Infect Dis Ther (2014) 3:45–53
DOI 10.1007/s40121-014-0026-x

ORIGINAL RESEARCH

Impact of a Multidisciplinary Culture Follow-up Program of Antimicrobial Therapy in the Emergency Department

Lisa E. Dumkow · Rachel M. Kenney · Nancy C. MacDonald · Joseph J. Carreno · Manu K. Malhotra · Susan L. Davis

To view enhanced content go to www.infectiousdiseases-open.com
Received: March 14, 2014 / Published online: April 29, 2014

ABSTRACT

Introduction: Antimicrobial prescribing in the emergency department is predominantly empiric, with final microbiology results either unavailable or reported after most patients are discharged home. Systematic follow-up processes are needed to ensure appropriate antimicrobial therapy at this transition of care. The objective of this study was to assess the impact of a culture follow-up (CFU) program on the frequency of emergency department (ED) revisits within 72 h and hospital admissions within 30 days compared to the historical standard of care (SOC). Additionally, infection characteristics and antimicrobial therapy were compared.

Methods: A single group, pre-test post-test quasi-experimental study was conducted comparing a retrospective SOC group to a prospective CFU group. CFU was implemented using computerized decision-support software and a multidisciplinary team of pharmacists and emergency physician staff.

Results: Over the four-month intervention period the CFU group evaluated 197 cultures and modified antimicrobial therapy in 25.5%. The rate of combined ED revisits within 72 h and hospital admissions within 30 days was 16.9% in the SOC group and 10.2% in the CFU group ($p = 0.079$). When evaluating the uninsured population alone, revisits to the ED within 72 h were reduced from 15.3% in the SOC group to 2.4% in the CFU group ($p = 0.044$).

These findings were presented in part as an abstract at the 52nd ICAAC in San Francisco, September 2012.

Electronic supplementary material The online version of this article (doi:10.1007/s40121-014-0026-x) contains supplementary material, which is available to authorized users.

L. E. Dumkow
Mercy Health St. Mary's, Grand Rapids, MI, USA

L. E. Dumkow · R. M. Kenney · N. C. MacDonald · S. L. Davis
Department of Pharmacy Services, Henry Ford Hospital, Detroit, MI, USA

J. J. Carreno · S. L. Davis (✉)
Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University and Henry Ford Hospital, 259 Mack Ave, Detroit, MI 48201, USA
e-mail: sldavis@wayne.edu

J. J. Carreno
Albany College of Pharmacy and Health Sciences, Albany, NY, USA

M. K. Malhotra
Department of Emergency Medicine, Henry Ford Hospital, Detroit, MI, USA

Conclusion: Implementation of a multidisciplinary CFU program was associated with a reduction in ED revisits within 72 h and hospital admissions within 30 days. One-fourth of patients required post-discharge intervention, representing a large need for antimicrobial stewardship expansion to ED practice models.

Keywords: Antimicrobial stewardship; Culture follow-up; Emergency department; Infectious diseases; Transition of care; Urinary tract infections

INTRODUCTION

The increasing emergence of antimicrobial resistance in both the community and inpatient settings has become an alarming public health concern. Infections caused by resistant organisms have been shown to increase morbidity, mortality, and healthcare costs [1]. The emergence of antimicrobial resistance has been linked to the overuse and inappropriate prescribing of antimicrobial therapy [2, 3]. Because it serves as a link in transitions of care, the emergency department (ED) represents an important target for interventions aimed at decreasing inappropriate antimicrobial use, especially in the outpatient setting. ED's across the United States are estimated to treat over 100 million patients annually, with approximately 15.7% of patients discharged home with a prescription for an antimicrobial agent [4–7]. In the ED setting, many patients are discharged home prior to culture and susceptibility results becoming final. It has been reported that 5.6% of patients discharged from the ED receive an inappropriate medication at discharge [4]. While institution-specific empiric therapy guidelines can help to align therapy with national guidelines and institutional-specific antibiogram data, pathogens are not always susceptible to empiric therapy choices. Prescribing of inappropriate antimicrobials puts patients at risk for clinical failure and subsequent revisit to the ED and readmission to the hospital [8, 9]. Therefore, further process improvements such as structured culture follow-up programs must be considered to improve antimicrobial use in the ED setting.

Cosgrove and colleagues recently published a call to action for antimicrobial stewardship in the ED, highlighting the importance of judicious antimicrobial use and also the important opportunity for antimicrobial stewardship collaboration [10]. ED clinicians play a prominent role in antimicrobial stewardship; not only are they tasked with choosing an appropriate antimicrobial regimen but also sending indicated cultures and performing follow-up. Pharmacists also play a prominent role in antimicrobial stewardship programs (ASPs) within hospitals and health systems due to their knowledge of antimicrobial activity, dosing, and drug interactions [11–13]. Several institutions have described their experience with antimicrobial stewardship in the emergency department [14–17]; however, the optimal targets for intervention in this setting have not been established.

The authors implemented a multidisciplinary culture follow-up (CFU) program in October 2011 with the purpose of expediting the identification of patients discharged from the ED with bacteremia and improving the quality of urinary tract infection management at the transition of care from ED to home. The authors hypothesized that the multidisciplinary culture-follow-up program would be associated with a reduction in ED revisits and hospitalizations.

METHODS

Study Design and Setting

This study was conducted at an 802-bed teaching hospital in Detroit, Michigan, with an existing ASP presence in inpatient and ED services. The authors conducted a single pre-test, post-test quasi-experimental study comparing the standard of care (SOC) to a multidisciplinary (CFU) program. The CFU program was implemented primarily by a pharmacy practice resident (PGY1), with support and oversight from the infectious diseases and ED pharmacy specialists.

Compliance with Ethics

The study was approved by the Henry Ford Health System Institutional Review Board and all procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 and 2008. The requirement for informed consent was waived.

Selection of Participants

Patients were included who were 18 years of age or older, presented to the main campus ED, were discharged to home from the ED, and had a blood or urine culture taken which yielded a positive result. For patients with multiple ED visits meeting these criteria, the first visit was included in the study population. Patients in both arms were identified using an electronic screening tool in the hospital's computerized decision support software program (Theradoc™ Hospira, Salt Lake City, UT, USA). Patients were excluded if they were less than 18 years of age, presented to a satellite ED, were admitted for inpatient treatment, or were discharged to hospice care. Consecutive adult patients presenting to the ED between January 1 and April 30, 2011 and meeting the inclusion criteria were retrospectively reviewed for inclusion into the SOC control group. Consecutive patients presenting to the ED between November 7, 2011 and February 6, 2012 were prospectively identified and reviewed for inclusion in the CFU group. Patients from the total population were considered to have a symptomatic urinary tract infection if they had a positive urine culture and concurrent urinary symptoms (excluding dysuria, frequency, or flank pain) or bacteriuria in pregnancy.

Intervention

Prior to the CFU program, the SOC for CFU consisted of prescriber-dependent follow-up. Each prescriber was responsible for performing culture follow-up for any patient whom they saw and discharged directly home from the ED. During both study phases, the microbiology laboratory called the responsible ED physician with critical values for positive blood culture Gram stain results.

In the CFU program, computerized decision support software alerted the CFU pharmacist to any new positive urine or blood culture results Monday through Friday. On weekends, CFU was performed at the discretion of the ED prescribers without additional pharmacist intervention. During weekdays, the CFU pharmacist screened the patients' medical record for inclusion criteria, ED and discharge antimicrobial therapy, and other patient characteristics. Patient characteristics evaluated included antibiotic allergies, pregnancy status, insurance status, serum creatinine, creatinine clearance, and diagnostic criteria for

symptomatic urinary tract infection. Among patients with symptomatic urinary tract infection or bacteriuria in pregnancy, appropriateness of antimicrobial therapy was defined by the pharmacist according to the following: drug selection according to institutional ASP guideline and susceptibility, drug selection and dose appropriate for patient characteristics, and duration at least the minimum recommended. If a therapeutic change was determined necessary, the CFU pharmacist created a patient-specific report including the patient's name, contact information, culture data, and the recommended therapy. Categorization of inappropriate therapy was confirmed with the ED physician through discussion of this patient-specific report. The pharmacist and ED physician then determined the plan for follow-up. The physician was responsible for contacting the patient by telephone to assess the patient's symptoms and communicate whether a new prescription was needed or if the patient should return to the ED for treatment. In the event that a patient was unable to be contacted via telephone, a letter was mailed to the address on record or another contact method was used. Intervention was not performed in the CFU group for patients deemed to have asymptomatic bacteriuria (unless in pregnancy).

Data Collection

For all patients in the study population, data were extracted from electronic medical records by trained investigators using a standardized case report form. Data collected included patient demographics, infection and microbiological characteristics, empiric antimicrobial therapy, ED revisit within 72 h, and hospital admission within 30 days. Time to appropriate therapy was recorded in days and calculated as the day from initial ED discharge to the day that the ED physician made their first follow-up contact attempt with the patient. The primary endpoint for analysis was a composite of patient revisit to the ED within 72 h of index ED discharge or admission to the hospital within 30 days of index ED discharge. A revisit to the ED was defined as any unplanned presentation for the same condition within 72 h of initial discharge [18, 19].

Analysis

The study was powered to detect a 12% reduction in ED revisit or hospital admission per patient compared to the previous standard of care using a two-sided test with a significance of 0.05 and 80% power [15]. The authors calculated that 139 patients per phase would need to be included in this study ($n = 276$ patients total). Based on the findings of Rynn and colleagues [16] the authors anticipated that 25% of patients would require therapeutic modification.

For all study endpoints as well as patient and infection characteristics, categorical data were compared using Chi square or Fisher's exact test; continuous data were compared using Student's t or Mann–Whitney U tests, as appropriate for the distribution of the data. Characteristics found to be associated with the outcome in bivariate tests with a $p < 0.2$ and clinical rationale were considered for inclusion in a multivariable logistic regression model. The primary population for analysis was the total number of cultures; subgroup analyses were conducted for each culture site as specified a priori. Post-hoc subgroup analysis according to insurance status was also performed. A $p < 0.05$ was considered significant for all comparisons. Statistical analysis was completed using SPSS 19.0 (IBM, Inc., Armonk, NY, USA).

RESULTS

Characteristics of Study Subjects

A total of 320 patients with 321 cultures were included in the final analysis. Over the four-month intervention period 651 cultures were screened and 197 met inclusion criteria for the CFU group. In the four-month retrospective SOC group, 324 cultures were screened and 124 were included for comparison. Cultures were excluded from analysis based on patient age or hospice status, because the patient was admitted to the hospital for treatment, or because the culture was taken at a satellite ED. The overwhelming majority of patients in both groups had positive urine cultures (307 out of 321). Patient characteristics are displayed in Table 1; patients in the SOC group were more likely to be uninsured compared to the CFU group [59 (47.6%) vs. 41 (20.8%) $p < 0.01$].

Infection and Treatment Characteristics

Of the 307 urine cultures included, 100% of patients in both the SOC and the CFU group had a urinalysis sample taken at baseline. In the SOC group 73.3% of patients had documentation of symptomatic urinary tract infection while 74.9% of the CFU group were symptomatic ($p = 0.764$). *Escherichia coli* was the most commonly identified urinary pathogen in both groups. In the SOC group, sulfamethoxazole-trimethoprim (TMP-SMX) was the most often prescribed agent for empiric treatment, followed by ciprofloxacin and cephalexin. In the CFU group, ciprofloxacin was the most commonly prescribed agent for empiric treatment, followed by nitrofurantoin and TMP-SMX. The average length of empiric therapy was 8.45 days in the SOC group and 7.59 days in the CFU group.

Table 1 Baseline demographics

	Standard of care ($n = 124$)	**Pharmacist-managed CFU ($n = 197$)**	***p* value**
Age (mean ± SD)	45.4 ± 20.6	48.2 ± 22.2	0.539
Female, *n* (%)	95 (76.6)	147 (74.6)	0.743
Race, *n* (%)			0.164
African American	95 (76.6)	155 (78.7)	
Other	29 (23.4)	41 (20.8)	
Pregnancy status			
% females, *n* (%)	22 (23.2)	29 (19.7)	0.669
Uninsured patients, *n* (%)	59 (47.6)	41 (20.8)	<0.01
Culture type (%)			0.424
Urine	120 (96.8)	187 (94.9)	
Blood	4 (3.2)	10 (5.1)	

CFU culture follow-up, *SD* standard deviation

A total of 14 blood cultures were included in the final analysis, 4 in the SOC group and 10 in CFU. Streptococcal species were the most common organisms identified in blood followed by Enterobacteriaceae; there were no *Staphylococcus aureus* blood stream infections in the study population. Only one patient in the CFU group required follow-up; the other nine cultures received adequate follow-up based on their initial gram stain report, prior to the pharmacist reviewing their cultures.

Outcomes

Empiric therapy was considered appropriate for 63.1% of the SOC cultures and 73% of CFU cultures ($p = 0.081$). Modification of antibiotic therapy was needed in 25.5% of the cases screened in the CFU group. The most common reason for intervention was pathogen non-susceptibility (38/50, 76%), followed by dose adjustments (5/50, 10%), increasing duration of therapy (4/50, 8%), and admission to the hospital for intravenous therapy (2/50, 4%). Of the 50 patients requiring intervention, the median time to follow-up and receipt of appropriate therapy was 2 days (interquartile range 2–3 days). Follow-up contact was made by telephone (87.5%), letter (8.9%), or through communication with the patients' primary care physician (3.6%).

The combined primary endpoint of ED revisit within 72 h or hospital admission within 30 days was 16.9% in the SOC group and 10.2% in the CFU group ($p = 0.079$) (see Table 2) Of the 21 patients having either an ED revisit or hospital admission in the SOC group, 76.2% returned due to an infection-related issue, while 55% of the 20 patients admitted in the CFU group returned for an infection-related issue ($p = 0.153$). In the subset of patients without medical insurance, 59 in the SOC group and 41 in the CFU group, the 72-h revisits to the ED were significantly reduced from 15.3% in the SOC group to 2.4% in the CFU group ($p = 0.044$). There was no difference in the incidence of hospital admissions at 30 days in this subset.

The subset of patients with urinary tract infections were evaluated further to determine the effect of various factors on the combined endpoint. Covariates found to be associated with the outcome in bivariate analyses included study group (OR = 0.53, $p = 0.073$), presence of dysuria at baseline (OR = 0.36, $p = 0.022$), and presence of urinary frequency at baseline (OR = 0.39, $p = 0.054$). Insurance status was not associated with the outcome (OR = 0.67, $p = 0.25$), nor was adequate empiric therapy (OR = 0.54, $p = 0.092$). In restricted multivariable logistic regression, presence of dysuria and frequency were combined into one variable ($\chi^2 = 69.817$, $p < 0.001$). After controlling for the presence of dysuria or frequency, the intervention reduced revisit and admission (adjusted OR = 0.477, 95% CI 0.234–0.973, $p = 0.042$).

Table 2 Combined primary endpoint and components

	SOC group ($n = 124$)	CFU group ($n = 197$)	p value
ED revisit within 72 h, n (%)	12 (9.7)	12 (6.1)	0.239
Hospital admission within 30 days, n (%)	13 (10.5)	14 (7.1)	0.295
Combined ED revisit within 72 h and hospital admission within 30 days, n (%)	21 (16.9)	20 (10.2)	0.079

CFU culture follow-up, *ED* emergency department, *SOC* standard of care

DISCUSSION

This study has found that implementation of a multidisciplinary CFU program resulted in an approximately 7% decrease in combined ED revisits within 72 h and hospital admissions at 30 days when compared to a non-standardized follow-up method. While this finding was statistically significant only in the multivariate analysis, this program improved quality of antimicrobial utilization and follow-up. Interestingly, the subgroup analysis in the uninsured population suggests that this intervention could have a dramatic impact in populations with limited access to care.

Other characteristics found to be associated with improved outcome were documented urinary frequency and dysuria; the authors speculate that this may be related to improved awareness and aggressive antimicrobial therapy among ED providers responding to these well-defined symptoms of urinary tract infections. In addition, the authors noted a numerical increase in appropriate empiric therapy and a significant increase in the use of nitrofurantoin in the CFU group, corresponding to a change in national and institutional recommendations for cystitis [20]. Despite this, intervention by the multidisciplinary CFU providers was still necessary in 25.5% of cases, and the most common reason for intervention was pathogen non-susceptibility. This is similar to reports from antimicrobial stewardship programs in other EDs with intervention rates ranging from 15 to 25% [15, 16]. This variance may be due in part to the population that each institution chooses to target. Whilst the authors limited their intervention to urine and blood cultures, others have also included sexually transmitted diseases, skin and skin structure infection, and respiratory tract infections.

There are potential limitations to this study that must be considered. The multidisciplinary CFU was only available for culture follow-up Monday–Friday. During weekend shifts, prescribers were instructed to continue culture follow-up with their same pre-intervention method; in nearly all cases this resulted in delaying intervention until the pharmacist initiated follow-up on Monday. Another limitation was reliance on electronic physician documentation to confirm if the patient was reached for changes in therapy. Calculating the time to appropriate therapy was, therefore, based on the day the physician contacted the patient. Limitations may also exist due to the quasi-experimental design, including potential bias in the assessment of empiric appropriate treatment, the lack of study group randomization, and potential for regression toward the mean in the post-intervention group [21]. A quasi-experimental design was selected for the study because withholding multidisciplinary follow-up from randomly selected patients would be impractical and potentially unethical. Last, while the authors believe the decrease in ED revisits and hospital admissions was significant to their institution, this study did not achieve the effect size for which it was designed, possibly due to the numerical increase in appropriate empiric therapy also seen after implementation of the CFU group when compared to the SOC. The impact of this study may have been greater with the inclusion of follow-up for sexually transmitted diseases (STDs) and other sites of bacterial culture.

CONCLUSION

Over a 4-month period, a multidisciplinary culture follow-up program in the ED was

effective in improving the quality of care, but did not achieve a statistical reduction in ED revisit and hospital admission compared to standard of care. Interventions targeting infection management in high-risk ED patients may show an even greater impact. Antimicrobial stewardship interventions at the transition of care were required in one-fourth of patients, supporting the need for continued expansion of antimicrobial stewardship services in the ED.

ACKNOWLEDGMENTS

All named authors meet the ICMJE criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published.

The authors wish to thank Edward G. Szandzik, Director of Pharmacy Services, Henry Ford Hospital and Health Network, Detroit, MI, USA, for administrative support of this project as well as editorial review of the manuscript.

Conflict of interest. SL Davis has served as a paid consultant with Forest Laboratories Inc., Durata Therapeutics, and Pfizer Inc. and has received research support from Cubist Pharmaceuticals in the subject area of antimicrobial stewardship.

LE Dumkow, RM Kenney, NC MacDonald, JJ Carreno and MK Malhotra declare no conflict of interest.

Compliance with ethics. The study was approved by the Henry Ford Health System Institutional Review Board and all procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 and 2008. The requirement for informed consent was waived.

Funding. Sponsorship for this study was funded by a residency research award from the American Society of Health System Pharmacists (ASHP) Research and Education Foundation (Bethesda, MD, USA).

REFERENCES

1. Shlaes DM, Gerding DN, John JF Jr, Craig WA, Bornstein DL, Duncan RA, et al. Society for Healthcare Epidemiology of America and Infectious Diseases Society of America Joint Committee on the Prevention of Antimicrobial Resistance: guidelines for the prevention of antimicrobial resistance in hospitals. Clin Infect Dis. 1997;25(3):584–99.

2. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ (Clinical research ed). 2010;340:c2096.

3. Karras D. Antibiotic misuse in the emergency department. Acad Emerg Med. 2006;13(3):331–3.

4. Chin MH, Wang LC, Jin L, Mulliken R, Walter J, Hayley DC, et al. Appropriateness of medication selection for older persons in an urban academic emergency department. Acad Emerg Med. 1999;6(12):1232–42.

5. National Research Council. Hospital-based emergency care: at the breaking point. Washington, DC: The National Academies Press; 2007.

6. Hafner JW Jr, Belknap SM, Squillante MD, Bucheit KA. Adverse drug events in emergency department patients. Ann Emerg Med. 2002;39(3):258–67.

7. Niska R, Bhuiya F, Xu J. National Hospital Ambulatory Medical Care Survey: 2007 Emergency Department Summary. National Health Statistics Reports; no 26. National Center for Health Statistics; 2010.

8. Micek ST, Welch EC, Khan J, Pervez M, Doherty JA, Reichley RM, et al. Resistance to empiric antimicrobial treatment predicts outcome in severe sepsis associated with Gram-negative bacteremia. J Hosp Med. 2011;6(7):405–10.

9. Ramphal R. Importance of adequate initial antimicrobial therapy. Chemotherapy. 2005;51(4): 171–6.

10. May L, Cosgrove S, L'Archeveque M, Talan DA, Payne P, Jordan J, et al. A call to action for antimicrobial stewardship in the emergency department: approaches and strategies. Ann Emerg Med. 2013;62(1):69–77.e2.

11. ASHP statement on pharmacy services to the emergency department. Am J Health Syst Pharm. 2008;65:2380–83.

12. ASHP statement on the pharmacist's role in antimicrobial stewardship and infection prevention and control. Am J Health Syst Pharm. 2010;67(7):575–7.

13. Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis. 2007;44(2):159–77.

14. Baker SN, Acquisto NM, Ashley ED, Fairbanks RJ, Beamish SE, Haas CE. Pharmacist-managed antimicrobial stewardship program for patients discharged from the emergency department. J Pharm Pract. 2012;25(2):190–4.

15. Randolph TC, Parker A, Meyer L, Zeina R. Effect of a pharmacist-managed culture review process on antimicrobial therapy in an emergency department. Am J Health Syst Pharm. 2011;68(10): 916–9.

16. Rynn KO, Hughes FL. Development of a culture review follow-up program in the emergency department. ACCP Conference Abstract No. 292. Pharmacotherapy. 2001;21(10):1299.

17. Wymore ES, Casanova TJ, Broekemeier RL, Martin JK, Jr. Clinical pharmacist's daily role in the emergency department of a community hospital. Am J Health Syst Pharm. 2008;65(5):395–6, 8–9.

18. Lindsay P, Schull M, Bronskill S, Anderson G. The development of indicators to measure the quality of clinical care in emergency departments following a modified-Delphi approach. Acad Emerg Med. 2002;9(11):1131–9.

19. Nunez S, Hexdall A, Aguirre-Jaime A. Unscheduled returns to the emergency department: an outcome of medical errors? Qual Saf Health Care. 2006;15(2):102–8.

20. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011;52(5):e103–20.

21. Harris AD, Bradham DD, Baumgarten M, Zuckerman IH, Fink JC, Perencevich EN. The use and interpretation of quasi-experimental studies in infectious diseases. Clin Infect Dis. 2004;38(11): 1586–91.