions, such as a prospective audit, and that interventions should be monitored and reported. The update also noted the importance of efforts surrounding common infections, such as CAP, UTI, and skin and soft tissue infection.[11] Investigators have found that an ASP team with an ASP lead pharmacist has a positive impact on de-escalation of antibiotic use, adherence to guidelines, and various outcomes.[12-14] Their studies and the CDC guidelines highlight the importance of ASP teams and ASP pharmacists on the improvement of antimicrobial use. Further evidence is needed to support the effect of clinical pharmacists.

Efforts of an ASP, including decreased duration of therapy, can increase from clinical pharmacist review and such interventions as therapy duration and antibiotic selection. In a study by Boyd et al,[15] ASP pharmacists provided coaching to clinical pharmacists to reduce the use of ceftriaxone, fluoroquinolones, and clindamycin. The investigators reported a decrease in the use of these antibiotics and a significant decrease in hospital-acquired *Clostridioides difficile* infections (rate ratio, 0.78; 95% CI, 0.743 to 0.833; $P<.001$). Additional studies are needed to focus on selected infectious disease states and therapy duration.

The Mayo Clinic Health System — Southwest Wisconsin Antimicrobial Stewardship Committee has committed to decreasing antibiotic use through optimization of antibiotic selection and dose, assessment of administration routes (eg, changes from intravenous [IV] to oral), and reduction in treatment duration. Limited ASP resources have led to the development of a program that uses clinical pharmacists, under the direction of the hospital ASP team, to implement ASP principles focused on selected infectious disease states. The objective of the present study was to assess whether clinical pharmacists, under the direction of an ASP team, can reduce treatment durations for CAP and UTI in accordance with institutional guidelines in a tertiary hospital affiliated with a health system.

PATIENTS AND METHODS

A community-based, single-center, retrospective chart review was completed to assess primary and secondary outcomes between the 6-month preaudit and postaudit periods of April 1, 2018, through September 30, 2018, and of April 1, 2019, through September 30, 2019, for patients with CAP and non—catheter-associated UTI. Community-acquired pneumonia and UTI were targeted collectively in this assessment because these were common disease states often encountered by our institution, were commonly cotreated by clinicians, and were identified for optimization of both antibiotic selection and treatment duration by our antimicrobial stewardship committee. Additionally, institutional guidelines were readily available, and both indications had similar treatment recommendations for application: to reserve fluoroquinolone use only when the preferred treatment was not an option.

Patients 18 years and older were included who had diagnoses of pneumonia or UTI on the basis of *International Statistical Classification of Diseases*, *Tenth Revision*, codes. Urinary tract infection included uncomplicated cystitis, complicated cystitis, and pyelonephritis. Patients were excluded if they had *persistent clinical instability* (defined as being hemodynamically unstable and requiring vasopressor support for >24 hours), tissue necrosis (eg, necrotizing pneumonia and tuberculosis), bloodstream infections, meningitis, endocarditis, and infections of *Staphylococcus aureus*, *Pseudomonas*, *Legionella*, *Burkholderia*, multidrug-resistant organisms, or fungi. Other exclusion criteria were a history of IV antibiotic therapy in the previous 90 days or immunocompromised status (ie, received an organ transplant, has human immunodeficiency virus infection, or has neutropenia with an absolute neutrophil count of $<500/mm^3$). Patients with a diagnosis of UTI were excluded if they had a complex urologic anatomy (ie, urinary

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tract obstruction, anatomic abnormality, stent, tube, or diversion).

After education sessions conducted by an ASP pharmacist to the clinical pharmacist team to detail institutional guidelines for CAP and UTI, a clinical pharmacist completed daily audits for patients with CAP and UTI. On receipt of an antibiotic order for verification, clinical pharmacists opened an electronic intervention documentation tool and applied a standardized assessment template which provided a subsequent prompt to the clinical pharmacists for daily assessments for appropriate treatments. The standardized assessment template (Figure 1) guided clinical pharmacists to review antibiotic indication and day of therapy and to assess antibiotic selection, dose, frequency, and duration in accordance with institutional guidelines. Opportunities for optimization were identified by clinical pharmacists and communicated to providers (hospital-based physicians, advanced nurse practitioners, and physician-assistants) through an electronic message, with a paging system, or in person. All clinical pharmacists received support and periodic reinforcement from an ASP pharmacist throughout the audit period.

Our institutional guidelines promote the use of β-lactam–based regimens over fluoroquinolone-based regimens for CAP and pyelonephritis and nitrofurantoin or trimethoprim-sulfamethoxazole regimens over fluoroquinolone-based regimens for cystitis. The treatment duration for these regimens is 5 to 7 days for CAP and pyelonephritis, 3 to 5 days for uncomplicated cystitis, and 7 days for complicated cystitis.

The study's primary outcome was the total duration of antibiotic therapy for patients with diagnosed CAP or non–catheter-associated UTI. *Duration* was defined as 1 calendar day of therapy and assessed as the total duration and the duration of oral and IV therapies. These oral and IV treatments were counted individually. For example, if a patient received ceftriaxone on hospital days 1 through 3 and had a therapy transition to cefdinir on hospital days 3 through 5, the patient had a total duration of 5 days, an IV duration of 3 days, and an oral duration of 3 days.

Secondary outcomes included duration of oral antibiotic therapy, duration of IV antibiotic therapy, length of hospital stay, *fluoroquinolone use* (defined as use beyond a single dose that may have been provided in the emergency department), adherence to institutional guidelines, and 30-day readmission.

The Mayo Clinic Institutional Review Board deemed the present study to have exempt status.

Categorical variables were compared between the preaudit and postaudit groups by using the Pearson χ^2 test. Continuous variables were compared between groups by using the Kruskal-Wallis rank sum test. A sample size of 50 patients per group (with CAP or UTI indication, or both) was needed for 80% power to detect a difference of 1.4 days. *P* values less than .05 were considered statistically significant. All analyses were performed with R Software (R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org/).

RESULTS

In total, 64 patients with CAP or UTI, or both, made up the 6-month preaudit group from April through September 2018 (Figure 2). The 6-month postaudit group had 51 patients from April through September 2019. The baseline characteristics were similar between the 2 groups except sex. A significantly higher percentage of women were in the postaudit group (78.4% vs 59.4%; *P*=.03) (Table 1).

The primary outcome of total duration of antibiotic therapy was a median of 7 days in

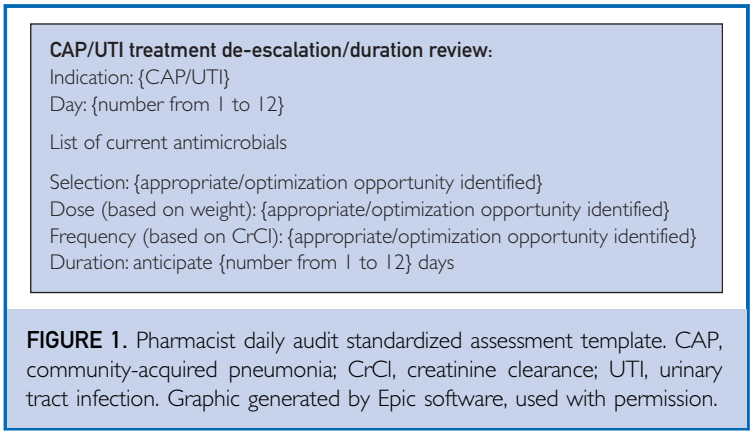

FIGURE 1. Pharmacist daily audit standardized assessment template. CAP, community-acquired pneumonia; CrCl, creatinine clearance; UTI, urinary tract infection. Graphic generated by Epic software, used with permission.

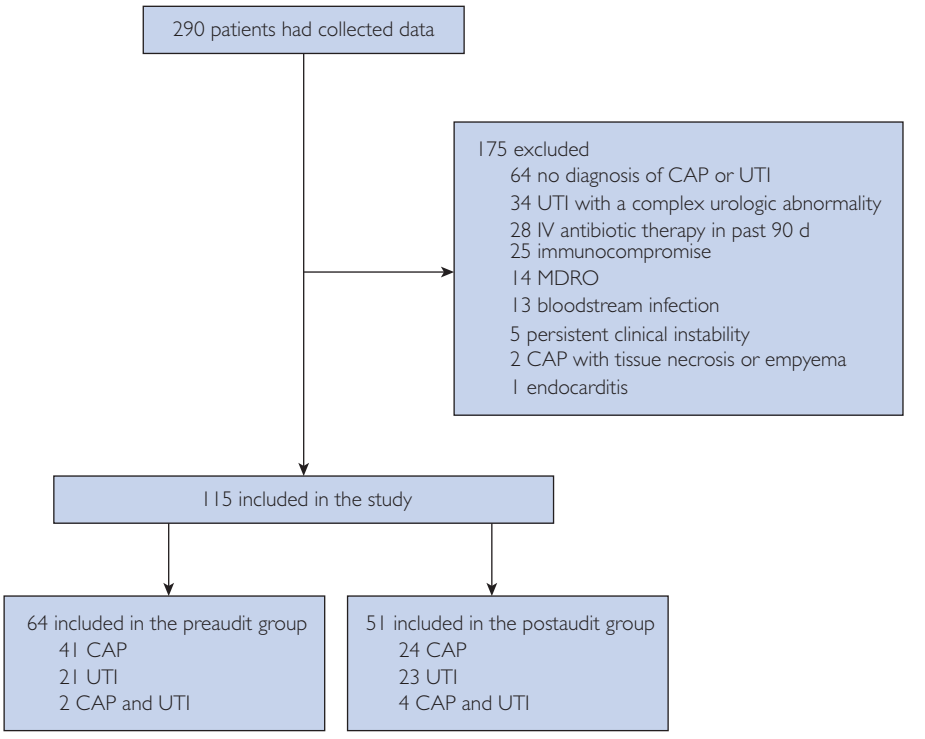

FIGURE 2. Flowchart of patient inclusion in the study. Some patients excluded from the study had >1 concern that caused exclusion; hence, the list of concerns totals 186 patients vs the actual 175 patients. CAP, community-acquired pneumonia; IV, intravenous; MDRO, multidrug-resistant organism; UTI, urinary tract infection.

the preaudit group and 6 days in the postaudit group (*P*=.55) (Table 2). For the secondary outcomes, the median duration of IV therapy was 2 days in both preaudit and postaudit groups. The median duration of oral therapy was 4.5 days in the preaudit group vs 5.0 days in the postaudit group (*P*=.87). The length of stay was 2.8 days in the preaudit group and 2.9 days in the postaudit group (*P*=.74). Fluoroquinolone use was significantly less in the postaudit group (13.7% vs 37.5%; *P*=.007). Adherence to guideline-suggested duration of therapy was seen in 68.8% of patients in the preaudit group and 76.5% in the postaudit group (*P*=.36). Thirty-day readmission rates were higher in the preaudit group (17.2% vs 6.1%; *P*=.007).

Subgroup analyses of primary and secondary outcomes were completed for CAP diagnoses only, UTI diagnoses only, and the 3-month periods of July through September 2018 and of July through September 2019 (ie, all diagnoses, UTI separately, and CAP separately). For CAP diagnoses in the 3-month periods, fluoroquinolone was used less frequently in the postaudit group (0.0% [0 of 7] vs 40.0% [8 of 20]). For the UTI subgroup, fluoroquinolone use was 33.3% (7 of 21) in the preaudit group and 4.3% (1 of 23) in the postaudit group (*P*=.01); 30-day readmission rates were 19.0% (4 of 21) in the preaudit group and 0.0% (0 of 23) in the postaudit group (*P*=.03). For UTI diagnoses in the 3-month periods, institutional guidelines were followed at a higher rate in the postaudit group (100% [11 of 11] vs 69.2% [9 of 13]). In the 3-month subgroup, fluoroquinolone use was 35.3% (12 of 34) in the preaudit group and significantly less at 5.3% (1 of 19) in the postaudit group (*P*=.02). The other comparisons among subgroups were not statistically significant (data not shown).

DISCUSSION

Use of clinical pharmacists daily, under direction of an ASP team, to target common disease states encountered in the inpatient setting (eg, CAP and UTIs) permitted the expansion of antimicrobial stewardship services. Standardized application was used for directed education and feedback, electronic health record intervention templates that facilitated adherence to institutional guidelines, and reduced antibiotic exposure (including fluoroquinolones) for patients. Application of the intervention template also facilitated transitions of care because it provided a summary of the patient's

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antibiotic history that facilitated the ease of review by the pharmacist when completing discharge medication reconciliation, thereby preventing the need to comb through a patient's health record to determine antibiotic treatment duration.

This real-world application of antimicrobial stewardship practices by clinical pharmacists in a community inpatient setting permitted innovative use of available resources collectively. The use allowed for the application of institutional guidelines, standardized clinical pharmacist assessment of antibiotics for CAP and UTI treatment, and standardized electronic intervention documentation, which permitted service expansion without the need for expanding personnel resources.

Antimicrobial stewardship pharmacists are recognized for their effect on antimicrobial stewardship outcomes in the inpatient setting.[12-14] The present study adds to the literature by describing the specific influence that general clinical pharmacists have in supporting antimicrobial stewardship activities in the inpatient setting under the direction of ASPs, thus increasing the antimicrobial stewardship reach.[15]

Therapy was reduced by 1 day in the postaudit group compared with the preaudit group. However, this effect did not meet our statistical significance goals to detect a difference of 1.4 days with the population size selected for study evaluation. Reduction in therapy duration, along with a shift to preferred antimicrobial therapy based on indication, has the potential to reduce patient adverse effects, drug interactions, costs, and resistance potential. This potential applies to all antimicrobial stewardship principles to help improve overall antimicrobial use.[1-4] Future studies with a larger sample size are necessary to further explore and validate these findings because studies with 200 patients have the minimum sample size required to detect a mean treatment duration difference of 1 day with 80% power with use of a 2-sample *t* test with an SD of 2.5 and a type I error of 0.05.

TABLE 1. Baseline Demographic Characteristics[a,b]

Characteristic	Group		*P* value
	Preaudit (n=64)	Postaudit (n=51)	
Age (y)	77.2 (67.0-85.0)	74.0 (65.9-88.4)	.82[c]
Female sex	38 (59.4)	40 (78.4)	.03[d]
Residence	(n=62)	(n=50)	
Community	52 (83.9)	44 (88.0)	.43[d]
Skilled nursing facility	8 (12.9)	6 (12.0)	
Other	2 (3.2)	0 (0.0)	
Allergy/ADR to β-lactam antibiotic			
None	55 (85.9)	44 (86.3)	.56[d]
ADR	5 (7.8)	2 (3.9)	
Allergy	4 (6.2)	4 (7.8)	
ADR and allergy	0 (0.0)	1 (2.0)	
Received oral antibiotics ≤90 d before admission	19 (29.7)	13 (25.5)	.62[d]

[a]ADR, acute drug resistance.
[b]Data are presented as median (interquartile range) or as No. (percentage).
[c]Kruskal-Wallis rank sum test.
[d]Pearson χ^2 test.

Fluoroquinolone use was significantly (*P*=.004) reduced with clinical pharmacist daily audits, resulting in an increased use of preferred β-lactam antibiotics. Across the institution, several efforts have been made to reduce fluoroquinolone use because of increasing resistance and important adverse effects, and clinical pharmacists have the ability to take a lead role in this effort. In addition, no adverse impact on outcomes was noted when

TABLE 2. Outcome Comparisons Between Groups for 6-mo Intervals[a]

Outcome	Group		*P* value
	Preaudit (n=64)	Postaudit (n=51)	
Duration (d)			
Total therapy	7.0 (5.0-8.0)	6.0 (5.0-8.0)	.55[b]
Intravenous therapy	2.0 (1.0-3.0)	2.0 (1.0-3.0)	.45[b]
Oral therapy	4.5 (3.0-6.0)	5.0 (3.0-5.5)	.87[b]
Length of hospital stay (d)	2.8 (2.0-5.6)	2.9 (1.8-6.2)	.74[b]
Patients who received fluoroquinolone >48 h	24 (37.5)	7 (13.7)	.007[c]
Adherence to institutional guidelines	44 (68.8)	39 (76.5)	.36[c]
30-d readmission	11 (17.2)	3 (6.1)[d]	.08[c]

[a]Data are presented as median (interquartile range) or as No. (percentage).
[b]Kruskal-Wallis rank sum test.
[c]Pearson χ^2 test.
[d]Sample, n=49.

comparing the groups, such as 30-day readmission rates in the group receiving the daily audit with the reduction of treatment duration.

A subgroup assessment was completed to determine whether changes were more impactful in the first 3 months of the pilot compared with the later 3 months. We observed a substantial reduction of fluoroquinolone use for both CAP and UTI cases in the 3-month subgroup. We speculate that onboarding a pharmacist to the institution treatment guidelines and a pilot of the audit processes, as well as ongoing day-to-day prospective audit education and feedback with providers, resulted in improved reduction results for the later one half of our assessment period.

Implementation of daily audits was completed with use of a full-time equivalent neutral manner. The clinical pharmacists noted that it did not take a substantial portion of time to complete these daily audits.

Limitations of the study include the limiting of exclusion criteria of immunosuppression to a strict definition and not performing a complete medication review for immunosuppressive medications, such as long-term prednisone treatment. Data were gathered on the basis of a provider diagnosis of CAP or UTI, or both, and a chest radiograph, symptoms, and culture data were not reviewed during data collection. Another limitation was the decreased interventions likely in the first half of the postaudit period because of the ongoing education of and reminders to clinical pharmacists.

CONCLUSION

Clinical pharmacists' daily audits contribute importantly to ASP efforts in inpatient settings. Daily audits, with use of standardized assessment templates, for selected infectious disease indications may allow for shorter treatment durations, improved adherence to guideline-directed therapy, and expanded antimicrobial stewardship reach. The present study adds to the limited literature about clinical pharmacist efforts on antimicrobial stewardship for CAP and UTI and identifies the high-impact areas affected by the clinical pharmacist's work. The model used in this study has potential for use at other hospital sites as a part of the clinical pharmacist's daily workflow.

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Abbreviations and Acronyms: **ASP** = antimicrobial stewardship program; **CAP** = community-acquired pneumonia; **CDC** = Centers for Disease Control and Prevention; **IV** = intravenous; **UTI** = urinary tract infection

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